Bibliographic Data

Application No: 18/418,030

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☐ No ☐ Met After Allowance

Verified and Acknowledged: /MANAHIL MIRGHANI ALI ABDALHAMEED/ Examiner's Signature | Initials

Title: METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
01/19/2024	707	1622	092459-0423/8032.US06
RULE			

APPLICANTS

Heron Therapeutics, Inc., San Diego, CA, UNITED STATES

INVENTORS

Thomas B. Ottoboni, Belmont, CA, UNITED STATES

Han Han, Sunnyvale, CA, UNITED STATES

CONTINUING DATA

This application is a CON of 18535853 12/11/2023

18535853 is a CON of 17180593 02/19/2021 PAT 11878074

17180593 is a CON of 16820311 03/16/2020 PAT 11173118

16820311 is a CON of 15965638 04/27/2018 PAT 10624850

15965638 is a CON of 15012532 02/01/2016 PAT 9974742

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

02/01/2024

**** SMALL ENTITY ****

STATE OR COUNTRY

UNITED STATES

ADDRESS

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531
UNITED STATES

FILING FEE RECEIVED

$2,800

Bibliographic Data

Application No: 18/418,030

Foreign Priority claimed: ○ Yes ◉ No

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UNITED STATES

ADDRESS

FILING FEE RECEIVED

$2,800

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	01/19/2024 06:33:42 PM Z ET	092459-0423/8032.US06

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9379	FILED BY	Judy Steinkraus
PATENT CENTER #	64020839	AUTHORIZED BY	Judy Mohr
CUSTOMER #	108547	FILING DATE	-
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Thomas B. Ottoboni

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 500417	E202411I37049800	Judy Steinkraus

PRE-AUTHORIZED ACCOUNT
500417

PRE-AUTHORIZED CATEGORY
37 CFR 1.16 (National application filing, search, and examination fees); 37 CFR 1.17 (Patent application and reexamination processing fees); 37 CFR 1.19 (Document supply fees); 37 CFR 1.21 (Miscellaneous fees and charges)

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2830	PROCESSING FEE, EXCEPT IN PROVISIONAL APPLICATIONS	56.00	1	56.00
2817	REQUEST FOR PRIORITIZED EXAMINATION	1680.00	1	1680.00
2111	UTILITY PATENT APPL. SEARCH FEE	280.00	1	280.00
4011	BASIC FILING FEE- UTILITY	64.00	1	64.00

2311	EXAMINATION OF ORIGINAL PATENT APPLICATION	320.00	1	320.00
2202	EACH CLAIM IN EXCESS OF 20	40.00	10	400.00
			TOTAL AMOUNT:	**$2,800.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	**01/19/2024 06:33:42 PM Z ET**	**092459-0423/8032.US06**

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Application Information

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CONFIRMATION #	9379	FILED BY	Judy Steinkraus
PATENT CENTER #	64020839	FILING DATE	-
CUSTOMER #	108547	FIRST NAMED INVENTOR	Thomas B. Ottoboni
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Judy Mohr

Documents

TOTAL DOCUMENTS: 9

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
ADSaia0014-ADS_jls.pdf	9	Application Data Sheet	2174 KB
Track-1_aia0424.pdf	1	Track One Request	183 KB
Application_Transmittal_Nonprov.pdf	2	Transmittal of New Application	564 KB
Parent_Signed_Declarations.pdf	2	Oath or Declaration filed	180 KB
New_POA_to_File.pdf	1	Power of Attorney	105 KB
373c_thru_2024_aia0096.pdf	6	Miscellaneous Incoming Letter	344 KB

Drawings_mdr.pdf	4	Drawings-only black and white line drawings	966 KB
0423_8032US06_Specification_19 Jan 2024_jmm-APP.TEXT.docx	46	Application body structured text document	110 KB

Warning: All artifacts (SmartArt, Drawings, Charts, etc) have been replaced with images. Bookmarks were found and have been removed. Images have been detected in the abstract section. Please review. You may be missing a drawing heading.

0423_8032US06_Specification_19 Jan 2024_jmm.pdf	46	Auxiliary PDF of Application	278 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
ADSaia0014-ADS_jls.pdf	309A11CC9A2B83CFCF27395406CA80A515DC35554D8434AA353FAF1E09BA5BF22DD1D88DB3992088D81BC9B92D46CC86610A0DB056692ED9D54EADDE997ADEBD
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0423_8032US06_Specification_19 Jan 2024_jmm-APP.TEXT.docx	FC161D96D1D4C1931DB6FAEF554CB237BC40B16986C5DA31CA2D23D46E1640ACB9E39762D16F2776655F435B64FDD358DEA28D2A76FA62A7718785033C2BB3B2
0423_8032US06_Specification_19 Jan 2024_jmm.pdf	AA09643F0BE7F577BB5EC39860E2203259D8C3CBAD5C34FE91489B53036A64F7D317F57B083DF6B812F6EA4150EBE104F0ADB9C419E5B2F22EEF21184459F459

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New International Application Filed with the USPTO as a Receiving Office

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PTO/AIA/14 (01-22)
Approved for use through 05/31/2024. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	092459-0423/8032.US06
	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Thomas	B.	Ottoboni	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Belmont	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	c/o Heron Therapeutics, Inc.
Address 2	4242 Campus Point Court, Suite 200

City	San Diego	State/Province	CA
Postal Code	92121	Country	US

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Han		Han	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Sunnyvale	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	c/o Heron Therapeutics, Inc.
Address 2	4242 Campus Point Court, Suite 200

City	San Diego	State/Province	CA
Postal Code	92121	Country	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

PTO/AIA/14 (01-22)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	092459-0423/8032.US06
	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

☐ An Address is being provided for the correspondence Information of this application.			
Customer Number	108547		
Email Address		Add Email	Remove Email

Application Information:

Title of the Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST		
Attorney Docket Number	092459-0423/8032.US06	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	4	**Suggested Figure for Publication (if any)**	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	108547		

PTO/AIA/14 (01-22)
Approved for use through 05/31/2024. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	092459-0423/8032.US06
	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	18/535853	2023-12-11
Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
18/535853	Continuation of	17/180593	2021-02-19
Prior Application Status	Patented		Remove

Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
17/180593	Continuation of	16/820311	2020-03-16	11173118	2021-11-16
Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
16/820311	Continuation of	15/965638	2018-04-27	10624850	2020-04-21
Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
15/965638	Continuation of	15/012532	2016-02-01	9974742	2018-05-22

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button. Add

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)

PTO/AIA/14 (01-22)
Approved for use through 05/31/2024. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	092459-0423/8032.US06
	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

PTO/AIA/14 (01-22)
Approved for use through 05/31/2024. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	092459-0423/8032.US06
	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

PTO/AIA/14 (01-22)
Approved for use through 05/31/2024. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	092459-0423/8032.US06
	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1 Remove

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

◉ Assignee	○ Legal Representative under 35 U.S.C. 117	○ Joint Inventor
○ Person to whom the inventor is obligated to assign.	○ Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Heron Therapeutics, Inc.		
Mailing Address Information For Applicant:			
Address 1	4242 Campus Point Court, Suite 200		
Address 2			
City	San Diego	**State/Province**	CA
Country	US	Postal Code	92121
Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button. Add

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

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	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

Assignee 1

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

Remove

If the Assignee or Non-Applicant Assignee is an Organization check here. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1			
Address 2			
City		**State/Province**	
Country i		Postal Code	
Phone Number		Fax Number	
Email Address			

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	092459-0423/8032.US06
	Application Number	
Title of Invention	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	092459-0423/8032.US06
First Named Inventor	Thomas B. OTTOBONI
Title	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANT
Priority Mail Express® Label No.	Via Patent Center

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

1. ☐ **Fee Transmittal Form** (PTO/SB/17 or equivalent)
2. ☑ **Applicant asserts small entity status.** See 37 CFR 1.27
3. ☐ **Applicant certifies micro entity status.** See 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent.
4. ☑ **Specification** [*Total Pages* 46] Both the claims and abstract must start on a new page. *(See MPEP § 608.01(a) for information on the preferred arrangement)*
5. ☑ **Drawing(s)** (35 U.S.C. 113) [*Total Sheets* 4]
6. **Inventor's Oath or Declaration** [*Total Pages* 2] *(including substitute statements under 37 CFR 1.64 and assignments serving as an oath or declaration under 37 CFR 1.63(e))*
   a. ☐ Newly executed (original or copy)
   b. ☑ A copy from a prior application (37 CFR 1.63(d))
7. ☑ **Application Data Sheet** ** See note below.* See 37 CFR 1.76 (PTO/AIA/14 or equivalent)
8. **CD-ROM or CD-R** in duplicate, large table, or Computer Program (*Appendix*)
   ☐ Landscape Table on CD
9. **Nucleotide and/or Amino Acid Sequence Submission** (*if applicable, items a. – c. are required*)
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ACCOMPANYING APPLICATION PAPERS

10. ☐ **Assignment Papers** (cover sheet & document(s))
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11. ☑ **37 CFR 3.73(c) Statement** (*when there is an assignee*) ☑ **Power of Attorney**
12. ☐ **English Translation Document** (*if applicable*)
13. ☐ **Information Disclosure Statement** (PTO/SB/08 or PTO-1449)
    ☐ Copies of citations attached
14. ☐ **Preliminary Amendment**
15. ☐ **Return Receipt Postcard** (*MPEP § 503*) (*Should be specifically itemized*)
16. ☐ **Certified Copy of Priority Document(s)** (*if foreign priority is claimed*)
17. ☐ **Nonpublication Request** Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent.
18. ☑ **Other:** Track 1 Request

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METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. Application No. 18/535,853, filed December 11, 2023, pending, which is a continuation of U.S. Application No. 17/180,593, filed February 19, 2021, now allowed, which is a continuation of U.S. Application No. 16/820,311, filed March 16, 2020, now U.S. Patent No. 11,173,118, which is a continuation of U.S. Application No. 15/965,638, filed April 27, 2018, now U.S. Patent No. 10,624,850, which is a continuation of U.S. Application No. 15/012,532, filed February 1, 2016, now U.S. Patent No. 9,974,742, each of which is incorporated herein in its entirety.

TECHNICAL FIELD

[0002] The disclosure relates generally to emulsion formulations and systems for the intravenous or parenteral administration of an NK-1 receptor antagonist for treatment of emesis. The emulsion formulations are stable for prolonged periods of time. Also described are methods for preparing the stable NK-1 receptor antagonist emulsions and pharmaceutical formulations.

BACKGROUND

[0003] Emesis is a critical problem experienced as a result of anticancer cytotoxic therapy. Up to 80% of patients will experience chemotherapy-induced nausea and vomiting (CINV) without prophylactic therapy (Vieira dos Santos et al., 2012, J Natl Cancer Inst, 104:1280-1292). Navari et al. (1999, N Engl J Med, 340:190-195) showed that neurokinin-1 (NK-1) receptor antagonists improve CINV when used in combination with cisplatin-based chemotherapy. NK-1 receptor antagonists block binding of substance P to the receptor, thereby preventing or limiting induction of vomiting pathways mediated by the NK-1 receptor (Aziz, 2012, Ann Palliat Med, 1:130-136).

[0004] NK-1 receptor antagonists currently approved and marketed include aprepitant and rolapitant HCl, which are both available in oral form. Not surprisingly, oral dosage forms can create a problem for patients suffering from emesis, specifically, for example, on days two and three of chemotherapy. Accordingly, it is desirable to have injectable formulations to simplify treatment for these patients. Described herein are emulsions formulated for administering to a patient by injection. These emulsions are formulated to contain neurokinin-1 receptor antagonists which may be poorly soluble in aqueous solvents or unstable in aqueous-based liquid formulations.

[0005] Liquid formulations containing NK-1 receptor antagonists having poor solubility and/or poor gastrointestinal permeability characteristics can be very challenging to formulate for purposes of long-term storage and for administration. One means of addressing this challenge is to prepare an emulsion which may both allow preparation of an injectable formulation as well as enhance bioavailability of the active agent once administered.

[0006] Intravenous emulsions should have a very small droplet size to circulate in the bloodstream without causing capillary blockage and embolization. These size limits are typified by USP33-NF28 General Chapter <729> for Globule Size Distribution in Lipid Injectable Emulsions, hereinafter referred to as USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm (PFAT5) not exceeding 0.05%, irrespective of the final lipid concentration.

[0007] Emulsion formulations must be physically stable. The droplet size limits defined in USP <729> apply throughout the assigned shelf life. All true emulsions are thermodynamically unstable and may over time undergo a range of processes which tend to increase the droplet size. These include direct droplet coalescence, when two droplets collide and form a single new droplet; and aggregation, in which droplets adhere together to form larger masses. Aggregation may in some cases be a precursor of further coalescence into larger droplets. These processes may result in large aggregates rising to the surface of the container, a phenomenon known as 'creaming', and ultimately to free oil being visible on the emulsion surface, known as 'cracking'.

[0008] Emulsion formulations must also be chemically stable. The drug substance may degrade; for example, lipophilic drugs will partition into the oil phase, which will confer some degree of protection, but hydrolytic degradation may still occur at the oil-water interface. Possible chemical degradation within parenteral fat emulsions includes oxidation of unsaturated fatty acid residues present in triglyceride and lecithin, and hydrolysis of phospholipids leading to the formation of free fatty acids (FFA) and lysophospholipids. Such degradants lower pH, which may then promote further degradation. Thus, pH should be controlled during manufacture and parenteral emulsion formulations may include a buffering agent to provide additional control. Any decrease in pH over the assigned shelf-life may be indicative of chemical degradation.

[0009] In the present application, emulsion formulations were prepared and characterized to identify a formulation and process that will allow an NK-1 receptor antagonist compound to be

incorporated into an emulsion for intravenous injection and remain stable during the shelf life of the formulation.

BRIEF SUMMARY

[0010] The following aspects and embodiments thereof described and illustrated below are meant to be exemplary and illustrative, not limiting in scope.

[0011] In one aspect, a pharmaceutical composition suitable for intravenous administration is provided which comprises a stable emulsion comprising an oil phase, wherein the oil phase comprises a neurokinin 1 (NK-1) receptor antagonist, a surfactant and a co-surfactant; and an aqueous phase, wherein the aqueous phase comprises water, a tonicity agent, and a pH modifier.

[0012] In some embodiments, the NK-1 receptor antagonist is selected from the group consisting of aprepitant, rolapitant, netupitant, lanepitant, vestipitant, orvepitant maleate, casopitant, ezlopitant, serlopitant, befetupitant and maropitant, or a pharmaceutically acceptable salt thereof. In other embodiments, the NK-1 receptor antagonist is poorly soluble in water.

[0013] In some embodiments, the NK-1 receptor antagonist is selected from the group consisting of rolapitant, netupitant, casopitant, ezlopitant, vestipitant, serlopitant, maropitant, and orvepitant.

[0014] In some embodiments, the NK-1 receptor antagonist is not aprepitant.

[0015] In some embodiments, the composition is an oil-in-water emulsion comprising an oil wherein the oil is selected from the group consisting of coconut oil, olive oil, soybean oil, safflower oil, triglycerides, octyl and decyl glycerate, ethyl oleate, glyceryl linoleate, ethyl linoleate, glyceryl oleate, cholesteryl oleate/linoleate or a mixture thereof. In other embodiments, the oil is hydrolyzed. In still other embodiments, the oil is structurally modified.

[0016] In some embodiments, the emulsifier comprises a phospholipid. In another embodiment, the emulsifier is selected from the group consisting of egg phospholipids, soy phospholipids, phosphatidylcholines, phosphatidylethanolamines, phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids, mixed chain phospholipids, lysophospholipids, hydrogenated phospholipids, partially hydrogenated phospholipids, and mixtures thereof.

[0017] In some embodiments, the co-surfactant comprises an alcohol. In other embodiments, the co-surfactant is ethanol.

[0018] In some embodiments, the pH modifier comprises an oleate or pharmaceutically acceptable salt thereof. In other embodiments, the oleate is sodium, potassium or ammonium oleate. In yet other embodiments, the pH modifier is sodium oleate or a pharmaceutically acceptable salt thereof.

[0019] In some embodiments, the pH modifier comprises a buffer. In other embodiments, the buffer is selected from the group consisting of phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer and borate buffer. In still other embodiments, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer.

[0020] In some embodiments, the pH modifier comprises an oleate and a buffer. In other embodiments, the oleate is sodium oleate and the buffer is Tris buffer.

[0021] In some embodiments, the pH modifier is selected from the group consisting of sodium hydroxide, potassium hydroxide, magnesium hydroxide, sodium carbonate, Tris, sodium linoleate, sodium oleate, potassium oleate, ammonium oleate, potassium carbonate, potassium linoleate, and mixtures thereof.

[0022] In some embodiments, the composition comprises about 5 wt/wt% (weight/weight %) to 15 wt/wt%, 5 wt/wt% to 10 wt/wt%, 7 wt/wt% to 10 wt/wt%, 8 wt/wt% to 9 wt/wt%, or 9 wt/wt% to 10 wt/wt% oil. In another embodiment, the composition comprises about 8 wt/wt5, 8.5 wt/wt%, 9 wt/wt%, 9.5 wt/wt%, 10 wt/wt%, or 10.5 wt/wt% oil. In still other embodiments, the oil is soybean oil.

[0023] In some embodiments, the composition comprises about 10 wt/wt% to 20 wt/wt%, 12 wt/wt% to 17 wt/wt%, 13 wt/wt% to 16 wt/wt%, 13 wt/wt% to 15 wt/wt%, 14 wt/wt% to 15 wt/wt%, or 13 wt/wt% to 14 wt/wt% emulsifier. In other embodiments, the composition comprises about 13 wt/wt%, 13.5 wt/wt%, 14 wt/wt%, 14.5 wt/wt%, 15 wt/wt%, 16 wt/wt%, 17 wt/wt%, 18 wt/wt%, 19 wt/wt% or 20 wt/wt% emulsifier. In still other embodiments, the emulsifier is a lecithin. In other embodiments, the lecithin is an egg yolk lecithin.

[0024] In some embodiments, the composition comprises about 0.05 wt/wt% to 1.5 wt/wt%, 0.1 wt/wt% to 1.0 wt/wt%, 0.2 wt/wt% to 0.8 wt/wt%, 0.3 wt/wt% to 0.7 wt/wt%, 0.4 wt/wt% to 0.6 wt/wt%, 0.4 wt/wt% to 0.5 wt/wt% oleate or salt thereof. In other embodiments, the composition comprises about 0.05 wt/wt%, 0.1 wt/wt%, 0.2 wt/wt%, 0.3 wt/wt%, 0.4 wt/wt%, 0.45 wt/wt%, 0.5 wt/wt%, 0.6 wt/wt%, 0.7 wt/wt%, 0.8 wt/wt%, 0.9 wt/wt%, 1.0 wt/wt% or 1.5 wt/wt% oleate or salt thereof. In still other embodiments, the oleate is sodium oleate. In still another embodiment, the oleate or sodium oleate is the pH modifier.

[0025] In some embodiments, the composition comprises about 20 wt/wt% to 50 wt/wt%, 30 wt/wt% to 50 wt/wt%, 35 wt/wt% to 45 wt/wt%, 30 wt/wt% to 45 wt/wt%, 37 wt/wt% to 42 wt/wt%, 38 wt/wt% to 40 wt/wt%, 30 wt/wt%, 31 wt/wt%, 32 wt/wt%, 33 wt/wt%, 34 wt/wt%, 35 wt/wt%,

36 wt/wt%, 37 wt/wt%, 38 wt/wt%, 39 wt/wt%, 40 wt/wt%, 41 wt/wt%, 42 wt/wt%, 43 wt/wt%, 44 wt/wt%, 45 wt/wt%, 46 wt/wt%, 47 wt/wt%, 48 wt/wt%, 49 wt/wt%, 50 wt/wt% of oil expressed as a percentage of the weight of the oil per the sum of weight of oil, emulsifier and oleate in a unit of the composition. In other embodiments, the oil is soybean oil.

[0026] In some embodiments, the composition comprises about 20 wt/wt% to 50 wt/wt%, 30 wt/wt% to 50 wt/wt%, 35 wt/wt% to 45 wt/wt%, 30 wt/wt% to 45 wt/wt%, 37 wt/wt% to 42 wt/wt%, 38 wt/wt% to 40 wt/wt%, 30 wt/wt%, 31 wt/wt%, 32 wt/wt%, 33 wt/wt%, 34 wt/wt%, 35 wt/wt%, 36 wt/wt%, 37 wt/wt%, 38 wt/wt%, 39 wt/wt%, 40 wt/wt%, 41 wt/wt%, 42 wt/wt%, 43 wt/wt%, 44 wt/wt%, 45 wt/wt%, 46 wt/wt%, 47 wt/wt%, 48 wt/wt%, 49 wt/wt%, 50 wt/wt% of oil expressed as a percentage of the weight of the oil per the sum of weight of oil and emulsifier in a unit of the composition. In other embodiments, the oil is soybean oil.

[0027] In some embodiments, the composition comprises about 40 wt/wt% to 80 wt/wt%, 50 wt/wt% to 70 wt/wt%, 55 wt/wt% to 65 wt/wt%, 57 wt/wt% to 63 wt/wt%, 58 to 60 wt/wt%, 35 wt/wt% to 40 wt/wt%, 30 wt/wt% to 40 wt/wt%, 50 wt/wt%, 51 wt/wt%, 52 wt/wt%, 53 wt/wt%, 54 wt/wt%, 55 wt/wt%, 56 wt/wt%, 57 wt/wt%, 58 wt/wt%, 59 wt/wt%, 60 wt/wt%, 61 wt/wt%, 62 wt/wt%, 63 wt/wt%, 64 wt/wt%, 65 wt/wt%, 66 wt/wt%, 67 wt/wt%, 68 wt/wt%, 69 wt/wt%, 70 wt/wt% of emulsifier expressed as a percentage of the weight of emulsifier per the sum of weight of oil, emulsifier and oleate in a unit of the composition. In other embodiments, the emulsifier is a lecithin. In still other embodiments, the lecithin is an egg yolk lecithin.

[0028] In some embodiments, the composition comprises about 40 wt/wt% to 80 wt/wt%, 50 wt/wt% to 70 wt/wt%, 55 wt/wt% to 65 wt/wt%, 57 wt/wt% to 63 wt/wt%, 58 to 60 wt/wt%, 35 wt/wt% to 40 wt/wt%, 30 wt/wt% to 40 wt/wt%, 50 wt/wt%, 51 wt/wt%, 52 wt/wt%, 53 wt/wt%, 54 wt/wt%, 55 wt/wt%, 56 wt/wt%, 57 wt/wt%, 58 wt/wt%, 59 wt/wt%, 60 wt/wt%, 61 wt/wt%, 62 wt/wt%, 63 wt/wt%, 64 wt/wt%, 65 wt/wt%, 66 wt/wt%, 67 wt/wt%, 68 wt/wt%, 69 wt/wt%, 70 wt/wt% of emulsifier expressed as a percentage of the weight of emulsifier per the sum of weight of oil and emulsifier in a unit of the composition. In other embodiments, the emulsifier is a lecithin. In still other embodiments, the lecithin is an egg yolk lecithin.

[0029] In some embodiments, the ratio of oil to NK-1 receptor antagonist (wt%:wt%) in the composition ranges from about 5:1 to 20:1, 5:1 to 15:1, 5:1 to 10:1, 11:1 to 20:1, 11:1 to 15:1, 12:1 to 16:1, 12:1 to 14:1, 11:1 to 15:1, 12:1 to 14:1, 12.5:1 to 13.5:1, 13:1 to 14:1, or 12:1 to 15:1. In other embodiments, the ratio of oil to NK-1 receptor antagonist (wt%:wt%) in the composition is

about 11:1 to 20:1, 11:1 to 15:1, 12:1 to 16:1, 12:1 to 14:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 11:1, 11.5:1, 12:1, 12.5:1, 13:1, 13.5:1, 14:1, 14.5:1 or 15:1, 15.5:1, 16:1.

[0030] In some embodiments, the ratio of emulsifier to NK-1 receptor antagonist (wt%:wt%) in the composition ranges from about 10:1 to 30:1, 10:1 to 20:1, 15:1 to 30:1, 20:1 to 25:1, 18:1 to 22:1, 19:1 to 20:1, or 10:1 to 30:1. In other embodiments, the ratio of emulsifier:NK-1 receptor antagonist (wt%:wt%) in the composition is about 10:1, 11:1, 13:1, 14:1, 15:1, 18:1, 19:1, 20:1, 21:1, 22:1 23:1, 24:1, 25:1, or 30:1.

[0031] In some embodiments, the ratio of (emulsifier plus oil) to NK-1 receptor antagonist (wt%:wt%) in the composition ranges from about 20:1 to 40:1, 25:1 to 35:1, 30:1 to 35:1, or 32:1 to 34:1. In other embodiments, the ratio of (emulsifier plus oil) to NK-1 receptor antagonist is about 25:1, 26:1, 27:1, 28:1, 29:1 30:1, 31:1, 32:1, 33:1, 34:1, 35:1, 36:1, 37:1, 38:1 or 40:1.

[0032] In some embodiments, the ratio of emulsifier to oil (wt%:wt%) in the composition ranges from about 0.5:1, to 4:1, 1:1 to 2:1, 1.25:1 to 1.75:1, or 1.4:1 to 1.6:1. In other embodiments, the ratio of emulsifier to oil (wt%:wt%) in the composition is about 0.5:1, 0.5:1, 0.6:1, 0.7:1, 0.8:1, 0.9:1, 1:1, 1.1:1, 1.2:1, 1.3:1, 1.4:1, 1.5:1, 1.6:1, 1.7:1, 1.8:1, 1.9:1, 2:1, 1.05:1, 1.15:1, 1.25:1, 1.35:1, 1.45:1, 1.55:1, 1.65:1, 1.75:1, 1.85:1, or 1.95:1.

[0033] In some embodiments, a therapeutic dose of the pharmaceutical composition comprises about 1 to 4 g, 1.5 to 3 g, 1.8 to 2.8 g, 2.3 to 2.8 g, 1.8 to 2.3 g, 1 g, 1.1 g, 1.2 g, 1.3 g, 1.4 g, 1.5 g, 1.6 g, 1.7 g, 1.8 g. 1.9 g, 2 g, 2.1 g, 2.2 g, 2.3 g, 2.4 g, 2.5 g, 2.6 g, 2.7 g, 2.8 g. 2.9 g, 3 g, 3.1 g, 3.2 g, 3.3 g, 3.4 g, 3.5 g, 3.6 g, 3.7 g, 3.8 g. 3.9 g, 4 g emulsifier. In other embodiments, the emulsifier is a lecithin. In still other embodiments, the emulsifier is egg yolk lecithin.

[0034] In some embodiments, a therapeutic dose of the pharmaceutical composition comprises about 0.5 to 3 g, 1 to 2.5 g, 1 to 2 g, 1 to 1.5 g, 1.5 g to 2 g, 0.5g 0.6 g, 0.7 g, 0.8 g, 0.9 g, 1 g, 1.1 g, 1.2 g, 1.3 g, 1.4 g, 1.5 g, 1.6 g, 1.7 g, 1.8 g. 1.9 g, 2 g, 2.1 g, 2.2 g, 2.3 g, 2.4 g, 2.5 g oil. In other embodiments, the oil is soybean oil.

[0035] In some embodiments, a therapeutic dose of the pharmaceutical composition comprises about 50 to 600 mg, 100 to 600 mg, 100 to 500 mg, 100 to 400 mg, 100 to 300 mg, 100 to 200 mg, 200 to 400 mg, 50 to 250 mg, 75 to 200 mg, 100 to 150 mg, 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180 mg, 190 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, or 600 mg of the NK-1 receptor antagonist.

[0036] In some embodiments, the composition comprises about 0 wt/wt% to 10 wt/wt%, 1 wt/wt% to 9 wt/wt%, 2 wt/wt% to 6 wt/wt%, 2 wt/wt% to 4 wt/wt% or 2 wt/wt% to 3 wt/wt% co-surfactant.

In other embodiments, the composition comprises less than 10 wt/wt%, less than 9 wt/wt%, less than 8 wt/wt%, less than 7, less than 6 wt/wt%, less than 5 wt/wt%, less than 4 wt/wt%, less than 3 wt/wt%, less than 2 wt/wt% or less than 1 wt/wt% co-surfactant.

[0037] In some embodiments, the composition comprises about 0 wt/wt% to 10 wt/wt%, 1 wt/wt% to 9 wt/wt%, or 2 wt/wt% to 6 wt/wt% ethanol. In other embodiments, the composition comprises less than 10 wt/wt%, less than 9 wt/wt%, less than 8 wt/wt%, less than 7, less than 6 wt/wt%, less than 5 wt/wt%, less than 4 wt/wt%, less than 3 wt/wt%, less than 2 wt/wt% or less than 1 wt/wt% ethanol.

[0038] In some embodiments, the aqueous phase of the emulsion comprises a tonicity agent, a pH modifier, and water.

[0039] In some embodiments, the aqueous phase of the emulsion comprises an osmotic agent, a pH modifier, and water.

[0040] In some embodiments, the aqueous phase of the emulsion comprises a tonicity agent, an osmotic agent, a pH modifier, and water.

[0041] In some embodiments, the aqueous phase further comprises a buffer.

[0042] In some embodiments, the aqueous phase comprises a buffer but does not comprise a pH modifier which is different from the buffer. In other embodiments, the buffer functions as both a pH modifier agent and a buffer.

[0043] In some embodiments, when the aqueous phase comprises a buffer, the composition contains no tonicity agent.

[0044] In some embodiments, the buffer is selected from the group consisting of phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer and borate buffer. In other embodiments, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer.

[0045] In some embodiments, the aqueous phase comprises a buffer, that when mixed with the oil phase will provide a substantially isotonic oil in water emulsion.

[0046] In some embodiments, the osmotic agent is selected from the group consisting of glycerol, sorbitol, xylitol, mannitol, glucose, trehalose, maltose, sucrose, raffinose, lactose, dextran, polyethylene glycol, or propylene glycol. In other embodiments, the osmotic agent is an inorganic salt such as sodium chloride and mixtures thereof.

[0047] In some embodiments, the composition has a pH of about 6 to 9, 7 to 9, 7.5 to 9, 7.5 to 8.5, 8 to 9, 6 to 8, 7 to 8, or 6, 7, 8 or 9.

[0048] In some embodiments, the composition comprises about 0 wt/wt% to 25 wt/wt%, 2 wt/wt% to 20 wt/wt%, 3 wt/wt% to 15 wt/wt%, or 3 wt/wt% to 8 wt/wt% tonicity agent. In other embodiments, the composition comprises about 1 wt/wt%, 2 wt/wt%, 3 wt/wt%, 4 wt/wt%, 5 wt/wt%, 6 wt/wt%, 7 wt/wt%, 8 wt/wt%, 9 wt/wt%, or 10 wt/wt%, 11 wt/wt%, 12 wt/wt%, 13 wt/wt%, 14 wt/wt%, 15 wt/wt%, 16 wt/wt%, 17 wt/wt%, 18 wt/wt%, 19 wt/wt%, or 20 wt/wt%, 21 wt/wt%, 22 wt/wt%, 23 wt/wt%, 24 wt/wt%, 25 wt/wt% tonicity agent. In still other embodiments, the composition comprises no tonicity agent.

[0049] In some embodiments, the composition comprises about 0 wt/wt% to 25 wt/wt%, 2 wt/wt% to 20 wt/wt%, 3 wt/wt% to 15 wt/wt%, or 3 wt/wt% to 8 wt/wt% osmotic agent. In other embodiments, the composition comprises about 1 wt/wt%, 2 wt/wt%, 3 wt/wt%, 4 wt/wt%, 5 wt/wt%, 6 wt/wt%, 7 wt/wt%, 8 wt/wt%, 9 wt/wt%, or 10 wt/wt%, 11 wt/wt%, 12 wt/wt%, 13 wt/wt%, 14 wt/wt%, 15 wt/wt%, 16 wt/wt%, 17 wt/wt%, 18 wt/wt%, 19 wt/wt%, or 20 wt/wt%, 21 wt/wt%, 22 wt/wt%, 23 wt/wt%, 24 wt/wt%, 25 wt/wt% osmotic agent. In still other embodiments, the composition comprises no osmotic agent.

[0050] In some embodiments, the aqueous phase comprises a dose of dexamethasone sodium phosphate in a therapeutic dose of the pharmaceutical composition. In other embodiments, the dose of dexamethasone sodium phosphate ranges from about 0.5 mg to 30 mg, 0.5 mg to 25 mg, 1 mg to 20 mg, 10 mg to 20 mg, or 3 mg to 16 mg. In still other embodiments, the dose of dexamethasone sodium phosphate is about 9 mg or 16 mg in a therapeutic dose of the pharmaceutical composition. In these embodiments comprising a dose of dexamethasone, the therapeutic dose of the pharmaceutical composition comprises about 50 to 600 mg, 100 to 600 mg, 100 to 500 mg, 100 to 400 mg, 100 to 300 mg, 100 to 200 mg, 200 to 400 mg, 50 to 250 mg, 75 to 200 mg, 100 to 150 mg, 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180 mg, 190 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, or 600 mg of the NK-1 receptor antagonist.

[0051] In some embodiments, the oil phase comprises a dose of dexamethasone in a therapeutic dose of the pharmaceutical composition. In other embodiments, the dose of dexamethasone ranges from about 0.5 mg to 30 mg, 0.5 mg to 20 mg, 1 mg to 18 mg, 10 mg to 20 mg, or 3 mg to 16 mg. In other embodiments, the dose of dexamethasone is about 8 mg or 12 mg in a therapeutic dose of the pharmaceutical composition. In these embodiments comprising a dose of dexamethasone, the therapeutic dose of the pharmaceutical composition comprises about 50 to 600 mg, 100 to 600 mg, 100 to 500 mg, 100 to 400 mg, 100 to 300 mg, 100 to 200 mg, 200 to 400 mg, 50 to 250 mg, 75 to 200 mg, 100 to 150 mg, 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180

mg, 190 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, or 600 mg of the NK-1 receptor antagonist

[0052] In some embodiments, the emulsion comprises about 0.002 wt/wt% to 0.2 wt/wt%, 0.003 wt/wt% to 0.16 wt/wt%, 0.02 wt/wt% to 0.1 wt/wt% dexamethasone sodium phosphate.

[0053] In some embodiments, the composition is a stable system maintaining an intensity-weighted mean particle size as determined by dynamic light scattering (DLS) of about 50 nm to 1000 nm, 50 to 500 nm, 50 nm to 400 nm, 50 nm to 300 nm, 50 nm to 200 nm or 50 nm to 100 nm. In another embodiment, the average droplet size is maintained below 500 nm for a period of at least 1 month, 3 months, 6 months, 9 months, 12 months, 2 years or 3 years at room temperature. In other embodiments, the average droplet size is maintained below 500 nm for a period of at least 1 month, 3 months, 6 months, 9 months, 12 months, 2 years or 3 years at 5 °C.

[0054] In another aspect, a method for preparing an emulsion comprising an NK-1 receptor antagonist compound and suitable for parenteral administration is provided.

[0055] In some embodiments, the administration is intravenous administration.

[0056] In some embodiments, the method comprises: a) preparing an oil phase by dissolving the antagonist compound and an emulsifier in ethanol, then adding in oil to generate an oil-based mixture; b) preparing an aqueous phase by mixing water, optionally with a tonicity agent, optionally with an osmotic agent and optionally with a pH modifier and optionally with a buffer to generate an aqueous mixture; c) combining the oil-based mixture and the aqueous mixture and subjecting this to high speed homogenization to generate a crude emulsion; and d) subjecting the crude emulsion to high pressure homogenization to generate a fine emulsion.

[0057] In some embodiments, preparing the oil phase further comprises dissolving dexamethasone with the antagonist compound and the emulsifier in the ethanol.

[0058] In some embodiments, the method comprises: a) combining a NK-1 receptor antagonist, an emulsifier, and an alcohol with an oil to generate an oil phase; (b) combining water, a tonicity agent, a pH modifier, and optionally a buffer to generate an aqueous phase; (c) homogenizing the oil phase with the aqueous phase to generate the pharmaceutical emulsion; and (d) sterilizing the pharmaceutical emulsion. In other embodiments, the homogenizing comprises high speed homogenization.

[0059] In some embodiments, the method comprises: a) preparing an oil phase by dissolving the antagonist compound and an emulsifier in ethanol and oil to generate an oil-based mixture; b) preparing an aqueous phase by mixing water, optionally with a tonicity agent, optionally with an

osmotic agent and optionally with a pH modifier and optionally with a buffer to generate an aqueous mixture; c) combining the oil-based mixture and the aqueous mixture and subjecting this to homogenization to generate a crude emulsion; and d) subjecting the crude emulsion to homogenization to generate a fine emulsion. In other embodiments, the subjecting the homogenization to generate a crude emulsion is high-speed homogenization. In still other embodiments, the homogenization to generate a fine emulsion is a high pressure homogenization.

[0060] In some embodiments, preparing the oil phase further comprises dissolving dexamethasone with the antagonist compound and the emulsifier in the ethanol and oil.

[0061] In some embodiments, preparing the aqueous phase further comprises mixing dexamethasone with the water, tonicity agent, pH modifier, and a buffer. In other embodiments, the dexamethasone is a salt of dexamethasone. In still other embodiments, the dexamethasone is dexamethasone sodium phosphate.

[0062] In some embodiments, the method further comprises sterilizing the fine emulsion to generate the final emulsion, wherein the final emulsion is suitable for injection into a subject.

[0063] In some embodiments, the dissolution in ethanol is performed at a temperature of about 25 °C to 80 °C, 40 °C to 75 °C, 60 °C to 70 °C, or at about 25 °C, 35 °C, 45 °C, 60 °C, 65 °C, 70 °C or 75 °C.

[0064] In some embodiments, the high-speed homogenization is performed at a speed of about 2,000 rpm (revolutions per minute) to 25,000 rpm. In other embodiments, the high-speed homogenization is performed at a speed of about 20,000 rpm. In still other embodiments, the high-speed homogenization is performed at a speed of about 3600 rpm.

[0065] In some embodiments, the high-speed homogenization is performed for a time period of about 0.5 min to 1 hour, 1 min to 45 min, or 1 min to 30 min. In other embodiments, the high-speed homogenization is performed for a time period of about 20 to 40 min or for about 30 min.

[0066] In some embodiments, the high-speed homogenization is performed at about 10 °C to about 60 °C, 20 °C to about 60 °C, about 30 °C to about 50 °C, or about 35 °C to about 45 °C. In another embodiment, the high-speed homogenization is performed at about 25 °C, 30 °C, 35 °C, 40 °C, 45 °C or 50 °C.

[0067] In some embodiments, the high-pressure homogenization is performed at a pressure of about 10,000 psi (pounds per square inch) to 30,000 psi. In other embodiments, the high-pressure homogenization is performed at a pressure of about 20,000 psi.

[0068] In some embodiments, the high-pressure homogenization is performed with cooling. In another embodiment, the high-pressure homogenization is performed with cooling which is sufficient to bring the temperature of the emulsion at the outlet of the process to about 0 °C to about 60 °C, about 10 °C to about 40 °C, about 20 °C to about 30 °C, or to about 20 °C, 25 °C or 30 °C within the time period.

[0069] In some embodiments, the sterilizing the fine emulsion comprises filtering the fine emulsion through a nylon filter. In other embodiments, the nylon filter is a Posidyne® filter. In yet another embodiment, the filter has a pore size of about 0.2 μm (micrometers).

[0070] In another aspect, the compositions described herein are for treatment of a subject, and the composition is administered via injection to a subject in need.

[0071] In some embodiments, the compositions are for use in a method for the treatment of emesis induced by a chemotherapeutic agent, by radiation-induced nausea and vomiting, and/or by post-operative induced nausea and vomiting in a subject. In other embodiments, the treatment comprises administering to the subject a composition comprising an NK-1 receptor antagonist as described herein. In still other embodiments, the compositions are for use in preventing or treating acute and delayed nausea and vomiting.

[0072] Additional embodiments of the present compositions and methods and the like, will be apparent from the following description, drawings, examples, and claims. As can be appreciated from the foregoing and following description, each and every feature described herein, and each and every combination of two or more of such features, is included within the scope of the present disclosure provided that the features included in such a combination are not mutually inconsistent. In addition, any feature or combination of features may be specifically excluded from any embodiment of the present invention. Additional aspects and advantages of the present invention are set forth in the following description and claims, particularly when considered in conjunction with the accompanying examples and drawings.

BRIEF DESCRIPTION OF DRAWINGS

[0073] FIGS. 1A-1D provides microscope images of samples from Examples 1, 2, 3 and 6 after a freeze-thaw cycle. FIG. 1A: Example 1, FIG. 1B: Example 2, FIG. 1C: Example 3, FIG. 1D: Example 6

[0074] FIG. 2 shows plasma levels of aprepitant after injection of a fosaprepitant solution (●) or an aprepitant emulsion prepared as described herein (▲).

[0075] FIG. 3 shows plasma levels of aprepitant after injection of a solution of fosaprepitant (▲) or after injection of an emulsion containing aprepitant and dexamethasone prepared as described herein (●).

[0076] FIG. 4 shows plasma levels of dexamethasone after injection of a solution of dexamethasone sodium phosphate (●) or after injection of an emulsion containing aprepitant and dexamethasone prepared as described herein (▲).

DETAILED DESCRIPTION

[0077] Various aspects now will be described more fully hereinafter. Such aspects may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey its scope to those skilled in the art.

I. DEFINITIONS

[0078] As used in this specification, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to a "polymer" includes a single polymer as well as two or more of the same or different polymers, reference to an "excipient" includes a single excipient as well as two or more of the same or different excipients, and the like.

[0079] Where a range of values is provided, it is intended that each intervening value between the upper and lower limit of that range and any other stated or intervening value in that stated range is encompassed within the disclosure. For example, if a range of 1 μm to 8 μm is stated, it is intended that 2 μm, 3 μm, 4 μm, 5 μm, 6 μm, and 7 μm are also explicitly disclosed, as well as the range of values greater than or equal to 1 μm and the range of values less than or equal to 8 μm. As used herein, the term "about" means ±5%, ±10%, or ±20% of the value being modified.

[0080] The term "emulsion" or "emulsion formulation" means a colloidal dispersion of two immiscible liquids in the form of droplets, whose diameter, in general, is between 10 nanometers and 100 microns. An emulsion is denoted by the symbol O/W (oil-in-water) if the continuous phase is an aqueous solution and by W/O (water-in-oil) if the continuous phase is an oil. Other examples of emulsions such as O/W/O (oil-in-water-oil) include oil droplets contained within aqueous droplets dispersed in a continuous oil phase.

[0081] "Physically stable" emulsions will meet the criteria under USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm

(PFAT5) not exceeding 0.05%, at 5 °C or room temperature for a designated storage time period. In addition, physically stable emulsions will have no visible NK-1 receptor antagonist crystals upon storage at 5 °C or room temperature for a designated time period. Crystals are considered visible when viewed at magnification of 4X to 10X. An emulsion is physically stable if it meets the criteria under USP <729> and NK-1 receptor antagonist crystals are not visible upon storage at 5 °C or room temperature for a time period equal to or at least 1 week, 2 weeks, 4 weeks, 1 month, 2 months, 6 months, 1 year or 2 years.

[0082] "Chemically stable" emulsions of the disclosure are ones in which the concentration of the active component (i.e., the drug being delivered) does not change by more than about 20% under appropriate storage conditions for at least 1 month. In certain embodiments, the concentration the NK-1 receptor antagonist in an emulsion of the present disclosure does not change by more than about 5%, 10%, 15% or 20% under appropriate storage conditions for at least 1, 2, 3, 4, 5, 6, 9, 12, 15, 18, or 24 months.

[0083] In one example, the stable emulsion compositions of the disclosure are stable over a wide range of temperatures, e.g., −20 °C to 40 °C. The compositions of the disclosure may be stored at about 5 °C to about 25 °C.

[0084] "Oil phase" in a water-in-oil emulsion refers to all components in the formulation that individually exceed their solubility limit in the water phase; these are materials that generally have solubilities of less than 1% in distilled water, however, water phase components such as salts may decrease the solubility of certain oils resulting in their partitioning into the oil phase. The oil phase refers to the non-aqueous portion of a water-in-oil emulsion.

[0085] "Aqueous phase" or "water phase" in a water-in-oil emulsion refers to the water present and any components that are water soluble, i.e., have not exceeded their solubility limit in water. "Aqueous phase", as used herein, includes a water-containing liquid which can contain pharmaceutically acceptable additives such as acidifying, alkalizing, buffering, chelating, complexing and solubilizing agents, antioxidants and antimicrobial preservatives, humectants, suspending and/or viscosity modifying agents, tonicity and wetting or other biocompatible materials. The aqueous phase refers to the non-oil portion of a water-in-oil emulsion.

[0086] An "emulsifier" refers to a compound that deters the separation of the injectable emulsion into individual oil and aqueous phases. Emulsifiers useful in the present disclosure generally are (1) compatible with the other ingredients of the stable emulsions of the present disclosure, (2) do not

interfere with the stability or efficacy of the drugs contained in the emulsions, (3) are stable and do not deteriorate in the preparation, and (4) are non-toxic.

[0087] Suitable emulsifiers include, but are not limited to, propylene glycol mono- and di-fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, polyoxyethylene-polyoxypropylene co-polymers and block co-polymers, salts of fatty alcohol sulphates, sorbitan fatty acid esters, esters of polyethylene-glycol glycerol ethers, oil and wax based emulsifiers, glycerol monostearate, glycerine sorbitan fatty acid esters and phospholipids.

[0088] A "phospholipid" refers to a triester of glycerol in which the secondary alcohol and one of the primary alcohols has been esterified with fatty acids and the other primary alcohol has been esterified with a phosphate group. Exemplary phospholipids useful in the present invention include, but are not limited to, phosphatidyl chlorine, lecithin (a mixture of choline ester of phosphorylated diacylglyceride), phosphatidylethanolamine, phosphatidylglycerol, phosphatidic acid with about 4 to about 22 carbon atoms, and more generally from about 10 to about 18 carbon atoms and varying degrees of saturation. The phospholipids can have any combination of fatty acid as its fatty acyl side chain, for example, the phospholipids can have a saturated fatty acid such as a decanoic acid, lauric acid, myristic acid, palmitic acid, stearic acid, icosanoic acid, (a C20 saturated fatty acid); sodium behenic acid, or an unsaturated fatty acid such as myristoleic acid, palmitoleic acid, oleic acid, sodium linoleic acid, alpha linolenic acid, sodium arachidonic acid, eicosapentanoic acid, and the like. The two fatty acyl residues on the phospholipids may be the same or they may be different fatty acids. The phospholipid component of the drug delivery composition can be either a single phospholipid or a mixture of several phospholipids. The phospholipids should be acceptable for the chosen route of administration.

[0089] In one aspect, the phospholipids used as emulsifiers in the present invention are naturally occurring phospholipids from a natural origin. For example, naturally occurring lecithin is a mixture of the diglycerides of stearic, palmitic, and oleic acids, linked to the choline ester of phosphoric acid, commonly called phosphatidylcholine, and can be obtained from a variety of sources such as eggs and soya beans. Soy lecithin and egg lecithin (including hydrogenated versions of these compounds) have been characterized in various compositions and are generally recognized to be safe, have combined emulsification and solubilization properties, and tend to be broken down into innocuous substances more rapidly than most synthetic surfactants.

[0090] The term "lecithin" includes a complex mixture of acetone-insoluble phosphatides, of which phosphatidylcholine is a significant component. The term lecithin is also used as a synonym for

phosphatidylcholine. Useful lecithins include, but are not limited to, egg yolk-, egg-, soybean-, and corn-derived lecithin. In one embodiment, the emulsifier is lecithin, such as egg yolk-derived lecithin. The terms egg lecithin and egg yolk derived lecithin are used interchangeably throughout. The compositions described herein preferably comprise lecithin as an emulsifier.

[0091] The amount of phospholipids, by weight, in the emulsions of the present disclosure may be within a range of about 10 wt/wt% to about 20 wt/wt%, 11 wt/wt% to 19 wt/wt%, 11 wt/wt% to 15 wt/wt%, 12 wt/wt% to 13 wt/wt%, 13 wt/wt% to 14 wt/wt%, 13 wt/wt% to 20 wt/wt%, or 12 wt/wt% to 18 wt/wt%. In certain embodiments, the phospholipids in the emulsions are at a concentration, by weight, about 11 wt/wt%, 12 wt/wt%, 12.5 wt/wt%, 13 wt/wt%, 13.5 wt/wt%, 14 wt/wt%, 14.5 wt/wt%, or 15 wt/wt%.

[0092] "Oil" refers to an organic liquid of mineral, vegetable, animal, essential or synthetic origin, including, for example, aliphatic or wax-based hydrocarbons, aromatic hydrocarbons or mixed aliphatic and aromatic hydrocarbons.

[0093] The term "buffer" or "buffered" as used herein means a solution containing both a weak acid and its conjugate base, whose pH changes only slightly upon addition of acid or base. As used herein, the phrase "buffering agent" means a species whose inclusion in a solution provides a buffered solution. Buffers are well-known in the art and readily available. Buffers for use according to the methods and compositions described herein include but are not limited to phosphate, citrate, Tris, carbonate, succinate, maleate, borate, MES, Bis-Tris, ADA, aces,PIPES, MOPSO, Bis-Tri Propane, BES, MOPS, TES, HEPES, DIPSO, MOBS, TAPSO, Trizma, HEPPSO, POPSO, TEA, EPPS, Tricine, Gly-Gly, Bicine, GEPBS, TAPS, AMPD, TABS, AMPSO, CHES, CAPSO, AMP, CAPS, and CABS.

[0094] The term "therapeutic agent" describes any natural or synthetic compound which has a biological activity. A "therapeutically effective amount" means the amount that, when administered to an animal or subject for treating or preventing a disorder, condition, or disease, is sufficient to effect treatment for that disorder, condition, or disease.

[0095] As used herein, the term "emesis" includes nausea and vomiting.

[0096] The term "substantially" in reference to a certain feature or entity means to a significant degree or nearly completely (i.e. to a degree of 85% or greater) in reference to the feature or entity.

II. NK-1 RECEPTION ANTAGONIST EMULSION AND METHODS OF MAKING

[0097] The present disclosure is directed to stable pharmaceutical compositions including an NK-1 receptor antagonist, a surfactant or mixtures of surfactants, a co-surfactant, an oil, with an aqueous

phase. The composition can be an injectable emulsion and is in the form of an oil-in-water emulsion which remains stable over an extended period of time and which is suitable for dilution and intravenous administration.

[0098] The NK-1 receptor antagonist compound is present in the oil phase with an emulsifier, a co-surfactant and an oil. The oil phase is then combined with an aqueous phase comprising water and a tonicity agent as described below to generate the stable emulsion. Prior to combining the oil phase with the aqueous phase, the oil phase will have an oil:antagonist compound ratio of about 11:1 to 30:1, 11:1 to 15:1, or about 13:11. For example, in formulating an oil phase comprising aprepitant, use of an oil:aprepitant ratio of about 13:1 was surprisingly found to produce, when mixed with the water phase, an emulsion which is more stable as compared to an emulsion in which the oil phase contains an oil:aprepitant ratio of less than about 12:1 or 11:1, and/or greater than about 15:1, 20:1, or 30:1. Accordingly, in some embodiments the stable emulsion comprising an NK-1 receptor antagonist and to be administered to the subject can have an oil:antagonist compound ratio of about 11:1 to 30:, 11:1 to 15:1, or about 13:11. Also contemplated, however, are emulsions in which the oil:antagonist compound ratio is about 5:1 to 20:1, 5:1 to 15:1 or 5:1 to 10:1.

[0099] Moreover, the present compositions also possess favorable stability properties when the amount of emulsifier in the oil phase is greater than the amount of oil. For example, the oil phase contains an emulsifier:oil ratio of about 5:1 to 1:1, 3:1 to 1:1 or a ratio of about 1.5:1. Such ratios of emulsifier:oil have surprisingly been found to impart greater stability on a final emulsion which is suitable for injection into a patient. For example, an aprepitant emulsion having a phospholipid:oil ratio within the oil phase of about 1.5:1 was found to have greater stability than a similar aprepitant emulsion, wherein the oil phase comprises a phospholipid:oil ratio of about 0.01:1, 0.1:1, 0.5:1 or 0.9:1.

[0100] Suitable NK-1 receptor antagonists for use in the presently described pharmaceutical emulsions include RP 67580 ((3aR,7aR)-Octahydro-2-[1-imino-2-(2-methoxyphenyl)ethyl]-7,7-diphenyl-4H-isoindol)), WIN 51078 (17-β-Hydroxy-17-α-ethynyl-5-α-androstano[3,2-b]pyrimido[1,2-a]benzimidazole), l-733,060, (((2S,3S)-3-[[3,5-bis(Trifluoromethyl) phenyl]methoxy]-2-phenylpiperidine hydrochloride), l-703,606 (cis-2-(Diphenylmethel)-N- ([2-iodophenyl]methyl)-1-azabicyclo(2.2.2)octan-3-amine) MDL 105,212 (R)-1-[2-[3-(3,4-dichlorophenyl)-1-(3,4,5-trimethoxybenzoyl)-pyrrolidin-3-yl]-ethyl]-4-phenylpiperidine-4-carboxamide hydrochloride), serlopitant, maropitant, Antagonist D, aprepitant, fosaprepitant, R116301, CGP49823, CP-96345, CP-99994, GR-203040, MDL-103392, l-760735, SDZ-NKT-343,

nolpitanitium (SR-140333), AV608, rolapitant, SCH 900978, AV608, GSK424887 (GlaxoSmithKline), GSK206136 (GlaxoSmithKline), GR-205171, CP-99994, TAK 637 ((S)-7-(3,5-Bis-trifluoromethyl-benzyl)-9-methyl-5-p-tolyl-8,9,10,11-tetrahydro-7H-1,7,11a-triaza-cycloocta[b]naphthalene-6,12-dione), LY303870 ([(R)-1-[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4- (piperidin-1-yl)piperidin-1-yl)acetyl)amino]propane]), LY686017 ((2-chloro-phenyl)-{2-[5-pyridin-4-yl-1-(3,5-bistrifluoromethyl-benzyl)-1H-[1,2,3]triazol-4-yl]-pyridin-3-yl}-methanone), E-6006, casopitant/GW679769 ((2R,4S)-4-(4-acetylpiperazin-1-yl)-N-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl)ethyl]-2-(4-fluoro-2-methylphenyl)-N-methylpiperidine-1-carboxamide), vestipitant, orvepitant and orvepitant maleate, befetupitant, netupitant, ezlopitant, CP-122721, MPC-4505 (Myriad Genetics, Inc.), CP-122721 (Pfizer, Inc.), CJ-1 2,255 (Pfizer, Inc.), SRR 240600 (Sanofi-Aventis), or TA-5538 (Tanabe Seiyaku Co.) including all pharmaceutically acceptable salts thereof.

1. Oil Phase

[0101] The oil (hydrophobic) phase comprises an oil. Triglycerides are exemplary oils for use in the compositions described herein. In certain embodiments the oil is or comprises a vegetable oil. "Vegetable oil" refers to oil derived from plant seeds or nuts. Vegetable oils are typically "long-chain triglycerides" (LCTs), formed when three fatty acids (usually 14 to 22 carbons in length, with unsaturated bonds in varying numbers and locations, depending on the source of the oil) form ester bonds with the three hydroxyl groups on glycerol. In certain embodiments, vegetable oils of highly purified grade (also called "super refined") are used to ensure safety and stability of the oil-in-water emulsions. In certain embodiments hydrogenated vegetable oils, which are produced by controlled hydrogenation of the vegetable oil, may be used. Exemplary vegetable oils include but are not limited to almond oil, babassu oil, black currant seed oil, borage oil, canola oil, castor oil, coconut oil, corn oil, cottonseed oil, olive oil, peanut oil, palm oil, palm kernel oil, rapeseed oil, safflower oil, soybean oil, sunflower oil and sesame oil. Hydrogenated and/or or partially hydrogenated forms of these oils may also be used. In specific embodiments, the oil is or comprises safflower oil, sesame oil, corn oil, olive oil and/or soybean oil. In more specific embodiments, the oil is or comprises safflower oil, and/or soybean oil. The oil is present in the emulsion at about 9 wt/wt%, though this may vary between about 5 wt/wt% to 12 wt/wt% or 9 wt/wt% to 10 wt/wt%.

[0102] To generate the oil phase, the NK-1 receptor antagonist is first mixed with an emulsifier such as a phospholipid emulsifier. Examples 1-6 and 11-19 are examples in which NK-1 receptor antagonist emulsions made using an egg lecithin. A phospholipid emulsifier is added to a

concentration of greater than 10 wt/wt%, 11 wt/wt%, 12 wt/wt% or 13 wt/wt% of the emulsion but less than 15 wt/wt%, 17 wt/wt% or 20 wt/wt% of the emulsion.

[0103] The mixture of antagonist and emulsifier is dissolved in a co-surfactant such as a short chain alcohol (1 to 6 carbons). Examples 1-6 and 11-19 below are some examples in which the co-surfactant is ethanol. The mixture is mixed at an elevated temperature, such as at about 60 °C or 70 °C or at an elevated temperature within the range of about 50 °C or 70 °C, until the NK-1 receptor antagonist and emulsifier are dissolved. This mixture is then combined with the oil, such as soybean oil, by mixing again at an elevated temperature such as at about 60 °C to produce the oil phase containing the NK-1 receptor antagonist. Excess co-surfactant can be removed by standard evaporation methods including heating, or pressure reduction, or a combination thereof such employed in a rotary evaporator. In this process, about 10% to 100%, 20% to 95%, 80% to 100%, 90% to 100%, or 95% to 100% of the ethanol evaporates depending on preparation scale, any pressure reduction, and heating time.

[0104] In one embodiment, the NK-1 receptor antagonist and the emulsifier are dissolved in a co-surfactant and an oil. Examples 1-6 and 11-19 below are some examples in which the co-surfactant is ethanol and the oil is soybean oil, however, the methods can be used with any one or more of the co-surfactants and oils described herein. The mixture is mixed at an elevated temperature, such as at about 60 °C or 70 °C or at an elevated temperature within the range of about 50 °C or 70 °C, at least until the NK-1 receptor antagonist and emulsifier are dissolved to produce the oil phase containing the NK-1 receptor antagonist. The mixture of NK-1 receptor antagonist, emulsifier, co-surfactant and oil are mixed at the elevated temperature for about 15 min to 120 min, about 15 min to 45 min, about 30 min to 90 min, or for about 15 min, 30 min or 50 min.

[0105] Excess co-surfactant can be removed by standard evaporation methods including heating, or pressure reduction, or a combination thereof in a rotary evaporator. During this process, about 10% to 100%, 20% to 95%, 80% to 100%, 90% to 100%, or 95% to 100% of the ethanol evaporates depending on preparation scale, any pressure reduction, and heating time.

[0106] In one embodiment, dexamethasone is added to the oil phase comprising the NK-1 receptor antagonist, emulsifier and oil to generate an oil phase comprising both the NK-1 receptor antagonist and dexamethasone prior to mixing with the aqueous phase to generate the pharmaceutical emulsion for injection. Dexamethasone is added to the oil phase to provide a dose of about 12 mg dexamethasone.

2. Aqueous Phase

[0107] The aqueous phase of the NK-1 receptor antagonist emulsion can be a mixture of water and a tonicity agent, including those such as but not limited to sucrose, mannitol, glycerin or dextrose or a mixture thereof. Also included in the aqueous phase is a pH-modifying agent (pH modifier). Sodium oleate is used in Examples 1-3, 5, 6, and 11-15, and 17-19 below to adjust the pH of the emulsion to about 6 to 9, depending on the desired emulsion formulation. However, it is understood that the pH modifier can be other oleic acids or salts thereof including but not limited to sodium oleate, potassium oleate and ammonium oleate. The oleic acid can comprise about 0.1 wt/wt% to 1.0 wt/wt% or about 0.4 wt/wt% or 0.5 wt/wt% of the stable injectable emulsions as provided herein. The aqueous phase is produced by mixing water with the tonicity agent and pH modifier (e.g., sodium oleate). Additional pH modifiers that may be used include but are not limited to sodium hydroxide, potassium hydroxide, magnesium hydroxide, Tris, sodium carbonate and sodium linoleate. In some embodiments, the pH modifier comprises more than one pH modifier. For example, the aqueous phase may comprise both an oleate and a buffer such as a Tris buffer. The pH modifier used is effective for adjusting the pH of the emulsion to a preferred pH of about 6 to 9, 7 to 8, or about 6, 7, 8 or 9. The aqueous phase can readily form by mixing at room temperature.

[0108] The aqueous phase of the emulsion may further contain a buffering agent to promote stability of the emulsion formulation. The drug substance may degrade; for example, lipophilic drugs will partition into the oil phase, which will confer some degree of protection, but hydrolytic degradation may still occur at the oil-water interface. Possible chemical degradation within parenteral fat emulsions includes oxidation of unsaturated fatty acid residues present in triglyceride and lecithin, and hydrolysis of phospholipids leading to the formation of free fatty acids (FFA) and lysophospholipids. Such degradants lower pH, which may then promote further degradation. Thus, pH should be controlled during manufacture and emulsion formulations may include a buffering agent to provide additional control. Any decrease in pH over the assigned shelf-life may be indicative of chemical degradation. Suitable buffers are well known to the person skilled in the art and include but are not limited to a phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer or borate buffer. Tris buffer is used in Examples 11 and 19 below to adjust the pH of the emulsion to about 8 to 9. As shown in Examples 11 and 19, in some embodiments a buffer such as Tris buffer can be used in addition to another pH modifier (e.g., oleate or sodium oleate) to adjust or modify the pH of the emulsion. In some embodiments, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer. In a particular

embodiment, the aqueous phase comprises a buffer, that when mixed with the oil phase will provide a substantially isotonic oil in water emulsion.

[0109] Buffering agents useful for the presently described compositions include, but are not limited to, a phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer or borate buffer. In a particular embodiment, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer. In a particular embodiment, the aqueous phase comprises a buffer, that when mixed with the oil phase will provide a substantially isotonic oil in water emulsion. In some embodiments, when the aqueous phase contains a buffering agent, the aqueous phase does not include a tonicity agent. Also, when a buffer is added to the aqueous phase, a pH-adjusting agent may not be added to the aqueous phase. It is understood that a buffer can be added to the aqueous phase or the buffer can be added to the emulsion.

[0110] In some embodiments, the aqueous phase of the emulsion contains a tonicity agent such as sucrose. The tonicity agent is added to an aqueous phase having about 0% to 30%, 0% to 25% or about 20% of the tonicity agent (wt/wt). It was surprisingly found that a composition containing about 20% sucrose wt/wt in the aqueous phase produced an emulsion that was particularly stable as determined by freeze-thaw testing. Accordingly, preferred embodiments include an emulsion in which the aqueous phase comprises a tonicity agent which imparts greater chemical and/or physical stability as compared to an emulsion wherein the aqueous phase contains less than about 10%, 15% or 20% wt/wt tonicity agent or more than about 30%, 40% or 50% wt/wt tonicity agent.

[0111] In one embodiment, the aqueous phase further comprises dexamethasone sodium phosphate (also referred to as "dexamethasone phosphate"). Dexamethasone sodium phosphate is a corticosteroid which is freely soluble in water. Daily dosages for dexamethasone sodium phosphate range from about 0.5 mg to 20 mg, more preferably from about 14 mg to 18 mg or 16 mg, depending on the severity of the disease or disorder. Accordingly, an NK-1 receptor antagonist emulsion further comprising dexamethasone may contain dexamethasone sodium phosphate in the aqueous phase. Accordingly, the aqueous phase of an emulsion suitable for intravenous administration may contain about 0.5 mg to 20 mg, 14 mg to 18 mg or about 16 mg dexamethasone sodium phosphate.

[0112] In another embodiment, a solution of dexamethasone sodium phosphate can be mixed into the fine emulsion prior to sterile filtration to prepare an emulsion containing dexamethasone sodium phosphate in the aqueous phase,

3. Pharmaceutical Emulsion Formulations

[0113] The pharmaceutical compositions comprising NK-1 receptor antagonists as disclosed herein are sterile oil-in-water emulsions comprising the aqueous and oil phases described above. Also encompassed by the disclosure are methods for preparing stable emulsions comprising the receptor antagonist which are suitable for intravenous administration and which can be prepared according to the conventional manufacturing procedures using aseptic techniques.

[0114] The aqueous phase is combined with the oil phase, under high-speed homogenization to produce a coarse emulsion. Examples 1-6 and 12-19 provide examples of NK-1 receptor antagonist emulsions which are produced using compositions and methods disclosed herein. As described in these examples, the combined aqueous and oil phases is homogenized using an IKA Ultra-Turrax T25 dispersing instrument at a speed of 20,000 rpm for 1 min. The speed used in this first homogenization step may vary, for example, from 2000 rpm to 25,000 rpm, or from 15,000 rpm to 22,000 rpm. The time of the homogenization step can also vary, for example, from 0.5 min to 1 hour, or from 1 min to 45 min. This crude emulsion is then homogenized into a fine emulsion by a high-pressure homogenizer, which may be a microfluidizer. The interaction chamber and the cooling coil portions of the microfluidizer are cooled by water, such as by an ice bath. The temperature of the ice bath may be between 0 to 10 °C, or 2 to 6 °C. The temperature of the emulsion coming out of the high-pressure homogenization may be between 0 to 60 °C, 15 °C, to 60 °C, 20 °C to 40 °C, or at about 25 °C. The microfluidizer is first primed with water and then the crude emulsion is introduced. The output from the homogenizer is initially run to waste to remove priming water, and priming water and emulsion mixtures, and then collected in a clean vessel when the stream becomes consistent in appearance. The high-pressure homogenizer cycle may be repeated to sufficiently reduce oil droplet size. The pressure used for the homogenization may vary. The pressures may be between 5000 and 30,000 psi. The number of passes through the microfluidizer may vary in order to achieve the desired droplet size. The number of passes may be from about 2 to 20, 2 to 15, 4 to 15, 4 to 12 or 7 to 8.

[0115] The pharmaceutical formulation may then be passed through a filter system at room temperature, and/or autoclaved, to achieve sterilization. The filters used to achieve sterilization may be chosen by the skilled artisan and may have a nominal pore size of 0.2 μm. The filter material used may vary. In one embodiment, the filter is nylon. In another embodiment, the filter is a Posidyne® filter (covalent charge-modified Nylon 6,6 membrane which exhibits a net positively-charged zeta potential in aqueous solutions). For large scale production the method above may need to be

modified. A skilled practitioner could combine these materials in a different order and using different processing equipment to achieve the desired end result.

[0116] In one embodiment of the disclosure, the homogenization can be done in repeated cycles to achieve an emulsion in which the oil particle/globule size is less than 2 microns (μm) with intermediate cooling of the homogenized product to a temperature less than about 25 °C.

[0117] The final emulsion comprises an oil portion (oil phase) dispersed in an aqueous portion (aqueous phase). The ratio of components to the NK-1 receptor antagonist within the oil phase is an important characteristic of the emulsion which may affect stability of the formulation prepared for injection and each of these ratios within the final pharmaceutical emulsion are presented in more detail below. As described above, the oil phase comprises the NK-1 receptor antagonist, an oil and an emulsifier, examples of which are provided herein.

[0118] The final emulsion contains about 0.7 wt/wt% of the NK-1 receptor antagonist, but may range from about 0.2 wt/wt% to 1.5 wt/wt%, 0.4 wt/wt% to 1.0 wt/wt%, 0.6 wt/wt% to 0.7 wt/wt%, or 0.7 wt/wt% to 0.8 wt/wt%. The emulsion is prepared which can contain about 130 mg of the NK-1 receptor antagonist, however, preparations may also be prepared according to the present disclosure which contain about 100 mg to 1000 mg, 100 mg to 500 mg, 250 mg to 750 mg or 100 mg to 200 mg NK-1 receptor antagonist.

[0119] In one embodiment, the ratio of oil:NK-1 receptor antagonist (wt%:wt%) within the oil phase of the final emulsion is about 13:1 to 14:1, but can range from about 11:1 to 15:1, 12:1 to 14:1, 13:1 to 13.5:1, or 12:1 to 15:1. In another embodiment, the ratio of oil:NK-1 receptor antagonist is about 11:1, 11.5:1, 12:1, 12.5:1, 13:1, 13.5:1, 14:1, 14.5:1 or 15:1.

[0120] The ratio of emulsifier to NK-1 receptor antagonist in the final emulsion can be about 20:1 but may also vary. For example, the ratio of emulsifier:NK-1 receptor antagonist (wt%:wt%) within the oil portion ranges from about 15:1 to 30:1, 20:1 to 25:1, 18:1 to 22:1, 19:1 to 20:1, or 10:1 to 30:1. In one embodiment, the emulsifier:NK-1 receptor antagonist (wt%:wt%) is about 15:1, 18:1, 19:1, 20:1, 21:1, 22:1 or 23:1.

[0121] The ratio of components within the oil phase of the final emulsion may alternatively be expressed in the ratio of (emulsifier plus oil):NK-1 receptor antagonist (wt%:wt%). The ratio of (emulsifier plus oil):NK-1 receptor antagonist can be about 33:1, but the ratios for the present emulsion can range from about 20:1 to 40:1, 25:1 to 35:1, 30:1 to 35:1 or 33:1 to 37:1, or may be, for example, about 30:1, 32:1, 33:1, 34:1, 35:1, 36:1, 37:1, 38:1 or 40:1.

[0122] The composition of the present disclosure has a significant advantage in terms of reduced toxicity as compared to injectable formulations which may contain less desirable excipients such as detergents, e.g., Tween-20 or Tween-80. The present formulations take advantage of the ability to solubilize therapeutically effective amounts of a NK-1 receptor antagonist in an oil phase which can then be used to generate an emulsion suitable for injection. Accordingly, described herein are pharmaceutical emulsion compositions containing a NK-1 receptor antagonist and optionally dexamethasone or dexamethasone sodium phosphate, wherein the emulsion does not comprise a detergent.

[0123] The composition of the present disclosure gives a product suitable for parenteral use because of low particle size. The composition of the present disclosure is easy to use as the product can be diluted with an agent such as an aqueous solution of sucrose, an aqueous solution of maltose or dextrose 5% injection or normal saline to achieve the required concentration for parenteral administration. The composition of the present disclosure also has a prolonged shelf life and hence is suitable for a readily marketable product.

[0124] The compositions of the disclosure are both chemically and physically stable. A physically stable emulsion of the invention is one which can be stored under appropriate conditions for at least 1, 2, 3, 4, 5, 6, 9, 12, 15, 18, 24 or 36 months, without an increase in average droplet size above that allowed as stated in USP <729>. As well, the population of large-diameter fat globules should be within the limits stated in USP <729>.

[0125] Droplet size limits defined in USP <729> apply throughout the assigned shelf life, which for a commercial pharmaceutical formulation may extend to 2-3 years or longer. All true emulsions are thermodynamically unstable and may over time undergo a range of processes which tend to increase the droplet size. These include direct droplet coalescence, when two droplets collide and form a single new droplet, and aggregation, in which droplets adhere together to form larger masses. Aggregation may in some cases be a precursor of further coalescence into larger droplets. These processes may result in large aggregates rising to the surface of the container, a phenomenon known as 'creaming', and ultimately to free oil being visible on the emulsion surface, known as 'cracking'.

[0126] Droplet size limits are typified by USP33-NF28 General Chapter <729> for Globule Size Distribution in Lipid Injectable Emulsions, hereinafter referred to as USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm (PFAT5) not exceeding 0.05%, irrespective of the final lipid concentration.

[0127] Droplet size measurements such as those defined in USP<729> can measure the initial increases in size, and hence are predictive of emulsion physical stability, at early times, long before the formulation shows macroscopic visible changes. Accordingly, the emulsions as described herein are stable compositions having an intensity-weighted mean droplet diameter less than about 500 nm, 400 nm, 300 nm, 200 nm or 100 nm.

[0128] The oil or particle droplet size, i.e. diameter, according to the present disclosure is measured using a dynamic light scattering (DLS) instrument, such as the Malvern Zetasizer 4000, Malvern Zetasize Nano S90 or preferably the Malvern Zetasizer Nano ZS. Intensity-weighted particles sizes were recorded, since they do not require the knowledge of the refractive index of the particle. In Malvern Zetasizer instruments, there are two fits for determining the intensity-weighted diameter of the oil droplet size. The first is a cumulant fit that is used to determine the Z-average diameter; this fit can additionally give the polydispersity index (PDI). This cumulant fit is recommended for monodisperse samples possessing a PDI of lower than 0.2. The second is a non-negative least squares (NNLS) fit. This gives the Peak 1 diameter, Peak 2 diameter and Peak 3 diameter. This is more suitable for polydisperse samples having a PDI of greater than 0.2.

[0129] The emulsion preparations as described herein may further comprise a preservative in quantities that preserve the composition. Suitable preservatives used in some of the embodiments of present disclosure include, but are not limited to, disodium edetate, tocopherol, benzalkonium chloride, methyl, ethyl, propyl or butylparaben, benzyl alcohol, phenylethyl alcohol, benzethonium, chlorobutanol, potassium sorbate or combination thereof.

III. MEDICAL USE

[0130] The pharmaceutical compositions of the present disclosure can be used for the prevention or treatment of emesis and provide a non-oral option for patients undergoing highly or moderately emetogenic chemotherapy such as chemotherapy used in cancer patients. The disclosure thus encompasses a method of treatment comprising intravenously administering an emulsion comprising a NK-1 receptor antagonist as described herein to a subject undergoing highly or moderately emetogenic chemotherapy whether the chemotherapy is an initial treatment or repeat courses of the chemotherapy. The pharmaceutical emulsions described herein can be used, for example, in preventing or treating acute and delayed nausea and vomiting associated with the chemotherapy or radiotherapy.

[0131] Another embodiment relates to the use of the pharmaceutical formulations of the disclosure in the manufacture of a medicament for use preventing or treating emesis in a subject in need thereof.

[0132] The amount of the NK-1 receptor antagonist and optionally dexamethasone required for use in the methods of the disclosure may vary with the method of administration and condition of the patient, and the degree of therapy required, and will be ultimately at the discretion of the attendant physician or clinician.

IV. EXAMPLES

The following examples are illustrative in nature and are in no way intended to be limiting.

Example 1: Preparing Aprepitant Emulsions for Intravenous Injection

[0133] To prepare the aprepitant emulsion, an oil phase was first prepared by combining 750 mg of aprepitant and 15.0 g of egg lecithin (LIPOID E 80) with 12.0 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added in 10.0 g of soybean oil. Heating at 60 °C and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 5.60 g of sucrose and 0.500 g of sodium oleate in 70.0 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 1 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using non-negative least squares (NNLS) fit gave a Peak 1 diameter of 99 nm. The intensity-weighted mean particle size determined using cumulant fit provided a Z-average diameter of 87 nm. The zeta potential was measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.74. This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 1

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.750	0.679	1
Lipoid E 80	15.0	13.6	20
Soybean Oil	10.0	9.05	13.3
Ethanol[1]	8.59	7.78	11.5
Sucrose	5.60	5.07	7.5
Sodium Oleate	0.500	0.453	0.667
Water for Injection	70.0	63.4	93.3
Total	110	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 2: Preparing Aprepitant Emulsions for Intravenous Injection

[0134] To prepare the aprepitant emulsion, an oil phase was first prepared by combining 450 mg of aprepitant and 9.00 g of egg lecithin (LIPOID E 80) with 4.0 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added 6.00 g of soybean oil. Heating at 60 °C and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 3.36 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 2 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using NNLS fit gave a Peak 1 diameter of 127 nm. The intensity-weighted mean particle sized determined using cumulant fit provided a Z-average diameter of 101 nm. The zeta potential was measured to be -47 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.77. This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 2

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.450	0.714	1
Lipoid E 80	9.00	14.3	20
Soybean Oil	6.00	9.52	13.3
Ethanol[1]	1.89	3.00	4.20
Sucrose	3.36	5.33	7.47
Sodium Oleate	0.300	0.476	0.667
Water for Injection	42.0	66.7	93.3
Total	63.0	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 3: Preparing Aprepitant Emulsions for Intravenous Injection

[0135] To prepare the aprepitant emulsion, an oil phase was first prepared by combining 450 mg of aprepitant and 9.00 g of egg lecithin (LIPOID E 80) with 6.0 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added in 6.00 g of soybean oil. Heating at 60°C and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 15.62 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 3 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using NNLS fit gave a Peak 1 diameter of 88 nm. The intensity-weighted mean particle sized determined using cumulant fit provided a Z-average diameter of 68 nm. The zeta potential was measured to be -42 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.80. This aprepitant-containing emulsion is to be diluted with water for injection by 4-fold prior to injection.

Table 3

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.450	0.587	1
Lipoid E 80	9.00	11.7	20
Soybean Oil	6.00	7.83	13.3
Ethanol[1]	3.27	4.26	7.26
Sucrose	15.6	20.4	34.7
Sodium Oleate	0.300	0.391	0.667
Water for Injection	42.0	54.8	93.3
Total	76.6	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 4: Preparing an Alternate Aprepitant Emulsion Formulation for Intravenous Injection

[0136] An aprepitant emulsion was prepared which has less than 10% wt/wt of the phospholipid emulsifier and which was adjusted to a pH of less than 8.0. To prepare the aprepitant emulsion, an oil phase was first prepared by combining 450 mg of aprepitant and 6.67 g of egg lecithin (LIPOID E 80) with 7.2 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm. Heating and stirring was carried out until the ethanol was evaporated and a thick residue was observed. To the resultant solution was added in 6.00 g of soybean oil and an appropriate amount of ethanol to obtain a clear oil phase upon heating at 60°C. The aqueous phase was prepared by dissolving 3.36 g of sucrose in 50.5 ml of water for injection at 60°C. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. The pH of this crude emulsion was adjusted to 7.0 and then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 4 below. Within 4 days post preparation at room temperature, crystals were observed in the product by microscopy.

Table 4

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.450	0.672	1
Lipoid E 80	6.67	9.95	14.8
Soybean Oil	6.00	8.96	13.3
Sucrose	3.36	5.02	7.47
Water for Injection	50.5	75.4	112
Total	67.0	100	-

Example 5: Preparing Aprepitant Emulsions for Intravenous Injection

[0137] An aprepitant emulsion was prepared which contains oleic acid. To prepare the aprepitant emulsion, an oil phase was first prepared by combining 250 mg of aprepitant, 2.50 g of egg lecithin (LIPOID E 80), 15.0 g of soybean oil and 125 mg of oleic acid. Ten ml of ethanol was added to dissolve the mixture at 70 °C. The ethanol was removed by pressure reduction in a 70 °C water bath to yield a clear oil phase. A preheated aqueous phase containing 82.1 ml of water for injection at 70 °C was added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 5 below. Within 4 days post-preparation at room temperature, crystals were observed in the product by microscopy.

Table 5

Component	Amount (g)	Concentration (w/w%)	Ratio to aprepitant
Aprepitant	0.250	0.250	1
Lipoid E 80	2.50	2.50	10
Soybean Oil	15.0	15.0	60
Oleic Acid	0.125	0.125	0.5
Water for Injection	82.1	82.1	328
Total	100	100	-

Example 6: Preparing Emulsions Containing Aprepitant and Dexamethasone Sodium Phosphate for Intravenous Injection

[0138] To prepare an injectable emulsion containing aprepitant and dexamethasone sodium phosphate, an oil phase was first prepared by combining 773 mg of aprepitant and 15.5 g of egg lecithin (LIPOID E 80) with 10.3 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added in 10.3 g of soybean oil. Heating at 60 °C and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 5.77 g of sucrose and 0.515 g of sodium oleate in 71.1 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. Dexamethasone sodium phosphate (93.5 mg) dissolved in 1 ml of water for injection was mixed into the fine emulsion. This resultant fine emulsion containing both aprepitant and dexamethasone sodium phosphate was sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 6 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using NNLS fit gave a Peak 1 diameter of 95 nm. The intensity-weighted mean particle size determined using cumulant fit provided a Z-average diameter of 70 nm. The zeta potential was measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.92. This aprepitant and dexamethasone sodium phosphate containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 6

Component	Amount (g)	Concentration (w/w%)	Ratio to aprepitant
Aprepitant	0.773	0.688	1
Dexamethasone Sodium Phosphate	0.0935	0.0832	0.121
Lipoid E 80	15.5	13.8	20
Soybean Oil	10.3	9.17	13.3
Ethanol[1]	7.31	6.51	9.47
Sucrose	5.77	5.14	7.47
Sodium Oleate	0.515	0.459	0.667
Water for Injection	72.1	64.2	93.3
Total	112	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 7: Stability of the Aprepitant Emulsion at Room Temperature and 5 °C

[0139] Stability of the aprepitant emulsions prepared as described in Examples 1, 2 3 and 6 was measured by incubating each emulsion preparation at room temperature (about 25 °C) or at 5 °C. Mean particle size and percentage of fat globules above 5 μm were measured using DLS and light obscuration respectively to determine if they satisfy USP <729>. The emulsions were also inspected by microscopy for aprepitant crystals. Example 1 was stable at room temperature for 2 months, that is, the mean particle size and percentage of fat globules above 5 μm satisfied USP <729>. Additionally, no aprepitant crystals were visible by microscopy. After 2 months storage at room temperature, creaming was observed in Examples 1 and 6. This corresponded with the observation of aprepitant crystals. Examples 2 and 3 were stable at room temperature for 3 and 2 months respectively. After these time points, aprepitant crystals were observed in these formulations. Storage at 5 °C resulted in longer emulsion stability for Examples 1, 2, 3 and 6. Table 7 shows the characterizations of Examples 1, 2, 3 and 6 and their respective stabilities at room temperature and at 5 °C.

Table 7

Sample	PDI	Particle Size as Peak 1 Diameter (nm)	Particle Size as Z-Average Diameter (nm)	Zeta Potential (mV)	pH	Stability at 25 °C per USP <729> (months)	Stability at 5 °C per USP <729>
Example 1	0.122	99	87	-43	8.74	2	>10 months
Example 2	0.200	127	101	-47	8.77	3	>10 months
Example 3	0.219	88	68	-42	8.80	2	>10 months
Example 6	0.244	95	70	-43	8.92	2	>10 months

Example 8: Stability of the Aprepitant Emulsion to Freeze-Thaw Cycle

[0140] The aprepitant emulsions prepared according to Examples 1, 2, 3 and 6 were tested for stability upon exposure to a freeze-thaw cycle. Samples from the Examples 1, 2, 3 and 6 were stored at -20 °C overnight. They were thawed to room temperature the next day and visualized by microscopy. Prior to freezing, all samples did not present any visible particles under the microscope. FIG. 1 shows microscope images, at 10X, of emulsions after the freeze-thaw cycle (Examples 1, 2, 3 and 6 are shown as FIG. 1 A, B, C, and D, respectively). Emulsions prepared as described in examples 1, 2 and 6 showed visible particles after exposure to freezing. Only Example 3 was stable after freezing. As FIG. 1C shows, no visible particles were observed for the formulation of Example 3. This enhanced stability was conferred by the presence of a large concentration of sucrose (20 w/w% in Example 3 compared to 5 w/wt% in Examples 1, 2 and 6).

Example 9: Pharmacokinetics of an Aprepitant Emulsion

[0141] The pharmacokinetics of an aprepitant emulsion prepared according to Example 1 was determined. Two groups of six male Sprague-Dawley rats each were injected intravenously with, respectively, fosaprepitant in solution or aprepitant emulsion prepared according to Example 1. All drugs were administered at an effective concentration equivalent to 14 mg/kg aprepitant. Blood from all rats was collected at the appropriate time intervals and processed to plasma by centrifugation. Plasma samples were analyzed by LC-MS/MS for aprepitant and fosaprepitant, as appropriate. A plasma concentration versus time curve of aprepitant for the emulsion described in Example 1 and for fosaprepitant is presented in FIG. 2 (fosaprepitant in solution, ●; aprepitant emulsion, ▲). The

curves indicate the initial aprepitant level reached immediately after injection of the aprepitant emulsion was almost 3 times higher than the initial aprepitant level reached immediately after injection of the fosaprepitant solution. Plasma levels of aprepitant resulting from each injection, however, were essentially the same by the 3-hour time point indicating the formulations were bioequivalent except for a delay in the conversion of fosaprepitant to aprepitant.

Example 10: Pharmacokinetics of an Aprepitant and Dexamethasone Emulsion

[0142] The pharmacokinetics of an aprepitant and dexamethasone sodium phosphate combination emulsion prepared according to Example 6 was determined. Male Sprague-Dawley rats each were injected intravenously with fosaprepitant solution (group 1), dexamethasone sodium phosphate solution (group 2), or an emulsion containing aprepitant and dexamethasone sodium phosphate prepared according to Example 6 (group 3). Groups 1 and 2 consisted of six rats each; for group 3, twelve rats were injected with the aprepitant and dexamethasone sodium phosphate combination emulsion to allow for the collection of sufficient samples for the measurement of both active ingredients.

[0143] In groups 1 and 3, a dose was administered at an effective drug concentration equivalent to 2 mg/kg aprepitant. In groups 2 and 3, a dose was administered at an effective drug concentration equivalent to 0.24 mg/kg dexamethasone sodium phosphate. Blood from all rats was collected at the appropriate time intervals and processed to plasma by centrifugation. Plasma samples were analyzed by LC-MS/MS for dexamethasone, aprepitant, and fosaprepitant, as appropriate.

[0144] FIGS. 3 and 4 present the plasma concentration versus time curve of aprepitant and dexamethasone, respectively. FIG. 3 compares the aprepitant plasma concentration versus time curve resulting from injection of the emulsion described in Example 6 (FIG. 3, ●) vs. injection of a solution of fosaprepitant (FIG. 3, ▲). FIG. 4 compares the dexamethasone plasma concentration versus time curve resulting from injection of a dexamethasone sodium phosphate solution (FIG. 4, ●) vs. injection of the emulsion described in Example 6. The curves indicate that the aprepitant in the emulsion is released approximately simultaneously with the dexamethasone sodium phosphate. The presence of dexamethasone sodium phosphate in the emulsion does not affect the pharmacokinetics of aprepitant.

Example 11: Preparing Aprepitant Emulsions for Intravenous Injection

[0145] To prepare the aprepitant emulsion comprising a buffering agent, an oil phase is first prepared by combining 750 mg of aprepitant, 15.0 g of egg lecithin (LIPOID E 80), 10.0 g of soybean oil and 3.75 ml of ethanol. This mixture is dissolved by heating and stirring at 70 °C and 200 rpm for

30 min. The aqueous phase is prepared by dissolving 2.17 g of sucrose and 0.500 g of sodium oleate in a mixture of 4.1 ml of 1M Tris buffer (pH 8.4) and 65.9 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). Dynamic light scattering is used to determine the intensity-weighted particle size using NNLS fit to give the Peak 1 diameter, the intensity-weighted mean particle sized is determined using cumulant fit to provide the Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Example 12: Preparing Rolapitant Emulsions for Intravenous Injection

[0146] To prepare the rolapitant emulsion, an oil phase was first prepared by combining 1.080 g of rolapitant and 21.6 g of egg lecithin (LIPOID E 80) with 14.4 g of soybean oil and 5.40 ml of ethanol in a glass jar. This mixture was allowed to incubate at room temperature for 30 min followed by heating and stirring at 70°C and 200 rpm for another 30 min. The aqueous phase was prepared by dissolving 8.06 g of sucrose and 0.720 g of sodium oleate in 100.8 ml of water for injection by heating and stirring at 35°C and 300 rpm for 15 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was passed 8 times through a high-pressure microfluidizer (Microfluidizer® M-110P, F12Y interaction chamber) at a pressure of 20,000 psi. The outlet fine emulsion temperature was kept at approximately 25°C using cooling water. The resultant fine emulsion was sterilized by passing through a 0.2 μm nylon filter (Nalgene). Details of the emulsion composition are provided in Table 8 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using non-negative least squares (NNLS) fit gave a Peak 1 diameter of 127 nm (Table 9). The intensity-weighted mean particle size determined using cumulant fit provided a Z-average diameter of 100 nm. The pH and osmolality of the injectable emulsion were 8.51 and 318 mmol/kg respectively. This rolapitant-containing emulsion can be injected as is, or diluted for infusion with 0.9% saline or 5% dextrose.

Table 8

Component	Amount (g)	Concentration (w/w%)	Ratio to Rolapitant
Rolapitant	1.080	0.728	1
Lipoid E 80	21.6	14.55	20
Soybean Oil	14.4	9.70	13.3
Ethanol[1]	1.78	1.20	1.65
Sucrose	8.06	5.43	7.47
Sodium Oleate	0.720	0.485	0.667
Water for Injection	100.8	67.9	93.3
Total	148	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Table 9

Sample	PDI	Particle Size as Peak 1 Diameter (nm)	Particle Size as Z-Average Diameter (nm)	pH	Osmolality (mmol/kg)	Stability at 25°C per USP <729>	Stability at 5°C per USP <729>
Example 1	0.213	127	100	8.51	318	>1 months	>1 months

Example 13: Preparing Netupitant Emulsions for Intravenous Injection

[0147] To prepare the emulsion containing a therapeutically effective amount of netupitant, an oil phase is first prepared by combining about 750 mg of netupitant and 15.0 g of egg lecithin (LIPOID E 80) with 12.0 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added in 10.0 g of soybean oil. Heating at 60 °C and stirring at 200 rpm is continued for another 15 min. The aqueous phase is prepared by dissolving 5.60 g of sucrose and 0.500 g of sodium oleate in 70.0 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 10 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using non-negative least squares (NNLS) fit to obtain a Peak 1 diameter of the particle. The

intensity-weighted mean particle size is also determined using cumulant fit and provides a Z-average diameter. The zeta potential is measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion is also measured and is preferably about pH 7.8 to 8.8. This NK-1 receptor antagonist-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 10

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.750	0.679	1
Lipoid E 80	15.0	13.6	20
Soybean Oil	10.0	9.05	13.3
Ethanol[1]	8.59	7.78	11.5
Sucrose	5.60	5.07	7.5
Sodium Oleate	0.500	0.453	0.667
Water for Injection	70.0	63.4	93.3
Total	110	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 14: Preparing Netupitant Emulsions for Intravenous Injection

[0148] To prepare the netupitant emulsion, an oil phase is first prepared by combining about 450 mg of netupitant and 9.00 g of egg lecithin (LIPOID E 80) with 4.0 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added 6.00 g of soybean oil. Heating at 60 °C and stirring at 200 rpm is continued for about another 15 min. The aqueous phase is prepared by dissolving 3.36 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 11 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using NNLS fit to give a Peak 1 diameter. The intensity-weighted mean particle size is determined using cumulant fit provides a Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis

(Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion is also measured and is preferably about pH 7.8 to 8.8. This netupitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 11

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.450	0.714	1
Lipoid E 80	9.00	14.3	20
Soybean Oil	6.00	9.52	13.3
Ethanol[1]	1.89	3.00	4.20
Sucrose	3.36	5.33	7.47
Sodium Oleate	0.300	0.476	0.667
Water for Injection	42.0	66.7	93.3
Total	63.0	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 15: Preparing Netupitant Emulsions for Intravenous Injection

[0149] To prepare the netupitant emulsion, an oil phase is first prepared by combining 450 mg of netupitant and 9.00 g of egg lecithin (LIPOID E 80) with 6.0 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added in 6.00 g of soybean oil. Heating at 60°C and stirring at 200 rpm is continued for another 15 min. The aqueous phase is prepared by dissolving 15.62 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 12 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using NNLS fit gave a Peak 1 diameter. The intensity-weighted mean particle size is determined using cumulant fit provided a Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano

ZS). The pH of the injectable emulsion is also measured and is preferably about pH 7.8 to 8.8. This netupitant-containing emulsion is to be diluted with water for injection by 4-fold prior to injection.

Table 12

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.450	0.587	1
Lipoid E 80	9.00	11.7	20
Soybean Oil	6.00	7.83	13.3
Ethanol[1]	3.27	4.26	7.26
Sucrose	15.6	20.4	34.7
Sodium Oleate	0.300	0.391	0.667
Water for Injection	42.0	54.8	93.3
Total	76.6	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 16: Alternate Netupitant Emulsion Formulations for Intravenous Injection

[0150] A netupitant emulsion is prepared which has less than 10% wt/wt of the phospholipid emulsifier and which is adjusted to a pH of less than 8.0. To prepare the netupitant emulsion, an oil phase is first prepared by combining 450 mg of netupitant and 6.67 g of egg lecithin (LIPOID E 80) with 7.2 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm. Heating and stirring is carried out until the ethanol is evaporated and a thick residue is observed. To the resultant solution is added in 6.00 g of soybean oil and an appropriate amount of ethanol to obtain a clear oil phase upon heating at 60°C. The aqueous phase is prepared by dissolving 3.36 g of sucrose in 50.5 ml of water for injection at 60°C. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. The pH of this crude emulsion is adjusted to 7.0 and then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 13 below. Within 4 days post preparation at room temperature, the emulsion product is analyzed for the presence of crystals by microscopy.

Table 13

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.450	0.672	1
Lipoid E 80	6.67	9.95	14.8
Soybean Oil	6.00	8.96	13.3
Sucrose	3.36	5.02	7.47
Water for Injection	50.5	75.4	112
Total	67.0	100	-

Example 17: Alternate Netupitant Emulsion Formulations for Intravenous Injection

[0151] A netupitant emulsion is prepared which contains oleic acid. To prepare the netupitant emulsion, an oil phase is first prepared by combining 250 mg of netupitant, 2.50 g of egg lecithin (LIPOID E 80), 15.0 g of soybean oil and 125 mg of oleic acid. Ten ml of ethanol is added to dissolve the mixture at 70 °C. The ethanol is removed by pressure reduction in a 70 °C water bath to yield a clear oil phase. A preheated aqueous phase containing 82.1 ml of water for injection at 70 °C is added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 14 below. Within 4 days post preparation at room temperature, the emulsion product is analyzed for the presence of crystals by microscopy.

Table 14

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.250	0.250	1
Lipoid E 80	2.50	2.50	10
Soybean Oil	15.0	15.0	60
Oleic Acid	0.125	0.125	0.5
Water for Injection	82.1	82.1	328
Total	100	100	-

Example 18: Preparing Emulsions Containing Netupitant and Dexamethasone Sodium Phosphate for Intravenous Injection

[0152] To prepare an injectable emulsion containing netupitant and dexamethasone sodium phosphate, an oil phase are first prepared by combining 773 mg of netupitant and 15.5 g of egg lecithin (LIPOID E 80) with 10.3 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added in 10.3 g of soybean oil. Heating at 60 °C and stirring at 200 rpm is continued for another 15 min. The aqueous phase is prepared by dissolving 5.77 g of sucrose and 0.515 g of sodium oleate in 71.1 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. Dexamethasone sodium phosphate (93.5 mg) dissolved in 1 ml of water for injection is mixed into the fine emulsion. This resultant fine emulsion containing both netupitant and dexamethasone sodium phosphate is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 15 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using NNLS fit to determine a Peak 1 diameter. The intensity-weighted mean particle size is determined using cumulant fit to determine a Z-average diameter. The zeta potential is measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The preferred pH of the injectable emulsion is between about 8.5 and 9.5. This netupitant and dexamethasone sodium phosphate containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 15

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.773	0.688	1
Dexamethasone Sodium Phosphate	0.0935	0.0832	0.121
Lipoid E 80	15.5	13.8	20
Soybean Oil	10.3	9.17	13.3
Ethanol[1]	7.31	6.51	9.47
Sucrose	5.77	5.14	7.47
Sodium Oleate	0.515	0.459	0.667
Water for Injection	72.1	64.2	93.3
Total	112	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 19: Preparing NK-1 Receptor Antagonist Emulsions for Intravenous Injection

[0153] To prepare an NK-1 receptor antagonist emulsion comprising a buffering agent, an oil phase is first prepared by combining 750 mg of aprepitant, 15.0 g of egg lecithin (LIPOID E 80), 10.0 g of soybean oil and 3.75 ml of ethanol. This mixture is dissolved by heating and stirring at 70 °C and 200 rpm for 30 min. The aqueous phase is prepared by dissolving 2.17 g of sucrose and 0.500 g of sodium oleate in a mixture of 4.1 ml of 1M Tris buffer (pH 8.4) and 65.9 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). Dynamic light scattering is used to determine the intensity-weighted particle size using NNLS fit to give the Peak 1 diameter, the intensity-weighted mean particle sized is determined using cumulant fit to provide the Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Example 20: Stability of the Rolapitant Emulsion at Room Temperature and 5 °C

[0154] Stability of the rolapitant emulsion prepared as described in Example 12 was measured by incubating the emulsion preparation at room temperature (about 25 °C) or at 5 °C. Mean particle size and percentage of fat globules above 5 μm were measured using DLS and light obscuration respectively and demonstrated to satisfy USP <729> after 2 months of storage. The emulsions were also inspected by microscopy for rolapitant crystals and visually for the presence of emulsion creaming. The absence of crystals or emulsion creaming further indicated product stability.

Example 21: Stability of the Netupitant Emulsion at Room Temperature and 5 °C

[0155] Stability of the netupitant emulsions prepared as described in Examples 13-17 can be measured by incubating each emulsion preparation at room temperature (about 25 °C) or at 5 °C. Mean particle size and percentage of fat globules above 5 μm are measured using DLS and light obscuration respectively to determine if they satisfy USP <729>. The emulsions are also inspected by microscopy for netupitant crystals and/or visually for the presence of emulsion creaming. The absence of crystals or emulsion creaming indicates product stability.

Example 22: Stability of the Netupitant Emulsion to Freeze-Thaw Cycle

[0156] The netupitant emulsions prepared according to Examples 13-17 can be tested for stability upon exposure to a freeze-thaw cycle. Samples from the Examples 13-17 are stored at -20 °C overnight. The absence of visible particles when the samples are viewed under a microscope indicates product stability.

[0157] While a number of exemplary aspects and embodiments have been discussed above, those of skill in the art will recognize certain modifications, permutations, additions and sub-combinations thereof. It is therefore intended that the following appended claims and claims hereafter introduced are interpreted to include all such modifications, permutations, additions and sub-combinations as are within their true spirit and scope.

WHAT IS CLAIMED IS:

1. An injectable emulsion, comprising:
0.7-0.8 wt% aprepitant;
13 wt/wt% to 20 wt/wt% of an emulsifier;
an oil;
a co-emulsifier which is an alcohol;
a tonicity modifier;
a pH modifier; and
water;
wherein the pH of the emulsion ranges from about 7.5 to 9.0.

2. The emulsion of claim 1, wherein the emulsifier is a phospholipid.

3. The emulsion of claim 2, wherein the phospholipid is present in the emulsion at about 17 wt/wt%.

4. The emulsion of claim 2, wherein the phospholipid is present in the emulsion at about 18 wt/wt%.

5. The emulsion of claim 1, wherein the emulsifier is an egg lecithin.

6. The emulsion of claim 5, wherein the egg lecithin is present in the emulsion at about 17 wt/wt%.

7. The emulsion of claim 5, wherein the egg lecithin is present in the emulsion at about 18 wt/wt%.

8. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is between about 20:1 to 25:1.

9. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 23:1.

10. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 24:1.

11. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 25:1.

12. The emulsion of claim 1, wherein the oil in the emulsion is soybean oil.

13. The emulsion of claim 11, wherein the soybean oil is present at a concentration of about 9 wt/wt % to 10 wt/wt %.

14. The emulsion of claim 1, wherein the alcohol in the emulsion is ethanol.

15. The emulsion of claim 13, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

16. The emulsion of claim 13, wherein the ethanol is present in the emulsion at a concentration of about 2 wt/wt % to 3 wt/wt %.

17. The emulsion of claim 1, wherein the tonicity modifier in the emulsion is sucrose.

18. The emulsion of claim 16, wherein the sucrose is present at a concentration of about 3 wt/wt % to 8 wt/wt %.

19. The emulsion of claim 16, wherein the sucrose is present at a concentration of about 5 wt/wt %.

20. The emulsion of claim 1, wherein the pH modifier in the emulsion is sodium oleate.

21. The emulsion of claim 19, wherein the sodium oleate is present at a concentration of about 0.4 wt/wt % to 0.5 wt/wt %.

22. The emulsion of claim 1, wherein the aprepitant is present in the emulsion at about 0.7 wt/wt%.

23. The emulsion of claim 21, wherein the phospholipid is an egg lecithin.

24. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is between about 20:1 to 25:1.

25. The emulsion of claim 21, wherein the phospholipid is present at a concentration of about 17 wt/wt %.

26. The emulsion of claim 21, wherein the phospholipid is present at a concentration of about 18 wt/wt %.

27. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 23:1.

28. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 24:1.

29. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 25:1.

30. An injectable pharmaceutical emulsion, comprising:
about 0.7-0.8 wt% aprepitant;
an egg phospholipid emulsifier;
an oil;
a co-surfactant;
water; and
a pH modifier,
wherein the ratio of the emulsifier to aprepitant is about 20:1 to 25:1 (wt/wt%).

ABSTRACT OF THE DISCLOSURE

Disclosed herein are novel pharmaceutical formulations of a neurokinin-1 (NK-1) receptor antagonist suitable for parenteral administration including intravenous administration. Also included are formulations including both the NK-1 receptor antagonist and dexamethasone sodium phosphate. The pharmaceutical formulations are stable oil-in-water emulsions for non-oral treatment of emesis and are particularly useful for treatment of subjects undergoing highly emetogenic cancer chemotherapy.

Doc Code: TRACK1.REQ
Document Description: **TrackOne Request**

PTO/AIA/424 (11-23)

CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION UNDER 37 CFR 1.102(e) (Page 1 of 1)

First Named Inventor:	Thomas B. Ottoboni	Nonprovisional Application Number (if known):	To be assigned
Title of Invention:	METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently $0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.

2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed.

3. The applicable box is checked below:

I. ☑ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via USPTO patent electronic filing system.

---OR---

(b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.

ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, **or** the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.

II. ☐ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

i. A request for continued examination has been filed with, or prior to, this form.
ii. If the application is a utility application, this certification and request is being filed via USPTO patent electronic filing system.
iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature /Judy M. Mohr/	Date 2024-01-19
Name (Print/Typed) Judy M. Mohr	Practitioner Registration Number 38563

Note: *This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.**

☑ *Total of 1 forms are submitted.

PTO/AIA/01 (06-12)
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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [■] The attached application, or
- [ ] United States application or PCT international application number _____

filed on _____.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Thomas B. Ottoboni Date (Optional): FEB-1-2016

Signature: Thomas B Ottoboni

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [■] The attached application, or
- [ ] United States application or PCT international application number _____

filed on _____.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Han Han Date (Optional) :_____

Signature: _____

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

[X] Practitioners associated with Customer Number: 108547

OR

[ ] Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignment documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

[X] The address associated with Customer Number: 108547

OR

[ ]

Firm or individual name		
Address		
City	State	Zip
Country		
Telephone	Email	

Assignee name and address: Heron Therapeutics, Inc.
4242 Campus Point Court, Suite 200
San Diego, CA 92121

A copy of this form, together with a statement under 37 CFR 3.73(c) (Form PTO/AIA/96 or equivalent) is required to be filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of the practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee.

Signature DocuSigned by: Thomas Ottoboni	Date January 10, 2019 | 1:28 PM PST
Name Thomas B. Ottoboni	Telephone (650) 366-2626
Title Senior Vice President, Pharmaceutical and Translational Sciences; Chief Scientific Officer	

This collection of information is required by 37 CFR 1.31, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public, which is to update (and by the USPTO to process) the file of a patent or reexamination proceeding. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 18 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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STATEMENT UNDER 37 CFR 3.73(c)

First Named Inventor/Patent Owner: Heron Therapeutics, Inc.

Application No./Patent No.: To be assigned Filed/Issue Date: Herewith

Titled: METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Heron Therapeutics, Inc., a Corporation

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

   ☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

   ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☑ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 052128, Frame 0548, or for which a copy thereof is attached*.

B. ☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: _____ To: _____

   The document was recorded in the United States Patent and Trademark Office at

   Reel _____, Frame _____, or for which a copy thereof is attached*.

2. From: _____ To: _____

   The document was recorded in the United States Patent and Trademark Office at

   Reel _____, Frame _____, or for which a copy thereof is attached*.

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0031. Public burden for this form is estimated to average 12 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

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4. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

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5. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached*.

6. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached*.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☑ *As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Judy M. Mohr/	2024-01-19
Signature	Date
Judy M. Mohr	38563
Printed or Typed Name	Title or Registration Number

ASSIGNMENT

THIS ASSIGNMENT is by Thomas B. Ottoboni and Han Han (the "Assignors"), residing in Belmont, California and Sunnyvale, California, respectively. We, the Assignors, have invented certain inventions (the "Invention(s)") described in a United States Patent Application entitled EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF (the "Application") bearing Application No. 15/012,532, with a filing date of February 1, 2016.

JMM 4.30.19

4242 Campus Point Court, Suite 200

HERON THERAPEUTICS, INC., having a place of business at ~~123 Saginaw Drive~~, San Diego 92121 ~~Redwood City~~, CA ~~94063~~ ("Assignee"), desires to acquire the entire right, title and interest in and to the Inventions and the Application, and in and to any patents (collectively, "Patents") that may be granted for the Inventions in the United States or in any foreign countries.

JMM 4.30.19

For valuable consideration, the receipt and sufficiency of which we acknowledge, Assignors hereby sell, assign, and transfer to Assignee, its successors, legal representatives and assigns, the entire right, title and interest in and to: the Inventions, the Application, and any Patents; any divisions, continuations, and continuations-in-part of the Application and any other application claiming priority rights from the Application; any reissues, reexaminations, or extensions of any and all Patents; the right to file foreign applications directly in the name of Assignee; and the right to claim priority rights deriving from the Application (collectively, the "Rights"). Assignors warrant that they are the owners of the Rights, and that the Rights are unencumbered. Assignors also agree to not sign any writing or do any act conflicting with this assignment, and, without further compensation, to sign all documents and do such additional acts as Assignee deems necessary or desirable to: perfect Assignee's enjoyment of the Rights; prepare and prosecute the Application or any other applications for Patents; conduct proceedings regarding the Rights, including any litigation or interference proceedings; or perfect or defend title to the Rights.

[The remainder of this page is intentionally left blank.]

Assignors request the Commissioner of Patents to issue any Patent of the United States that may be issued on the Inventions to Assignee. This Assignment may be executed in counterparts.

Date: April 6 2016

Thomas B. Ottoboni

Date: April 6 2016

Han Han

WITNESSES TO SIGNATURE BY THOMAS B. OTTOBONI

1. _____ April 6, 2016
Signature Date

KHYLA LE
Print Name

119 POPPY CT
Street Address

MILLPITAS, CA 95035
City, Country & Postal Code

2. _____ 06 APR 2016
Signature Date

Jason Cutes
Print Name

263 Stanley Ave
Street Address

Pacifica, CA 94044
City, Country & Postal Code

OR

STATE OF _____

COUNTY OF _____

On _____ before me, _____, personally appeared **Thomas B. Ottoboni**, personally known to me (or proved to me on the basis of satisfactory evidence) to be the person whose name is subscribed to the within instrument and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of _____ that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

_____
Signature (Seal)

WITNESSES TO SIGNATURE BY HAN HAN

1. Kaylale — Signature; April 6, 2016 — Date

KAYLA LE — Print Name

119 POPPY CT — Street Address

MILPITAS, CA 95035 — City, Country & Postal Code

2. J. — Signature; 06 APR 2016 — Date

Jason Lutes — Print Name

263 Stanley Ave — Street Address

Pacifica CA 94044 — City, Country & Postal Code

OR

STATE OF _____

COUNTY OF _____

On _____ before me, _____, personally appeared Han Han, personally known to me (or proved to me on the basis of satisfactory evidence) to be the person whose name is subscribed to the within instrument and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of _____ that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

_____
Signature (Seal)

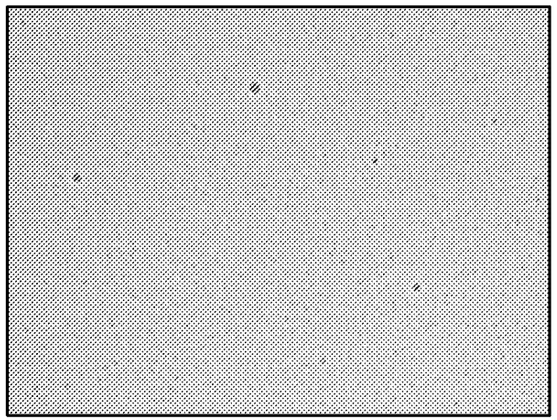


FIG. 1A

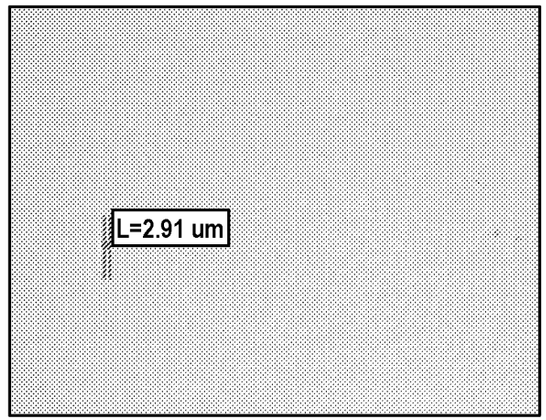


FIG. 1B

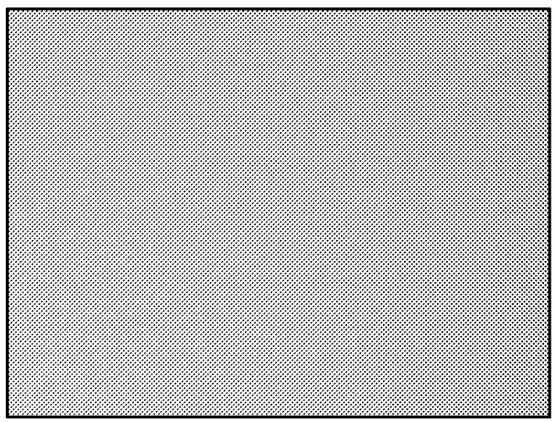


FIG. 1C

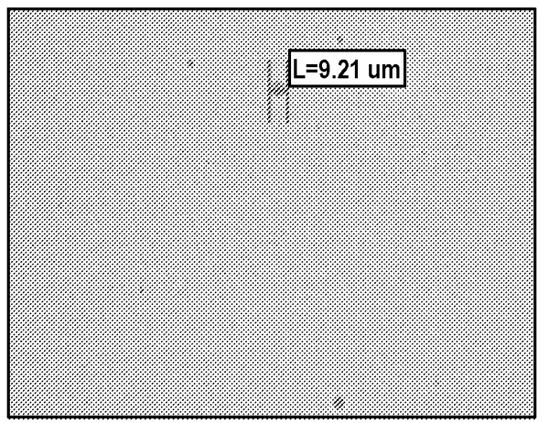


FIG. 1D

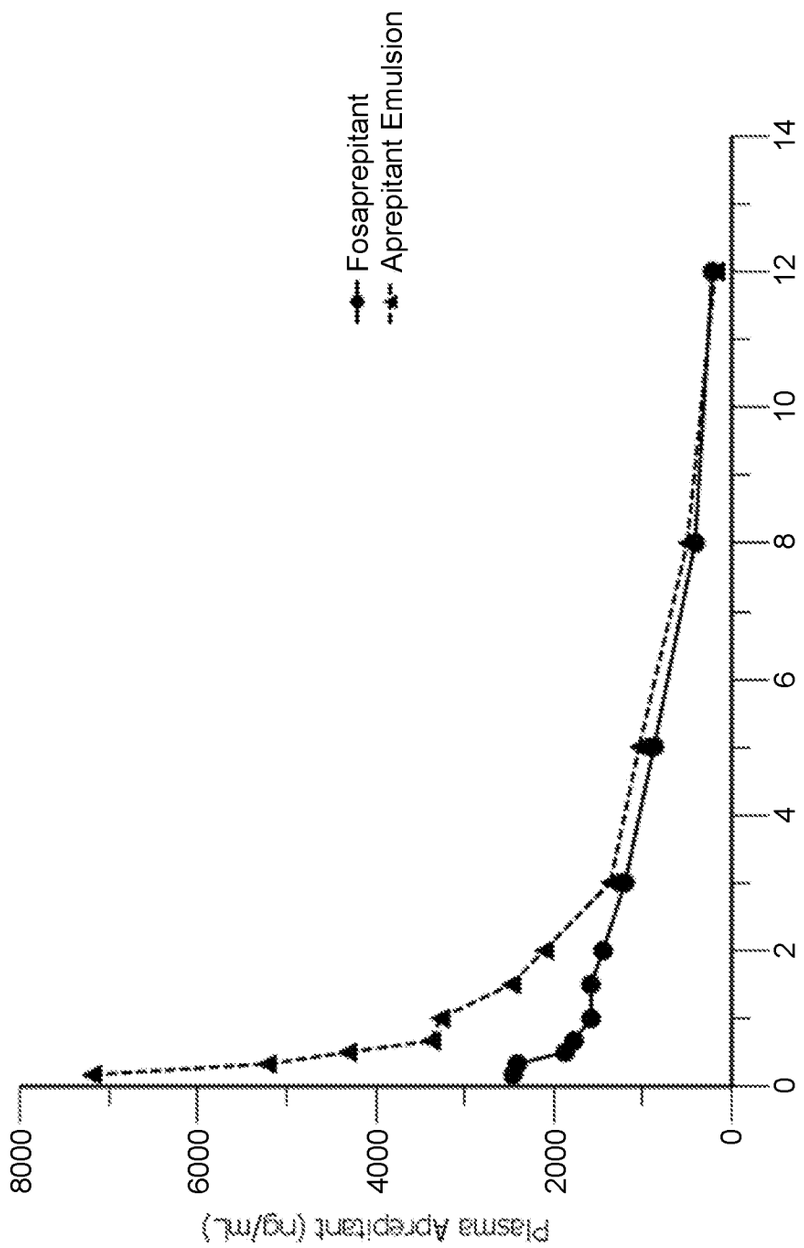

Fosaprepitant
Aprepitant Emulsion
Plasma Aprepitant (ng/mL)
8000
6000
4000
2000
0
0
2
4
6
8
10
12
14
Hours

FIG. 2

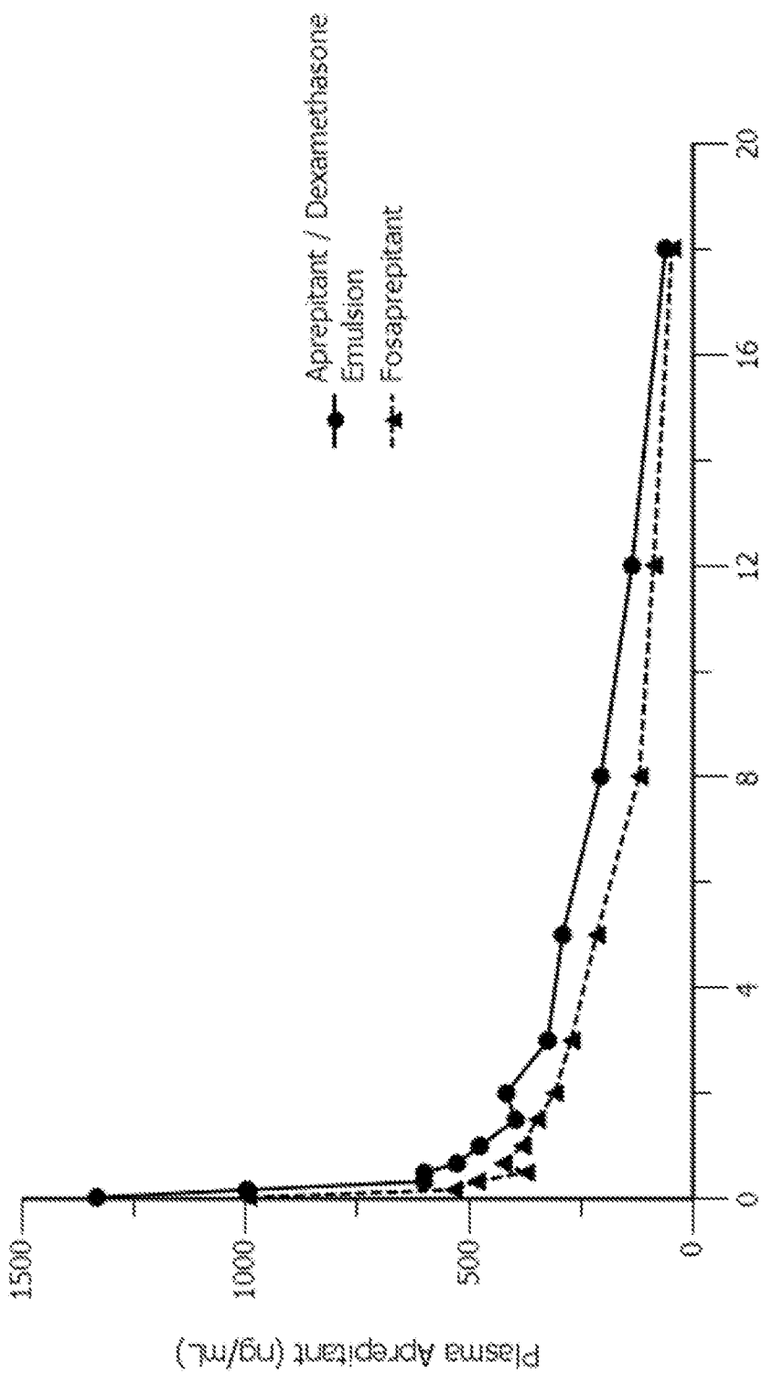

Aprepitant / Dexamethasone Emulsion
Fosaprepitant
Plasma Aprepitant (ng/mL)
1500
1000
500
0
0
4
8
12
16
20
Hours

FIG. 3

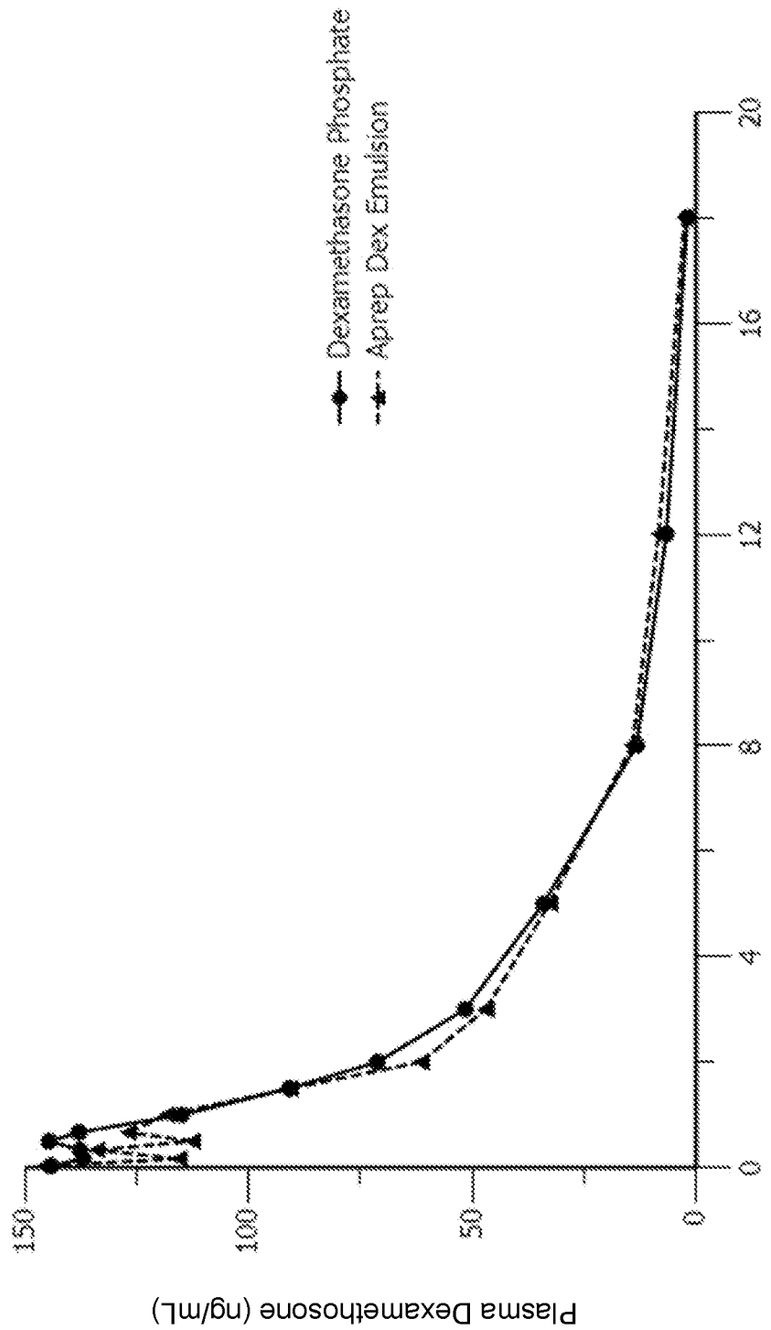

Dexamethasone Phosphate
Aprep Dex Emulsion
Plasma Dexamethosone (ng/mL)
150
100
50
0
0
4
8
12
16
20
Hours

FIG. 4

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
18/418,030	01/19/2024		1064	092459-0423/8032.US06	30	2

CONFIRMATION NO. 9379

108547
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

FILING RECEIPT

OC000000067791627

Date Mailed: 02/02/2024

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

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Inventor(s)

Thomas B. Ottoboni, Belmont, CA;
Han Han, Sunnyvale, CA;

Applicant(s)

Heron Therapeutics, Inc., San Diego, CA;

Power of Attorney: The patent practitioners associated with Customer Number 108547

Domestic Priority data as claimed by applicant

This application is a CON of 18/535,853 12/11/2023
which is a CON of 17/180,593 02/19/2021 PAT 11,878,074
which is a CON of 16/820,311 03/16/2020 PAT 11,173,118
which is a CON of 15/965,638 04/27/2018 PAT 10,624,850
which is a CON of 15/012,532 02/01/2016 PAT 9,974,742

Foreign Applications for which priority is claimed (You may be eligible to benefit from the Patent Prosecution Highway program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

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Permission to Access Search Results: Yes

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The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/418,030**

Projected Publication Date: 05/09/2024

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Preliminary Class

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06	9379

108547 7590 02/26/2024

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

EXAMINER
CENTRAL, DOCKET

ART UNIT	PAPER NUMBER
OPAP	

NOTIFICATION DATE	DELIVERY MODE
02/26/2024	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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PTOL-90A (Rev. 04/07)

Decision Granting Request for Prioritized Examination (Track I)	**Application No.** 18/418,030	**Applicant(s)** Ottoboni et al.	
	Examiner ANDREA SMITH	**Art Unit** OPET	**AIA (FITF) Status** Yes

1. THE REQUEST FILED 19 January 2024 IS **GRANTED** .

   The above-identified application has met the requirements for prioritized examination
   - A. ☑ for an original nonprovisional application (Track I).
   - B. ☐ for an application undergoing continued examination (RCE).

2. **The above-identified application will undergo prioritized examination**. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:
   - A. filing a **petition for extension of time** to extend the time period for filing a reply;
   - B. filing an **amendment to amend the application to contain more than four independent claims, more than thirty total claims** , or a multiple dependent claim;
   - C. filing a **request for continued examination** ;
   - D. filing a notice of appeal;
   - E. filing a request for suspension of action;
   - F. mailing of a notice of allowance;
   - G. mailing of a final Office action;
   - H. completion of examination as defined in 37 CFR 41.102; or
   - I. abandonment of the application.

Telephone inquiries with regard to this decision should be directed to ANDREA SMITH at (571)272-3226. In his/her absence, calls may be directed to Petition Help Desk at (571) 272-3282.

/ANDREA M SMITH/ Lead Paralegal Specialist, OPET	

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	**03/27/2024 01:38:29 PM Z ET**	**092459-0423/8032.US06**

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9379	FILED BY	Matthew Redlon
PATENT CENTER #	64856954	FILING DATE	01/19/2024
CUSTOMER #	108547	FIRST NAMED INVENTOR	Thomas B. Ottoboni
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Judy Mohr

Documents

TOTAL DOCUMENTS: 34

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
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Digest

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Aziz2012AnnPalliatMed130to136.pdf	9FF56112E35B502F244149BD84E7C30AD56754FC223DE05FB05675FA8EAB6E1A235FD2336B3F771998ACFFE35628F0B94B381295B4777741CA008485A0E9DA14
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Zhou2012ChineseJPharm1003t o1006EnglishTransOnly.pdf	E25FC748CA08471C2951852D30C3BCB317308E94D09227190 CF3A2B2EF70241AAF653960F9E848E64F44980E5A288347363 CE8C37616DA3514C937A3D37E3165
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wo2016044784.pdf	63429AD692153F5A9D967743F41B4BC102A89C2B8A79A74C8 F9E61AADB659161B6BA62AD561C0416D6C64A2414673F3BE3 90BE49197A242F3666A542E75AC80D
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wo2017135923.pdf

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9F7AAA3A4BE0050B03084FEEC71E6224

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Attorney Docket No.: 092459-0423/8032.US06

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	EXAMINER:
THOMAS B. OTTOBONI ET AL.	Manahil Mirghani Ali ABDALHAMEED
APPLICATION NO.: 18/418,030	ART UNIT: 1622
FILED: JANUARY 19, 2024	CONF. NO: 9379
FOR: **METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST**	

Information Disclosure Statement within Three Months of Application Filing or Before First Action – 37 C.F.R. § 1.97(b)

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

A. Timing of Submission

This information disclosure is being filed within three months of the filing date of this application or date of entry into the National Stage of an International Application or before the mailing date of a first Office Action on the merits or before the mailing date of a first Office Action on the merits after the filing of a Request for Continued Examination under 37 CFR §1.114, whichever occurs last (37 CFR 1.97(b)(4)). The references listed on the enclosed Form PTO-1449 (modified) may be material to the examination of this application; the Examiner is requested to make them of record in the application.

B. Cited Information

☒ Copies of cited references 1-29 which are issued patent(s) and/or published application(s) are not included (see 37 C.F.R. § 1.98(a) (2)(ii)).

☒ Copies of cited references 30-61 are enclosed.

C. Effect of Information Disclosure Statement (37 C.F.R. § 1.97(h))

This Information Disclosure Statement is not to be construed as a representation that: (i) a search has been made; (ii) additional information

material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the cited information is, or is considered to be, material to patentability. In addition, applicant does not admit that any enclosed item of information constitutes prior art to the subject invention and specifically reserves the right to demonstrate that any such reference is not prior art.

D. Fee Payment

No fees are believed due because this Information Disclosure Statement is being filed before the mailing date of the first Office Action. However, should the Commissioner determine that fees are due in order for this Information Disclosure Statement to be considered, the Commissioner is hereby authorized to charge such fees to Deposit Account No. 50-0417.

E. Patent Term Adjustment (37 C.F.R. § 1.704(d))

☐ The undersigned states that each item of information submitted herewith was cited in a communication from a foreign patent office in a counterpart application and that this communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty days prior to the filing of this statement. 37 C.F.R. § 1.704(d).

Respectfully submitted,
McDermott Will & Emery

Date: March 27, 2024

/Peter Brunovskis/
Peter Brunovskis
Registration No. 52,441

Correspondence Address:
Customer No. 108547

INFORMATION DISCLOSURE STATEMENT BY APPLICANT Form PTO-1449 (Modified) (Use several sheets if necessary)				***COMPLETE IF KNOWN***	
				Application Number	18/418,030
				Confirmation Number	9379
				Filing Date	January 19, 2024
				First Named Inventor	Thomas B. OTTOBONI
				Group Art Unit	1622
				Examiner Name	Manahil Mirghani Ali ABDALHAMEED
Sheet	1	of	3	Attorney Docket No.	092459-0423/8032.US06

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No.	U.S. Patent or Application NUMBER	Kind Code (if known)	Name of Patentee or Inventor of Cited Document	Date of Publication or Filing Date of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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	2.	9,561,229	B2	Ottoboni et al.	02-07-2017	
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	29.	2023/0072781	A1	Ottoboni et al.	03-09-2023	

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application(s).

INFORMATION DISCLOSURE STATEMENT BY APPLICANT Form PTO-1449 (Modified) (Use several sheets if necessary)				COMPLETE IF KNOWN	
				Application Number	18/418,030
				Confirmation Number	9379
				Filing Date	January 19, 2024
				First Named Inventor	Thomas B. OTTOBONI
				Group Art Unit	1622
				Examiner Name	Manahil Mirghani Ali ABDALHAMEED
Sheet	2	of	3	Attorney Docket No.	092459-0423/8032.US06

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Examiner Initials*	Cite No.	Foreign Patent or Application: Office	NUMBER	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication or Filing Date of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
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Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published.	
	43.	Applicant initiated interview, Examiners Summary, 31 August 2016, for U.S. Application Number: 15/083,071, now U.S. Patent Number: 9,561,229, 4 pages (2016)	
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EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application(s).

INFORMATION DISCLOSURE STATEMENT BY APPLICANT Form PTO-1449 (Modified) (Use several sheets if necessary)				***COMPLETE IF KNOWN***	
				Application Number	18/418,030
				Confirmation Number	9379
				Filing Date	January 19, 2024
				First Named Inventor	Thomas B. OTTOBONI
				Group Art Unit	1622
				Examiner Name	Manahil Mirghani Ali ABDALHAMEED
Sheet	3	of	3	Attorney Docket No.	092459-0423/8032.US06

OTHER NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published.	
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EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application(s).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
092459-0175		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2016/015992	1 February 2016 (01-02-2016)	
Applicant		
HERON THERAPEUTICS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [ ] the text is approved as submitted by the applicant
   [X] the text has been established by this Authority to read as follows:

   EMULSION COMPRISING AN NK-1 RECEPTOR ANTAGONIST

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [X] none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (January 2015)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
092459-0171		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2015/051050	18 September 2015 (18-09-2015)	19 September 2014 (19-09-2014)
Applicant		
HERON THERAPEUTICS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [X] none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2015/051050

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/00 A61K47/10 A61K47/44 A61K47/24 A61K47/12 A61K47/26
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2014/005606 A1 (PHARMATHEN SA [GR]; KARAVAS EVANGELOS [GR]; KOUTRIS EFTHIMOS [GR]; BIK) 9 January 2014 (2014-01-09) the whole document claim 1; table 9 -----	1-17
X	WO 2013/177501 A2 (INNOPHARMA INC [US]) 28 November 2013 (2013-11-28) the whole document paragraph [0032]; claims 1,2 -----	1-17
X	WO 2011/158053 A1 (NANOFORM CARDIOVASCULAR THERAPEUTICS LTD [GB]; FILIPCSEI GENOVEVA [HU]) 22 December 2011 (2011-12-22) the whole document example 5 ----- -/--	1-17

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 December 2015	18/12/2015

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Giese, Hans-Hermann

1

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 102 379 845 A (NANJING YOKO BIOLOG MEDICAL CO LTD) 21 March 2012 (2012-03-21) the whole document claim 1; example 1	1-17
A	WO 2005/016308 A1 (CHEN ANDREW XIAN [US]) 24 February 2005 (2005-02-24) claims; examples 6,8	1
A	WO 2009/124756 A1 (EUROPEAN MOLECULAR BIOLOGY LAB EMBL [DE]; UNIV MODENA E REGGIO EMILIA) 15 October 2009 (2009-10-15) the whole document	1

1

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		JP 2015521190 A	27-07-2015
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WO 2009124756 A1	15-10-2009	NONE	

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/015992

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/00 A61K47/24 A61K9/107 A61K31/454 A61K31/496 A61K31/5377
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2016/024092 A1 (WAN JIANSHENG [US] ET AL) 28 January 2016 (2016-01-28)	18-25
A	figure 3 paragraph [0004] examples 1-7	1-17, 26-28
A	CN 102 379 845 A (NANJING YOKO BIOLOG MEDICAL CO LTD) 21 March 2012 (2012-03-21) the whole document	1-28
A	US 2013/317016 A1 (HINGORANI TUSHAR [US] ET AL) 28 November 2013 (2013-11-28) paragraph [0054] - paragraph [0056]	1-28
A	WO 2014/209962 A1 (TIGERCAT PHARMA INC [US]) 31 December 2014 (2014-12-31) example 4 table 7	1-28

-/--

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 May 2016	03/06/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Sindel, Ulrike

1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/015992

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2014/005606 A1 (PHARMATHEN SA [GR]; KARAVAS EVANGELOS [GR]; KOUTRIS EFTHIMOS [GR]; BIK) 9 January 2014 (2014-01-09) claims 1-3	1-28

E	WO 2016/044784 A1 (HERON THERAPEUTICS INC [US]) 24 March 2016 (2016-03-24) claims 1-17	1-9, 11-16, 18-23, 26-28

1

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2016/015992

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/US2016/015992

TITLE: EMULSION COMPRISING AN NK-1 RECEPTOR ANTAGONIST

APPLICANT: HERON THERAPEUTICS, INC.

IPC CLASSIFICATION: A61K9/00, A61K47/24, A61K9/107, A61K31/454, A61K31/496, A61K31/5377

EXAMINER: Sindel, Ulrike

CONSULTED DATABASES:

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61K9/0019, A61K47/24, A61K9/1075, A61K31/454, A61K31/496, A61K31/5377

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:

EPO FORM F04442

Notice of References Cited	Application/Control No. 18/418,030	Applicant(s)/Patent Under Reexamination Ottoboni et al.	
	Examiner MANAHIL M ABDALHAMEED	Art Unit 1622	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date YYYY-MM-DD	Name	CPC Classification	US Classification
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*	B	US-9808465-B2	2017-11-07	Ottoboni; Thomas B.	A61K47/12	1/1
*	C	US-9974742-B2	2018-05-22	Ottoboni; Thomas B.	A61K9/1075	1/1
*	D	US-9974793-B2	2018-05-22	Ottoboni; Thomas B.	A61K47/24	1/1
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*	F	US-10500208-B2	2019-12-10	Ottoboni; Thomas B.	A61P43/00	1/1
*	G	US-10624850-B2	2020-04-21	Ottoboni; Thomas B.	A61K31/435	1/1
*	H	US-10953018-B2	2021-03-23	Ottoboni; Thomas B.	A61K47/44	1/1
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*	J	US-11744800-B2	2023-09-05	Ottoboni; Thomas B.	A61K31/573	707/750
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*		Document Number Country Code-Number-Kind Code	Date YYYY-MM-DD	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in YYYY-MM-DD format are publication dates. Classifications may be US or foreign.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT Form PTO-1449 (Modified) (Use several sheets if necessary)				COMPLETE IF KNOWN	
				Application Number	18/418,030
				Confirmation Number	9379
				Filing Date	January 19, 2024
				First Named Inventor	Thomas B. OTTOBONI
				Group Art Unit	1622
				Examiner Name	Manahil Mirghani Ali ABDALHAMEED
Sheet	1	of	3	Attorney Docket No.	092459-0423/8032.US06

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.	U.S. Patent or Application NUMBER	Kind Code (if known)	Name of Patentee or Inventor of Cited Document	Date of Publication or Filing Date of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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EXAMINER	DATE CONSIDERED
/MANAHIL MIRGHANI ALI ABDALHAMEED/	03/28/2024

*EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application(s).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.A./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT Form PTO-1449 (Modified) (Use several sheets if necessary)				COMPLETE IF KNOWN	
				Application Number	18/418,030
				Confirmation Number	9379
				Filing Date	January 19, 2024
				First Named Inventor	Thomas B. OTTOBONI
				Group Art Unit	1622
				Examiner Name	Manahil Mirghani Ali ABDALHAMEED
Sheet	2	of	3	Attorney Docket No.	092459-0423/8032.US06

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.	Foreign Patent or Application Office	NUMBER	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication or Filing Date of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
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Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published.	
	43.	Applicant initiated interview, Examiners Summary, 31 August 2016, for U.S. Application Number: 15/083,071, now U.S. Patent Number: 9,561,229, 4 pages (2016)	
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EXAMINER	DATE CONSIDERED
/MANAHIL MIRGHANI ALI ABDALHAMEED/	03/28/2024

*EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application(s).

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT Form PTO-1449 (Modified) (Use several sheets if necessary)				COMPLETE IF KNOWN	
				Application Number	18/418,030
				Confirmation Number	9379
				Filing Date	January 19, 2024
				First Named Inventor	Thomas B. OTTOBONI
				Group Art Unit	1622
				Examiner Name	Manahil Mirghani Ali ABDALHAMEED
Sheet	3	of	3	Attorney Docket No.	092459-0423/8032.US06

OTHER NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published.	
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EXAMINER	DATE CONSIDERED
/MANAHIL MIRGHANI ALI ABDALHAMEED/	03/28/2024

*EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application(s).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.A./

UNITED STATES PATENT AND TRADEMARK OFFICE

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United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06	9379

108547 7590 04/08/2024

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

EXAMINER
ABDALHAMEED, MANAHIL MIRGHANI ALI

ART UNIT	PAPER NUMBER
1622	

NOTIFICATION DATE	DELIVERY MODE
04/08/2024	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocketmwe@mwe.com

Office Action Summary	**Application No.** 18/418,030	**Applicant(s)** Ottoboni et al.	
	Examiner MANAHIL M ABDALHAMEED	**Art Unit** 1622	**AIA (FITF) Status** Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 19 January 2024.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 1-30 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-30 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Priority

This application filed on 01/09/2024 is a continuation of U.S. Application No. 18/535,853, filed 12/11/2023, which is a continuation of U.S. Application No. 17/180,593, filed 02/19/2021 (now U.S. Patent No. 11878074), which is a continuation of U.S. Application No. 16/820,311, filed 03/16/2020 (now U.S. Patent No. 11,173,118), which is a continuation of U.S. Application No. 15/965,638, filed 04/27/2018 (now U.S. Patent No. 10,624,850), which is a continuation of U.S. Application No. 15/012,532, filed 02/01/2016 (now U.S. Patent No. 9,974,742).

Information Disclosure Statement

The information disclosure statement (IDS) filed on 03/27/2024 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits, except where noted.

DETAILED ACTION

Claims 1-30 are pending.

Rejections 35 U.S.C. 112(b)

The following is a quotation of 35 U.S.C. 112(b):

> (b) CONCLUSION. — The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

Claims 13, 15-16, 18-19, 21, 23-29 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

The claims are rejected for insufficient antecedent basis. For example, claim 13 recites "the emulsion of **claim 11**, wherein the **soybean oil** is present at a concentration of about 9 wt/wt% to 10 wt/wt%". However, claim 11 is directed to **egg lecithin** not soybean oil. Similarly claim 15 recites "the emulsion of claim 13 wherein the ethanol is present in the emulsion at less than 10 wt/wt%, whereas claim 13 is directed to the amount of soybean not ethanol. The lack of antecedent basis is repeated throughout claims 15-16, 18-19, 21, 23-29. Applicant may overcome this rejection by changing the dependency of the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b). The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Double Patenting Rejection over US9561229B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 9561229B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-surfactant (ethanol); and water, wherein the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1

(wt/wt %); and wherein the injectable emulsion further comprises an osmotic agent (sucrose); and pH modifier (sodium oleate).

US9561229B2 recited in claims 1-21 an injectable pharmaceutical emulsion comprising 0.4 wt/wt % to 1.0 wt/wt % aprepitant; 13 wt/wt % to 15 wt/wt % egg yolk lecithin; 9 wt/wt % to 10 wt/wt % soybean oil; and a pH modifier, wherein the pH modifier is sodium oleate; wherein the pH of the emulsion ranges from 7.5 to 9.0, wherein the emulsion comprises 0.7 wt/wt % aprepitant, wherein the emulsion comprises 14 wt/wt % egg yolk lecithin, wherein the emulsion further comprises 3 wt/wt % to 8 wt/wt % sucrose, wherein the emulsion further comprises 2 wt/wt % to 6 wt/wt % ethanol. The US9561229B2 ratio of egg yolk lecithin to aprepitant (calculates 1:15 to 1:32.5) overlaps with the range in present claim 1. Thus, the range recited in present claim 1 is obvious over the amount of emulsifier and aprepitant claimed in the US9561229B2. Therefore, the conflicting claims 1-21 of US9561229B2 reads on the limitations of instant claims 1-30.

Double Patenting Rejection over US9808465B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6, 8-9, 12-15 of U.S. Patent No. US9808465B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from

about 20:1 to 25:1 (wt/wt %).

US9808465B2 recited in claims 1-6, 8-9, 12-15, a composition comprising an injectable physically stable emulsion wherein the emulsion comprises aprepitant; 11 wt/wt % to 15 wt/wt % of an emulsifier; an oil; a co-emulsifier which is an alcohol; a tonicity modifier; a pH modifier; and water; wherein the ratio of emulsifier : aprepitant ranges from about 18:1 to 22:1, wherein the ratio of the oil to the aprepitant within the oil phase of the emulsion ranges from about 10:1 to 15:1 (wt/wt %), wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the ethanol is less than 10 wt%, and wherein the emulsifier is an egg lecithin, wherein the pH modifier is sodium oleate, wherein the oil is soybean oil, wherein the alcohol in the emulsion is ethanol, and wherein the tonicity modifier in the emulsion is sucrose. The amount of aprepitant appears to be obvious considering the ratio between aprepitant to egg lecithin and 11-15% of egg lecithin (calculates to 0.6-0.8wt%). Therefore, the conflicting claims 1-6, 8-9, 12-15 of US9808465B2 reads on the limitations of instant claims 1-30.

Double Patenting Rejection over US9974742B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6, 9, and 12-14 of U.S. Patent No. 9974742B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from

about 20:1 to 25:1 (wt/wt %).

US9974742B2 recited in claims 1-6, 9, and 12-14, an injectable pharmaceutical emulsion comprising a neurokinase-1 (NK-1) receptor antagonist; 11 wt/wt % to 15 wt/wt % of an emulsifier; an oil; a co-surfactant which comprises an alcohol; a tonicity agent; a pH modifier; and water, wherein the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt %), wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 5:1 to 15:1 (wt/wt %), wherein the emulsifier is an egg lecithin, wherein the pH modifier is oleic acid or a salt thereof, wherein the oil is soybean oil, wherein the alcohol is ethanol, wherein the ethanol is present in the emulsion at less than 10 wt/wt %. The amount of aprepitant appears to be obvious considering the ratio between aprepitant to egg lecithin and 11-15% of egg lecithin (calculates to 0.6-0.8wt%). Therefore, the conflicting claims 1-6, 9, and 12-14 of US9974742B2 reads on the limitations of instant claims 1-30.

Double Patenting Rejection over US9974793B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 9974793B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from

about 20:1 to 25:1 (wt/wt %).

US9974793B2 recited in claims 1-22, a physically stable pharmaceutical emulsion, comprising 0.4-1.0 wt/wt% aprepitant; an emulsifier (egg yolk lecithin); an oil (soybean oil); and water; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 18:1 to 22:1, wherein the ratio of the oil to aprepitant (wt %:wt %) ranges from about 11:1 to 15:1, wherein the composition comprises 0.7 wt/wt % aprepitant; wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the composition comprises 11 wt/wt % to 15 wt/wt % emulsifier; wherein the composition comprises 9 wt/wt % to 10 wt/wt % oil; wherein the composition further comprises sodium oleate as a pH modifier; wherein composition further comprises 3 wt/wt % to 8 wt/wt % sucrose; wherein the composition further comprises 6 wt/wt % ethanol. Therefore, the conflicting claims 1-22 of US9974793B2 meets the limitations of instant claims 1-30.

Double Patenting Rejection over US9974794B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 9974794B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

US9974794B2 recited in claims 1-11, a physically stable emulsion pharmaceutical composition, comprising 0.4-1.0 wt/wt% aprepitant; 13-15 wt/wt% egg yolk lecithin); 9-10 wt/wt% soybean oil; sodium oleate as a pH modifier; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 18:1 to 22:1, wherein the composition comprises 0.7 wt/wt % aprepitant; wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the composition comprises 9 wt/wt % to 10 wt/wt % oil; wherein the composition further comprises wherein composition further comprises 3 wt/wt % to 8 wt/wt % sucrose; wherein the composition further comprises 6 wt/wt % ethanol. Therefore, the conflicting claims 1-11 of US9974794B2 meets the limitations of instant claims 1-30.

Double Patenting Rejection over US10500208B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-5, 7-9, 11-13 of U.S. Patent No. 10500208B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

US10500208B2 recited in claims 1-5, 7-9, and 11-13, an injectable emulsion comprising aprepitant; 11 wt/wt % to 15 wt/wt % of an emulsifier; an oil; a co emulsifier which is an alcohol; a tonicity

modifier; a pH modifier; and water; wherein the ratio of the emulsifier to the aprepitant in the emulsion ranges from about 15:1 to 30:1 (wt/wt %), wherein the ratio of the oil to the aprepitant in the emulsion ranges from about 11:1 to 15:1 (wt/wt %), wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the emulsifier is an egg lecithin, wherein the pH modifier is sodium oleate, wherein the oil is soybean oil, wherein the alcohol is less than 10 wt/wt % ethanol. The amount of aprepitant appears to be obvious considering the ratio between aprepitant to egg lecithin and 11-15% of egg lecithin (calculates to 0.7-1.0wt%). Therefore, the conflicting claims 1-5, 7-9, and 11-13 of US10500208B2 reads on the limitations of instant claims 1-30.

Double Patenting Rejection over US10624850B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6, 9, and 12-16 of U.S. Patent No. 10624850B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

US10624850B2 recited in claims 1-6, 9, and 12-16 an injectable pharmaceutical emulsion, wherein the emulsion comprises a neurokinase-1 (NK-1) receptor antagonist; 11 wt/wt % to 15 wt/wt % of an emulsifier (egg lecithin); an oil (soybean oil); a co-surfactant which comprises less than 10 wt/wt %

ethanol; a tonicity agent; a pH modifier (oleic acid or a salt thereof); and water, wherein the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt %), wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 5:1 to 15:1 (wt/wt %). The instant specification defined aprepitant as NK-1 receptor antagonist. The amount of aprepitant appears to be obvious considering the ratio between aprepitant to egg lecithin and 11-15% of egg lecithin (calculates to 0.6-0.8wt%). Therefore, the conflicting claims 1-6, 9, and 12-16 of US10624850B2 reads on the limitations of instant claims 1-30.

Double Patenting Rejection over US10953018B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 10953018B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

US10953018B2 recited in claims 1-18, a physically stable pharmaceutical emulsion, comprising 0.4-1.0 wt/wt% aprepitant; an emulsifier (11-15 wt/wt% egg yolk lecithin); an oil (9-10 wt/wt% soybean oil); and water; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 18:1 to 22:1; wherein the composition comprises 0.7 wt/wt % aprepitant; wherein the composition further

comprises sodium oleate as a pH modifier; wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the composition further comprises 3 wt/wt % to 8 wt/wt % sucrose. Therefore, the conflicting claims 1-18 of US10953018B2 meets the limitations of instant claims 1-30.

Double Patenting Rejection over US11173118B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-8, 11-12, and 14-17 of U.S. Patent No. 11173118B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

US11173118B2 recited in claims 1-8, 11-12, and 14-17, an injectable pharmaceutical emulsion comprising, a neurokinase-1 (NK-1) receptor antagonist; an emulsifier (egg lecithin); an oil (soybean oil); a co-surfactant (ethanol); and an aqueous phase; wherein the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt %); wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 5:1 to 15:1 (wt/wt %); wherein the aqueous phase comprises water and a tonicity agent and a pH modifying agent (oleate or a salt thereof). US11173118B2 1-8, 11-12, and 14-17 recites all the instant claimed elements including the pH modifier sodium oleate, and the US11173118B2 specification recited that the pH of the composition is 7.5-9. [Col. 6, ln. 15]. Therefore, the conflicting

claims 1-8, 11-12, and 14-17 of US11173118B2 meets the limitations of instant claims 1-30.

Double Patenting Rejection over US11744800B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 11744800B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

US11744800B2 recited in claims 1-21 an injectable pharmaceutical emulsion comprising aprepitant, about 14-15 wt/wt % egg lecithin (an emulsifier, phospholipid); about 9-10 wt/wt % soybean oil (an oil); about 3 wt/wt% ethanol (a co-surfactant); about 3-8 wt/wt % sucrose (an osmotic agent); sodium oleate (a pH modifier); and water, wherein the ratio of the egg lecithin to aprepitant ranges from about 18:1 to 22:1 (wt/wt %). The amount of aprepitant appears to be met considering the ratio between aprepitant to egg lecithin and 14-15% of egg lecithin (calculates to 0.78-0.8wt%). US11744800B2 1-21 recites all the instant claimed elements including the pH modifier sodium oleate, and the US11744800B2 specification recited that the pH of the composition is 7.5-9. [Col. 6, ln. 21]. Therefore, the conflicting claims 1-21 of US11744800B2 reads on the limitations of instant claims 1-30.

Double Patenting Rejection over US11878074B2

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 11878074B2. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

11878074B2 recites in claims 1-5, 7-9, and 11-14, an injectable pharmaceutical emulsion comprising: aprepitant; an emulsifier; an oil; a co-surfactant; and an aqueous phase, wherein the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt%); wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 5:1 to 15:1 (wt/wt%); wherein the emulsion comprises between about 11 wt/wt% to 15 wt/wt% of an emulsifier; wherein the emulsifier is a phospholipid; wherein the pH modifier is oleic acid or a salt thereof; wherein the oil is soybean oil; the alcohol is ethanol. The amount of aprepitant appears to be obvious considering the ratio between aprepitant to egg lecithin and 11-15% of egg lecithin (calculates to 0.6-0.8wt%). 11878074B2 1-5, 7-9, and 11-14 recites all the instant claimed elements including the pH modifier sodium oleate, and the 11878074B2 specification recited that the pH of the composition is 7.5-9. [Col. 6, ln. 15]. Therefore, the conflicting claims 1-5, 7-9, and 11-14 of 11878074B2 reads on the limitations of instant claims 1-30.

Double Patenting Rejection over U.S. co-pending Application No. 17/194,114

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-19, 21-28 of co-pending Application No. 17/194,114 (US20210186981A1). Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

Co-pending Application No. 17/194,114 recites in claims 1-19 and 21-28, a physically stable pharmaceutical emulsion comprising aprepitant; an emulsifier; an oil; and water; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 18:1 to 22:1, wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the composition comprises 11-15 wt/wt % emulsifier; wherein the emulsifier is egg yolk lecithin; wherein the composition comprises 9 -10 wt/wt % oil; wherein the oil is soybean oil; wherein the composition further comprises sodium oleate as a pH modifier; wherein the composition further comprises 3-8 wt/wt % sucrose; wherein the composition further comprises 6 wt/wt % ethanol. The amount of aprepitant appears to be obvious considering the ratio between aprepitant to egg lecithin and 11-15% of egg lecithin (calculates to 0.6-0.8wt%). Therefore, the conflicting claims 1-19 and 21-28 of co-pending Application No. 17/194,114 reads on the limitations of instant claims 1-30.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Double Patenting Rejection over U.S. co-pending Application No. 16/261,459

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 31, 39-46, 51, 54-62 and 65-71 of co-pending Application No. 16/261,459 (US20190231688A1). Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

Co-pending Application No. 16/261,459 recites in claims 31, 39-46, 51, 54-62 and 65-71, an emulsion comprising 100-200 mg of aprepitant; 10-20 wt/wt% of an emulsifier; an oil; less than 10 wt/wt% ethanol; a tonicity agent; a pH modifier and water; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 20:1 to 25:1, wherein the ratio of the oil to the aprepitant ranges from about 10:1 to 15:1 wt/wt%; wherein the pH of the emulsion ranges from about 7.5-9.0, wherein the emulsifier is 17 wt/wt % of phospholipid egg lecithin; wherein the oil is soybean oil; wherein the pH modifier sodium is oleate. The claimed amount of aprepitant, 0.7-0.8wt% appears to be obvious considering the amount of aprepitant and emulsifier recited in claims 45 (calculates to 0.5:1 to 0.4:0.8). Therefore, the conflicting claims 31, 39-46, 51, 54-62 and 65-71 of co-pending Application No. 16/261,459 reads on the limitations of instant claims 1-30.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Double Patenting Rejection over U.S. co-pending Application No. 18/408,463

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-28 of co-pending Application No. 18/408,463. Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

Co-pending Application No. 18/408,463 recites in claims 1-28, an injectable emulsion comprising aprepitant; 13-20 wt/wt% of an emulsifier (17 wt/wt% egg lecithin); an 9-10 wt/wt% oil (soybean oil); co-emulsifier (less than 10 wt/wt% ethanol); a tonicity modifier (3-8 wt/wt% sucrose); a pH modifier (sodium oleate); and water; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 20:1 to 25:1. wherein the pH of the emulsion ranges from about 7.5-9.0. The claimed amount of aprepitant appears to be obvious considering the ratio between aprepitant to egg lecithin and 13-20% of egg lecithin (calculates to 0.65-0.8wt%). Therefore, the conflicting claims 1-19 and 21-28 of co-pending Application No. 17/194,114 reads on the limitations of instant claims 1-30.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Double Patenting Rejection over U.S. co-pending Application No. 18/408,486

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claim claims 1-30 of co-pending Application No. 18/408,486 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

Co-pending Application No. 18/408,486 recites in claims 1-30, an injectable emulsion comprising 0.7-0.8 wt/wt% aprepitant; 13-20 wt/wt% of an emulsifier (17 wt/wt% egg lecithin); an 9-10 wt/wt% oil (soybean oil); co-emulsifier (less than 10 wt/wt% ethanol); a tonicity modifier (3-8 wt/wt% sucrose); a pH modifier (sodium oleate); and water; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 20:1 to 25:1. Co-pending Application No. 18/408,486 claims 1-30 recites all the instant claimed elements including the pH modifier sodium oleate, and the co-pending Application No. 18/408,486 specification recited that the pH of the composition is 7.5-9. [page 7, 0047] Therefore, the conflicting claims 1-30 of co-pending Application No. 18/408,486 reads on the limitations of instant claims 1-30.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Double Patenting Rejection over U.S. co-pending Application No. 18/535,853

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-20 of co-pending Application No. 18/535,853 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because:

The instant claims 1-30 recite an injectable pharmaceutical emulsion comprising 0.7-0.8wt% aprepitant, 13-20 wt/wt% of an emulsifier (phospholipid, egg lecithin); an oil (olive oil, soybean oil, etc.); a co-emulsifier (ethanol); a tonicity modifier (sucrose); a pH modifier (sodium oleate); and water, wherein the pH of the emulsion ranges from about 7.5-9.0, the ratio of the emulsifier to aprepitant ranges from about 20:1 to 25:1 (wt/wt %).

Co-pending Application No. 18/535,853 recites in claims 1-20, an injectable emulsion comprising 0.7-0.8 wt/wt% aprepitant; 11-15 wt/wt% of an emulsifier (egg lecithin); an 9-10 wt/wt% oil (soybean oil); co-emulsifier (6 wt/wt% ethanol); a tonicity modifier (3-8 wt/wt% sucrose); a pH modifier (sodium oleate); and water; wherein the ratio of the emulsifier to aprepitant (wt %:wt %) ranges from about 18:1 to 22:1, wherein the pH of the emulsion ranges from about 7.5-9.0. Therefore, the conflicting claims 1-20 of co-pending Application No. 18/535,853 meets the limitations of instant claims 1-30.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MANAHIL MIRGHANI ALI ABDALHAMEED whose telephone number is (571)272-1242. The examiner can normally be reached M-F 7:30 am - 5:00 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Havlin can be reached on 571-272-9066. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M.M.A./
Examiner, Art Unit 1622

/BAHAR CRAIGO/
Primary Examiner, Art Unit 1699

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06

CONFIRMATION NO. 9379

108547
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

PUBLICATION NOTICE

OC000000072393244

Date Mailed: 05/09/2024

Title:METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Publication No.US-2024-0148650-A1
Publication Date:05/09/2024

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be viewed using the USPTO's publicly available Searchable Databases via the Patent Public Search tool at www.uspto.gov. The direct link to access the Patent Public Search tool is currently https://ppubs.uspto.gov/pubwebapp/static/pages/ppubsbasic.html.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through Patent Center, the USPTO's electronic patent application filing and management system. The direct link to access this status information is currently https://patentcenter.uspto.gov/. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of Patent Center.

Further assistance in electronically accessing the publication, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Doc code : DISQ.E.FILE
Description : Electronic Terminal Disclaimer - Approved

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APPROVAL LETTER

APPLICATION #	FILING DATE	APPLICANT/PATENT UNDER REEXAMINATION
18/418,030	01/19/2024	Thomas Ottoboni

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Electronic terminal disclaimer filed on 07/02/2024

☑ Approved

This patent is subject to a Terminal Disclaimer

Approved / Disapproved by: Electronic Terminal Disclaimer automatically approved

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TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A PRIOR PATENT

APPLICATION #	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET #
18418030	01/19/2024	Thomas Ottoboni	092459-0423/8032.US06

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

☑ Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action

☑ This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

Owner	Percent interest
Heron Therapeutics, Inc.	100%
Total	100%

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending reference Application Number(s)

Application #	Filing Date
18408463	01/09/2024
18408486	01/09/2024
18535853	12/11/2023

as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on the reference application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.
In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term of any patent granted on said reference application, "as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application," in the event that any such patent granted on the pending reference application: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s)

Patent #
9561229
9808465
9974742
9974793
9974794
10500208
10624850
10953018
11173118
11744800
11878074

as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that

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- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
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- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

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Applicant claims the following entity status:
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I hereby declare that all statements made herein of my own knowledge are true and that all statemnts made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I certify, in accordance with 37 CFR 1.4(d)(4) that I am: An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application

Signature	Name	Registration #
/Peter Brunovskis/	Peter Brunovskis	52441

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* Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner). Form PTO/SB/96 may be used for making this certification. See MPEP 324.

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	07/02/2024 03:19:50 PM Z ET	092459-0423/8032.US06

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9379	FILED BY	Tawana Lefeged
PATENT CENTER #	66208338	AUTHORIZED BY	Peter Brunovskis
CUSTOMER #	108547	FILING DATE	01/19/2024
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Thomas B. Ottoboni

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 500417	E202472F20379415	Peter Brunovskis

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2814	STATUTORY DISCLAIMER, INCLUDING TERMINAL DISCLAIMER	170.00	1	170.00
			TOTAL AMOUNT:	$170.00

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National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	**07/02/2024 03:19:50 PM Z ET**	**092459-0423/8032.US06**

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9379	FILED BY	Tawana Lefeged
PATENT CENTER #	66208338	FILING DATE	01/19/2024
CUSTOMER #	108547	FIRST NAMED INVENTOR	Thomas B. Ottoboni
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Peter Brunovskis

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
petition-request.pdf	3	Terminal Disclaimer-Filed (Electronic)	55 KB
grantLetter.pdf	1	Terminal Disclaimer-Electronic-Approved	19 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
petition-request.pdf	BF071E62874641B635FC5AAF4E91A6D99E05E64A33AD2C02B DD5B60FA198491A17E7512B135FE755913277F21596DCB22A8

	3FDDD82BF0829439A08ACFA64E280
grantLetter.pdf	CEA090192A9FCA5B2AA2F843ADB9E09024DBB9650B72CC3396CEDF9FBDBC84EB2EEA465A2602953572229E41473214A55C1BE9370CC8182EC7E00340636A0227E

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New International Application Filed with the USPTO as a Receiving Office

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	**07/02/2024 03:29:30 PM Z ET**	**092459-0423/8032.US06**

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9379	FILED BY	Tawana Lefeged
PATENT CENTER #	66208664	FILING DATE	01/19/2024
CUSTOMER #	108547	FIRST NAMED INVENTOR	Thomas B. Ottoboni
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Peter Brunovskis

Documents

TOTAL DOCUMENTS: 3

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
092459-0423_Amendment.pdf		8	-	45 KB
092459-0423_Amendment-A....pdf	(1-1)	1	Amendment/Request for Reconsideration-After Non-Final Rejection	24 KB
092459-0423_Amendment-CLM.pdf	(2-4)	3	Claims	23 KB
092459-0423_Amendment-REM.pdf	(5-8)	4	Applicant Arguments/Remarks Made in an Amendment	34 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
092459-0423_Amendment.pdf	F0873ADAF0805C20D8C79F12E6FA0903D78122A9F7FE1F46F1D98AA7AF03DB692960104A92502E4D4C8579EB42F186DCB35C7B3DF4F26690EB0311FC32E939B6
092459-0423_Amendment-A....pdf	F65E9D5D51BC5CDD3EE5DA5A88D668E54F4489D173174A6044A9FBF7B2BD1DC0CA2F500FF92393D3F47A9E2E95812027BFD3F065DFD539A7F18FA0DDDBB6E615
092459-0423_Amendment-CLM.pdf	4194B9274214D14A0FAD18D83C34557E1530816B4AD081855E78DB16C45FDEE79B6573633FCC924C628D6344E4EBE93C48E12B4BA2D635B3DA4C3FC196ED19F4
092459-0423_Amendment-REM.pdf	34E462D3E3A2AE03C0AB1C4D6A7CFFDBBE6E4C7B5679448660047F3DE05EBDF78A1FEA038EBCA046879DA36F28DBA1BB2261E418F9A1312504DBCBB17EAB7144

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

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Attorney Docket No. 092459-0423/8032.US06

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	THOMAS B. OTTOBONI, et al.
APPLICATION NO.:	18/418,030
FILED:	JANUARY 19, 2024
FOR:	**METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST**

EXAMINER:	ABDALHAMEED, MANAHIL MIRGHANI ALI
ART UNIT:	1622
CONF. NO:	9379

Amendment Under 37 C.F.R. § 1.111

Mail Stop: Amendment
Commissioner for Patents
U.S. Patent & Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The present communication responds to the Office Action dated April 8, 2024 in the above-identified application.

Please amend the application as follows:

Amendments to the Claims begin on page 2.

Remarks begin on page 5 of this paper.

The remainder of this page is intentionally left blank.]

Amendments to the Claims

The following Listing of Claims, in which deleted text appears ~~struck through~~ or [[double-bracketed]] and inserted text appears underlined, will replace all prior versions, and listings, of claims in the application.

1. (Original) An injectable emulsion, comprising:
0.7-0.8 wt% aprepitant;
13 wt/wt% to 20 wt/wt% of an emulsifier;
an oil;
a co-emulsifier which is an alcohol;
a tonicity modifier;
a pH modifier; and
water;
wherein the pH of the emulsion ranges from about 7.5 to 9.0.

2. (Original) The emulsion of claim 1, wherein the emulsifier is a phospholipid.

3. (Original) The emulsion of claim 2, wherein the phospholipid is present in the emulsion at about 17 wt/wt%.

4. (Original) The emulsion of claim 2, wherein the phospholipid is present in the emulsion at about 18 wt/wt%.

5. (Original) The emulsion of claim 1, wherein the emulsifier is an egg lecithin.

6. (Original) The emulsion of claim 5, wherein the egg lecithin is present in the emulsion at about 17 wt/wt%.

7. (Original) The emulsion of claim 5, wherein the egg lecithin is present in the emulsion at about 18 wt/wt%.

8. (Original) The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is between about 20:1 to 25:1.

9. (Original) The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 23:1.

10. (Original) The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 24:1.

11. (Original) The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 25:1.

12. (Original) The emulsion of claim 1, wherein the oil in the emulsion is soybean oil.

13. (Currently Amended) The emulsion of claim 12 [[11]], wherein the soybean oil is present at a concentration of about 9 wt/wt % to 10 wt/wt %.

14. (Original) The emulsion of claim 1, wherein the alcohol in the emulsion is ethanol.

15. (Currently Amended) The emulsion of claim 14 [[13]], wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

16. (Currently Amended) The emulsion of claim 14 [[13]], wherein the ethanol is present in the emulsion at a concentration of about 2 wt/wt % to 3 wt/wt %.

17. (Original) The emulsion of claim 1, wherein the tonicity modifier in the emulsion is sucrose.

18. (Original) The emulsion of claim 16, wherein the sucrose is present at a concentration of about 3 wt/wt % to 8 wt/wt %.

19. (Original) The emulsion of claim 16, wherein the sucrose is present at a concentration of about 5 wt/wt %.

20. (Original) The emulsion of claim 1, wherein the pH modifier in the emulsion is sodium oleate.

21. (Original) The emulsion of claim 19, wherein the sodium oleate is present at a concentration of about 0.4 wt/wt % to 0.5 wt/wt %.

22. (Original) The emulsion of claim 1, wherein the aprepitant is present in the emulsion at about 0.7 wt/wt%.

23. (Original) The emulsion of claim 21, wherein the phospholipid is an egg lecithin.

24. (Original) The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is between about 20:1 to 25:1.

25. (Original) The emulsion of claim 21, wherein the phospholipid is present at a concentration of about 17 wt/wt %.

26. (Original) The emulsion of claim 21, wherein the phospholipid is present at a concentration of about 18 wt/wt %.

27. (Original) The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 23:1.

28. (Original) The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 24:1.

29. (Original) The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 25:1.

30. (Original) An injectable pharmaceutical emulsion, comprising:
about 0.7-0.8 wt% aprepitant;
an egg phospholipid emulsifier;
an oil;
a co-surfactant;
water; and
a pH modifier,
wherein the ratio of the emulsifier to aprepitant is about 20:1 to 25:1 (wt/wt%).

REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated April 8, 2024 are respectfully requested.

I. Amendments

Claims 13, 15, and 16 are amended to provide antecedent basis for a recited element. No new matter has been added. Claims 1-30 are pending in the instant application.

II. Rejections Under 35 U.S.C. § 112

Claims 13, 15-16, 18-19, 21, and 23-29 are rejected under 35 U.S.C. § 112(b) as indefinite for lack of antecedent basis. This rejection is traversed in view of the following.

The dependency of claims 13, 15, and 16 are amended to provide antecedent basis for the recited claim element. Accordingly, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112.

III. Obviousness Type Double-Patenting Rejection

The proffered nonstatutory double patenting rejections are grouped below according to Applicant's response.

GROUP 1: REJECTIONS ADDRESSED BY FILING A TERMINAL DISCLAIMER

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 9,561,229.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6, 8-9, and 12-15 of U.S. Patent No. 9,808,465.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6, 9, and 12-14 of U.S. Patent No. 9,974,742.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 9,974,793.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 9,974,794.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-5, 7-9, and 11-13 of U.S. Patent No. 10,500,208.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6, 9, and 12-16 of U.S. Patent No. 10,624,850.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 10,953,018.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-8, 11-12, and 14-17 of U.S. Patent No. 11,173,118.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 11,744,800.

Claims 1-30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 11,878,074.

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-28 of co-pending Application No. 18/408,463.

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claim claims 1-30 of co-pending Application No. 18/408,486.

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-20 of co-pending Application No. 18/535,853.

Without conceding to the validity of these rejections, Applicant herewith submits an executed terminal disclaimer filed in accordance with C.F.R. §1.321(b) and (c) which disclaims the terminal portion of any Patent issuing on the instant application that extends beyond the expiration of U.S. Patent Nos.: 9,561,229; 9,808,465; 9,974,742; 9,974,793; 9,974,794; 10,500,208; 10,624,850; 10,953,018; 11,173,118; 11,744,800; and 11,878,074; and beyond the expiration of any patent that issues from, 18/408,463, 18/408,486, and 18/535,853.

GROUP 2: REJECTION OVER A NOW ABANDONED APPLICATION

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-19 and 21-28 of co-pending Application No. 17/194,114. This application is abandoned; a Notice of Abandonment was mailed on March 7, 2024. Withdrawal of the rejection is requested.

GROUP 3: REJECTION OVER A LATER-FILED APPLICATION

Claims 1-30 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 31, 39-46, 51, 54-62, and 65-71 of co-pending Application No. 16/261,459.

Reconsideration and withdrawal is requested. The instant application has a patent term filing date of February 1, 2016. Application No. 16/261,459 has a patent term filing date of January 29, 2019, and is therefore later filed than the instant application. In accord with M.P.E.P. § 804, and in view of the terminal disclaimer filed herewith to resolve the other rejections, the nonstatutory double patenting rejection over Application No. 16/261,459 is the only remaining rejection. Since the instant case has an earlier patent term filing date the rejection should be withdrawn. (*See,* M.P.E.P. § 804 (I)(B)(1)(b)(i) "If a provisional nonstatutory double patenting rejection is the only rejection remaining in an application having the earlier patent term filing date, the examiner should withdraw the rejection in the application having the earlier patent term filing date and permit that application to issue as a patent, thereby converting the provisional nonstatutory double patenting rejection in the other application into a nonstatutory double patenting rejection upon issuance of the patent.").

IV. Conclusion

No fees are believed due with this communication. However, the Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. **50-0417**.

In view of the foregoing, the claims pending in the application comply with the requirements of 35 U.S.C. § 112 and patentably define over the applied art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (202) 756-8934.

Respectfully submitted,
McDermott Will & Emery LLP

Date: **July 2, 2024**

/Peter Brunovskis/
Peter Brunovskis, Ph.D.
Registration No. 52,441

Correspondence Address:
Customer No. 108547

DM_US 205241961-3.092459.0423

Respectfully submitted,
MCDERMOTT WILL & EMERY LLP

Date: **July 2, 2024**

/Peter Brunovskis/
Peter Brunovskis, Ph.D.
Registration No. 52,441

Correspondence Address:
Customer No. 108547

DM_US 205241961-3.092459.0423

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Without conceding to the validity of these rejections, Applicant herewith submits an executed terminal disclaimer filed in accordance with C.F.R. §1.321(b) and (c) which disclaims the terminal portion of any Patent issuing on the instant application that extends beyond the expiration of U.S. Patent Nos.: 9,561,229; 9,808,465; 9,974,742; 9,974,793; 9,974,794; 10,500,208; 10,624,850; 10,953,018; 11,173,118; 11,744,800; and 11,878,074; and beyond the expiration of any patent that issues from, 18/408,463, 18/408,486, and 18/535,853.

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In view of the foregoing, the claims pending in the application comply with the requirements of 35 U.S.C. § 112 and patentably define over the applied art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (202) 756-8934.

Notice of Allowability	Application No. 18/418,030	Applicant(s) Ottoboni et al.	
	Examiner MANAHIL M ABDALHAMEED	Art Unit 1622	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 07/02/2024.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 1-30 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☑ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☐ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/M.M.A./ Examiner, Art Unit 1622	/ROBERT H HAVLIN/ Supervisory Patent Examiner, Art Unit 1622

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Priority

This application filed on 01/09/2024 is a continuation of U.S. Application No. 18/535,853, filed 12/11/2023, which is a continuation of U.S. Application No. 17/180,593, filed 02/19/2021 (now U.S. Patent No. 11878074), which is a continuation of U.S. Application No. 16/820,311, filed 03/16/2020 (now U.S. Patent No. 11,173,118), which is a continuation of U.S. Application No. 15/965,638, filed 04/27/2018 (now U.S. Patent No. 10,624,850), which is a continuation of U.S. Application No. 15/012,532, filed 02/01/2016 (now U.S. Patent No. 9,974,742).

DETAILED ACTION

The Amendments and Applicant's Arguments submitted on 07/02/2024 have been received and its contents have been carefully considered. Claims 13, 15 and 16 were amended. Claims 1-30 are pending.

EXAMINER COMMENT AND REASONS FOR ALLOWANCE

Withdrawal Claim Rejections – 35 U.S.C. 112(b)

Rejection of claims 13, 15-16, 18-19, 21, 23-29 rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA) for insufficient antecedent basis, is withdrawn in view of Applicant's amendment to claims 13, 15 and 16 submitted on 07/02/2024.

Withdrawal Claim Rejections – Double Patenting

Rejection of claims 1-30 rejected under the nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 9561229B2, claims 1-6, 8-9, 12-15 of U.S. Patent No. US9808465B2, claims 1-6, 9, and 12-14 of U.S. Patent No. 9974742B2, claims 1-22 of U.S. Patent No. 9974793B2, claims 1-11 of U.S. Patent No. 9974794B2, claims 1-5, 7-9, 11-13 of U.S. Patent No. 10500208B2, claims 1-6, 9, and 12-16 of U.S. Patent No. 10624850B2, claims 1-18 of U.S. Patent No. 10953018B2, claims 1-8, 11-12, and 14-17 of U.S. Patent No. 11173118B2, claims 1-21 of U.S. Patent No. 11744800B2, claims 1-21 of U.S. Patent No. 11878074B2, claims 1-28 of co-pending Application No. 18/408,463, claims 1-30 of co-pending Application No. 18/408,486, claims 1-20 of co-pending Application No. 18/535,853, is withdrawn in view of the Terminal Disclaimer submitted by the Applicant on 07/02/2024.

Rejection of claims 1-30 rejected under the nonstatutory double patenting as being unpatentable over claims 1-19, 21-28 of copending Application No. 17/194,114, is withdrawn because Application No. 17/194,114 is abandoned on 03/7/2024.

Rejection of claims 1-30 rejected under the nonstatutory double patenting as being unpatentable over claims 31, 39-46, 51, 54-62 and 65-71 of co-pending Application No. 16/261,459, is withdrawn because the co-pending Application No. 16/261,459 has patent term filing date of 01/29/2019, whereas the instant application has a patent term filing date of 02/01/2016, and Pursuant to MPEP 1490, the nonstatutory double patenting rejections over copending applications No. 16/261,459 is withdrawn because the instant application has an earlier patent term filing date.

Terminal Disclaimer

The terminal disclaimer filed on 05/24/2024 disclaiming the terminal portion of any patent

granted on this application which would extend beyond the expiration date of any patent granted on U.S. Patent No. US9561229B2, US9808465B2, US9974742B2, US9974793B2, US9974794B2, US10500208B2, US10624850B2, US10953018B2, US11173118B2, US11744800B2, US11878074B2, and U. S. Application Number 18/408,463, 18/408,486, and 18/535,853 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

The closest prior art is considered to be W. Zhou et al. (CN102379845A, 03/21/2012).

Zhou teaches NK-1 antagonist, aprepitant microemulsion for injection, consisting of 0.05% ~ 2% aprepitant, 5% ~ 30% injection oil, 0.5% ~ 10% emulsification Agent, 1-10% emulsion aid, 5% -20% protective agent; 60-80% water for injection. Zhou teaches that the emulsifier is egg yolk phospholipid, the oil is soybean oil, and teaches that the emulsion comprises alcohol (ethanol) and a pH modifier, wherein the NK-1 antagonist aprepitant is used to treat patients at risk of vomiting induced by cancer chemotherapy. [Zhou, translated Espacenet document, page 3].

However, Zhou's ratio of emulsifier to aprepitant (the NK-1 antagonist) is below the ratio required by the claimed invention. It appears that the amount of emulsifier is critical in the claimed emulsion because, according to the instant specification, the aprepitant emulsion possess favorable stability properties when the amount of emulsifier in the oil phase is greater than the amount of oil, wherein the amount of emulsifier have been found to impart greater stability on a final emulsion compared to a similar aprepitant emulsion with the oil phase comprises emulsifier less than the claimed amount. [Instant

specification, pg. 16, 0099]. For example, the instant specification provides preparation of an alternate aprepitant emulsion, wherein the ratio of aprepitant: emulsion is 1: 14.8, wherein with 4 days post preparation, crystals were observed which indicates less stable emulsion. [Instant Specification, Example 4, pg. 28].

In order to arrive at the claimed composition, one of ordinary skill in the art would have to modify Zhou's aprepitant emulsion to increase the amount of phospholipid to 13-20 wt/wt% and increase the ratio of the emulsifier to the NK-1 receptor antagonist to about 20:1 to 25:1 (wt/wt%). However, Zhou's disclosure does not provide sufficient guidance and motivation to one of ordinary skill in the art to perform the modification to arrive at instantly claimed emulsion. Therefore, Zhou's disclosure does not anticipate or render the instant claims obvious.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MANAHIL MIRGHANI ALI ABDALHAMEED whose telephone number is (571)272-1242. The examiner can normally be reached M-F 7:30 am - 5:00 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

Robert Havlin can be reached on 571-272-9066. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M.M.A./
Examiner, Art Unit 1622

/ROBERT H HAVLIN/
Supervisory Patent Examiner, Art Unit 1622

Notice of References Cited	Application/Control No. 18/418,030	Applicant(s)/Patent Under Reexamination Ottoboni et al.	
	Examiner MANAHIL M ABDALHAMEED	Art Unit 1622	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date YYYY-MM-DD	Name	CPC Classification	US Classification
	A					
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date YYYY-MM-DD	Country	Name	CPC Classification
	N	CN-102379845-A	2012-03-21	CN	CAO Y	
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in YYYY-MM-DD format are publication dates. Classifications may be US or foreign.

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NOTICE OF ALLOWANCE AND FEE(S) DUE

108547 7590 08/02/2024

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

EXAMINER
ABDALHAMEED, MANAHIL MIRGHANI ALI

ART UNIT	PAPER NUMBER
1622	

DATE MAILED: 08/02/2024

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06	9379

TITLE OF INVENTION: METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	11/04/2024

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

108547 7590 08/02/2024
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06	9379

TITLE OF INVENTION: METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	11/04/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
ABDALHAMEED, MUSTAFA AL	1622	707-750000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. Fees submitted: ❑Issue Fee ❑Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via the USPTO patent electronic filing system ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

❑ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

❑ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06	9379

108547 7590 08/02/2024

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

EXAMINER	
ABDALHAMEED, MANAHIL MIRGHANI ALI	
ART UNIT	PAPER NUMBER
1622	

DATE MAILED: 08/02/2024

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).
https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to:

1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;
2) a federal, state, local, or international agency, in response to its request;
3) a contractor of the USPTO having need for the information in order to perform a contract;
4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;
5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c));
9) the Office of Personnel Management (OPM) for personnel research purposes; and
10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	**09/13/2024 04:41:43 PM Z ET**	**092459-0423/8032.US06**

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9379	FILED BY	Vickie Wall
PATENT CENTER #	67171301	AUTHORIZED BY	Judy Mohr
CUSTOMER #	108547	FILING DATE	01/19/2024
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Thomas B. Ottoboni

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 500417	**E20249CG43046249**	**Vickie Wall**

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2501	UTILITY ISSUE FEE	480.00	1	480.00
			TOTAL AMOUNT:	**$480.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
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P.O. Box 1450
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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/418,030	**09/13/2024 04:41:43 PM Z ET**	**092459-0423/8032.US06**

Title of Invention

METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

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CONFIRMATION #	9379	FILED BY	Vickie Wall
PATENT CENTER #	67171301	FILING DATE	01/19/2024
CUSTOMER #	108547	FIRST NAMED INVENTOR	Thomas B. Ottoboni
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Judy Mohr

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
092459-0423-8032.US06_IssueFeeTrans.pdf	1	Issue Fee Payment (PTO-85B)	412 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
092459-0423-8032.US06_IssueFeeTrans.pdf	9CBBDB3D4F3FE0DC054297C8C54D6298DE1A7FBD034CE2F10CB4C17CB7A0D4430C74CAF590788647654917 4C4A5E718C1171995188B1B628769F32CD59F5E338

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PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

108547 7590 08/02/2024
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

Vickie D. Wall	(Typed or printed name)
/Vickie D. Wall/	(Signature)
September 13, 2024	(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06	9379

TITLE OF INVENTION: METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	11/04/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
ABDALHAMEED,	1622	707-750000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 McDermott Will & Emery LLP
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: HERON THERAPEUTICS, INC.
(B) RESIDENCE: (CITY and STATE OR COUNTRY): San Diego, CA

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☒ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

☒ Electronic Payment via the USPTO patent electronic filing system ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. 50-0417

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

☐ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

☐ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Judy M. Mohr/ Date September 13, 2024

Typed or printed name Judy M. Mohr Registration No. 38563

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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	10/15/2024	12115255	092459-0423/8032.US06	9379

108547 7590 09/25/2024

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at https://patentcenter.uspto.gov/. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at https://certifiedcopycenter.uspto.gov/index.html. The Certified Copy Center may be reached at (800)972-6382.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (https://patentcenter.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional inventors):

Thomas B. Ottoboni, Belmont, CA;
Han Han, Sunnyvale, CA;

APPLICANT(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional applicants):

Heron Therapeutics, Inc., San Diego, CA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/418,030	01/19/2024	Thomas B. Ottoboni	092459-0423/8032.US06	9379

108547 7590 10/15/2024

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

EXAMINER
ABDALHAMEED, MANAHIL MIRGHANI ALI

ART UNIT	PAPER NUMBER
1622	

NOTIFICATION DATE	DELIVERY MODE
10/15/2024	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocketmwe@mwe.com

PTOL-90A (Rev. 04/07)

APPLICATION NO.	ISSUE DATE	PATENT NO.
18/418,030	15-Oct-2024	12115255

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001-1531

EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at https://patentcenter.uspto.gov

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit https://www.uspto.gov/electronicgrants

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 18/418,030	Filing Date 01/19/2024	☐ To be Mailed

ENTITY: ☐ LARGE ☑ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $40 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $ 192 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT	07/02/2024	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 30	Minus	** 30	= 0		x $40 =	0
	Independent (37 CFR 1.16(h))	* 2	Minus	*** 3	= 0		x $ 192 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $ 0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $ 0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/CAROLYN E THOMAS/
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".	
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.	

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 18/418,030

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	64		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	280		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	320		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	30 minus 20 =	* 10	x 40 =	400	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	2 minus 3 =	*	x =	0			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	1064		TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/418,030	Ottoboni et al.
	Examiner	**Art Unit**
	MANAHIL M ABDALHAMEED	1622

INTERNATIONAL CLASSIFICATION					
CLAIMED					
A61K	/	31	/	5377	
NON-CLAIMED					
	/		/		

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					

/MANAHIL MIRGHANI ALI ABDALHAMEED/ Examiner, Art Unit 1622	15 July 2024	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	30	
/ROBERT H HAVLIN/ Supervisory Patent Examiner, Art Unit 1622	16 July 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

U.S. Patent and Trademark Office — Part of Paper No.: 20240715

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/418,030	Ottoboni et al.
	Examiner	**Art Unit**
	MANAHIL M ABDALHAMEED	1622

☑ Claims renumbered in the same order as presented by applicant ☐ CPA ☑ T.D. ☐ R.1.47

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1	10	10	19	19	28	28								
2	2	11	11	20	20	29	29								
3	3	12	12	21	21	30	30								
4	4	13	13	22	22										
5	5	14	14	23	23										
6	6	15	15	24	24										
7	7	16	16	25	25										
8	8	17	17	26	26										
9	9	18	18	27	27										

/MANAHIL MIRGHANI ALI ABDALHAMEED/ Examiner, Art Unit 1622	15 July 2024	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	30	
/ROBERT H HAVLIN/ Supervisory Patent Examiner, Art Unit 1622	16 July 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

U.S. Patent and Trademark Office — Part of Paper No.: 20240715

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/418,030	Ottoboni et al.
	Examiner	**Art Unit**
	MANAHIL M ABDALHAMEED	1622

CPC						
Symbol					**Type**	**Version**
A61K	/	9	/	1075	F	2013-01-01
A61K	/	9	/	0019	I	2013-01-01
A61K	/	47	/	24	I	2013-01-01
A61K	/	47	/	44	I	2013-01-01
A61K	/	47	/	10	I	2013-01-01
A61K	/	31	/	435	I	2013-01-01
A61K	/	31	/	496	I	2013-01-01
A61K	/	31	/	43	I	2013-01-01
A61K	/	31	/	5377	I	2013-01-01
A61K	/	31	/	573	I	2013-01-01
G06F	/	16	/	9038	I	2019-01-01
G06N	/	20	/	00	I	2019-01-01
G06F	/	16	/	90344	I	2019-01-01

CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
A61K	/	31	/	5377	I	1	1	2013-01-01
A61K	/	2300	/	00	I	1	2	2013-01-01
A61K	/	31	/	573	I	2	1	2013-01-01
A61K	/	2300	/	00	I	2	2	2013-01-01
A61K	/	31	/	435	I	3	1	2013-01-01
A61K	/	2300	/	00	I	3	2	2013-01-01
A61K	/	31	/	496	I	4	1	2013-01-01
A61K	/	2300	/	00	I	4	2	2013-01-01

/MANAHIL MIRGHANI ALI ABDALHAMEED/ Examiner, Art Unit 1622	15 July 2024	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	30	
/ROBERT H HAVLIN/ Supervisory Patent Examiner, Art Unit 1622	16 July 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

U.S. Patent and Trademark Office — Part of Paper No.: 20240715

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/418,030	Ottoboni et al.
	Examiner	Art Unit
	MANAHIL M ABDALHAMEED	1622

CPC - Searched*		
Symbol	**Date**	**Examiner**
A61K9/1075	03/13/2024	MMA
A61K9/0019	03/13/2024	MMA
A61K31/43	03/13/2024	MMA
A61K31/496	03/13/2024	MMA
A61K31/5377	03/13/2024	MMA
A61K47/10	03/13/2024	MMA
A61K47/44	03/13/2024	MMA

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
SEARCH, Classification and Limited Classification search, Assignee search, Inventor search (DAV), see attached	03/13/2024	MMA
STN search, see attached	03/13/2024	MMA
PE2E Search: keyword search, Classification search, Assignee search, Inventor search (DAV), see attached	07/15/2024	
STNext search, see attached	07/15/2024	MMA

/M.M.A./ Examiner, Art Unit 1622	/BAHAR CRAIGO/ Primary Examiner, Art Unit 1699

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/418,030	Ottoboni et al.
	Examiner	Art Unit
	MANAHIL M ABDALHAMEED	1622

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
A61K	9	03/13/2024	MMA

/M.M.A./ Examiner, Art Unit 1622	/BAHAR CRAIGO/ Primary Examiner, Art Unit 1699

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/418,030	Ottoboni et al.
	Examiner	Art Unit
	MANAHIL M ABDALHAMEED	1622

CPC - Searched*		
Symbol	Date	Examiner
A61K9/1075	03/13/2024	MMA
A61K9/0019	03/13/2024	MMA
A61K31/43	03/13/2024	MMA
A61K31/496	03/13/2024	MMA
A61K31/5377	03/13/2024	MMA
A61K47/10	03/13/2024	MMA
A61K47/44	03/13/2024	MMA

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
SEARCH, Classification and Limited Classification search, Assignee search, Inventor search (DAV), see attached	03/13/2024	MMA
STN search, see attached	03/13/2024	MMA

/M.M.A./ Examiner, Art Unit 1622	/BAHAR CRAIGO/ Primary Examiner, Art Unit 1699

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/418,030	Ottoboni et al.
	Examiner	Art Unit
	MANAHIL M ABDALHAMEED	1622

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
A61K	9	03/13/2024	MMA

/M.M.A./ Examiner, Art Unit 1622	/BAHAR CRAIGO/ Primary Examiner, Art Unit 1699

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	17	(A61K9/1075 AND A61K9/0019 AND A61K31/43 AND A61K31/496 AND A61K31/5377 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:29 PM
L2	19	(A61K9/1075 AND A61K9/0019 AND A61K31/496 AND A61K31/5377 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:30 PM
L3	67	(A61K9/1075 AND A61K9/0019 AND A61K31/5377 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:30 PM
L4	1402	(A61K9/1075 AND A61K9/0019 AND A61K47/10 AND	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY,	OR	ON	ON	2024/03/13 03:31 PM

		A61K47/44)	CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L5	31	((A61K9/1075 AND A61K9/0019 AND A61K47/10 AND A61K47/44) AND aprepitant)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:32 PM
L6	3999	(aprepitant AND phospholipid AND oil AND ethanol AND water AND inject$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:33 PM
L7	31	((("Heron") near3 ("Therapeutics") near3 ("Inc"))).AS,AANM.	(USPAT)	OR	ON	ON	2024/03/13 03:34 PM
L8	83	((("Heron") near3 ("Therapeutics") near3 ("Inc"))).AS,AANM.	(US-PGPUB; USPAT)	OR	ON	ON	2024/07/15 06:38 AM
L9	8281	(aprepitant AND lecithin)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA,	OR	ON	ON	2024/07/15 06:44 AM

			EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L10	2244	(aprepitant AND lecithin AND soybean AND ethanol AND sucrose AND oleate AND inject$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/07/15 06:53 AM
L11	1578	(aprepitant AND lecithin AND soybean AND ethanol AND sucrose AND (sodium ADJ oleate) andwater AND inject$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/07/15 06:54 AM
L12	1032	(aprepitant AND lecithin AND soybean AND ethanol AND sucrose AND (sodium ADJ oleate) andwater AND inject$ AND emulsi$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO;	OR	ON	ON	2024/07/15 06:54 AM

			JPO; DERWENT; IBM_TDB)				
L13	368	(aprepitant AND lecithin AND soybean AND ethanol AND sucrose AND (sodium ADJ oleate) AND water AND inject$ AND emulsi$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/07/15 06:56 AM
L14	75	(A61K9/1075 AND A61K9/0019 AND A61K31/5377 AND A61K47/10)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/07/15 07:01 AM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N1	165	(A61K9/1075 AND A61K9/0019 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT)	OR	ON	ON	2024/03/13 03:31 PM
N2	22	(A61K9/1075 AND A61K9/0019 AND A61K31/5377 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT)	OR	ON	ON	2024/03/13 03:31 PM
N3	1154	(aprepitant AND phospholipid AND oil AND ethanol AND water AND inject$)	(US-PGPUB; USPAT)	OR	ON	ON	2024/03/13 03:33 PM

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DICTIONARY FILE UPDATES:  14 JUL 2024  HIGHEST RN 3047493-82-0

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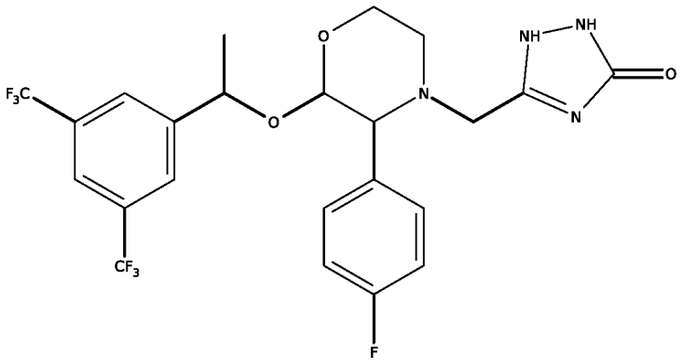
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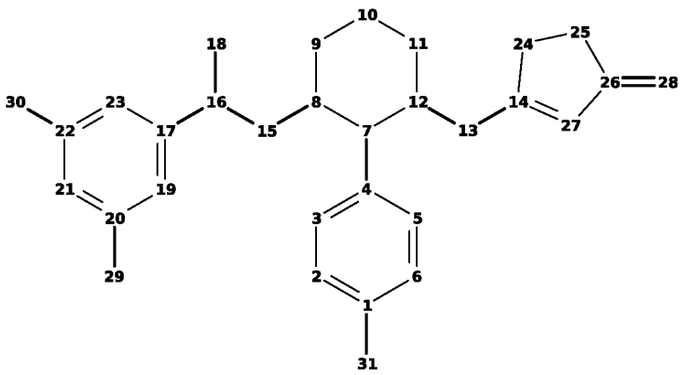
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=>
Uploading structure file: 2024_0133_Structure
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Node Attributes
Ring Nodes : 1 2 3 4 5 6 7 8 9 10 11 12 14 17 19 20 21 22 23 26 27
Chain Nodes : 13 15 16 18 28 31
Bond Attributes
Ring Bonds : 1-2 2-3 3-4 4-5 5-6 6-1 7-8 8-9 9-10 10-11 11-12 12-7 14-24 17-19 19-20 20-21 21-22 22-23 23-17 24-25 25-26 26-27 27-14
Chain Bonds : 1-31 4-7 8-15 12-13 13-14 15-16 16-17 16-18 20-29 22-30 26-28
Exact Bonds : 1-31 4-7 13-14 16-17 16-18 20-29 22-30
Normalized Bonds : 1-2 2-3 3-4 4-5 5-6 6-1 17-19 19-20 20-21 21-22 22-23 23-17
Exact/Normalized Bonds : 7-8 8-9 8-15 9-10 10-11 11-12 12-7 12-13 14-24

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15-16  24-25  25-26  26-27  26-28  27-14
Markush Attributes
Match Level (ATOM) : 1  2  3  4  5  6  7  8  9  10  11  12  14  17  19  20  21
22  23  24  25  26  27
Match Level (CLASS) : 13  15  16  18  28  29  30  31
Element Count Level (LIMITED) : 1  2  3  4  5  6  7  8  9  10  11  12  13  14
15  16  17  18  19  20  21  22  23  24  25  26  27  28  29  30  31



L1      STRUCTURE UPLOADED

=> S L1 SSS SAM

SAMPLE SEARCH INITIATED 12:21:11 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       53 TO ITERATE

100.0% PROCESSED         53 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          624 TO     1496
PROJECTED ANSWERS:               5 TO      234

L2            5 SEA SSS SAM L1

=> S L1 SSS FULL

FULL SEARCH INITIATED 12:21:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      805 TO ITERATE

100.0% PROCESSED        805 ITERATIONS                               68 ANSWERS
SEARCH TIME: 00.00.01

L3           68 SEA SSS FUL L1

=> FILE CAPLUS

COST IN U.S. DOLLARS                          SINCE FILE            TOTAL
                                                   ENTRY          SESSION
FULL ESTIMATED COST                               887.58           887.93

FILE 'CAPLUS' ENTERED AT 12:21:39 ON 15 JUL 2024
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FILE COVERS 1907 - 15 Jul 2024 VOL 187 ISS 6
FILE LAST UPDATED: 14 Jul 2024 (20240714/ED)

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substance identification.

=> S L3
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L4        1714 L3

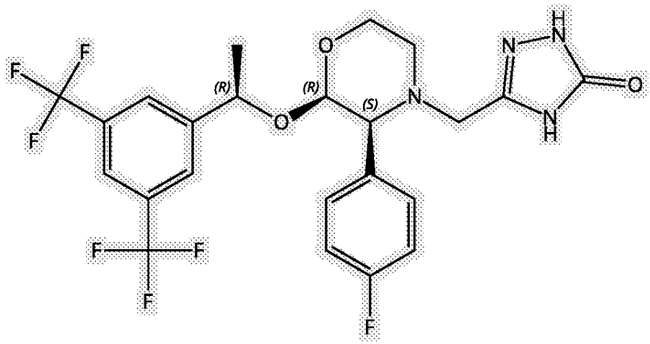
=> S L4 AND lecithin

         55781 LECITHIN
         63166 LECITHINS
         88634 LECITHIN
                 (LECITHIN OR LECITHINS)
L5          49 L4 AND LECITHIN

=> D L5 1-49 IBIB ABS HITIND HITSTR


L5   ANSWER 1 OF 49  CAPLUS  COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER:         2024:1135791  CAPLUS Full-text
DOCUMENT NUMBER:          187:43089
TITLE:                    Stable antiemetic emulsions for parenteral
                          administration
INVENTOR(S):              Dubewar, Ashish Anilrao; Bhise, Rahul Dhulaji; Mamidi,
                          Shanker; Mahadik, Mahadeo Vasant; Pillai, Sumitra
                          Ashokkumar
PATENT ASSIGNEE(S):       Slayback Pharma LLC, USA
SOURCE:                   Indian Pat. Appl., 56pp.
                          CODEN: INXXBQ
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
     PATENT NO.           KIND  DATE        APPLICATION NO.          DATE
     ---------------      ----  --------    ---------------------    --------
     IN 202241061823       A    20240503    IN 2022-41061823         20221031
     US 20240156829        A1   20240516    US 2023-18487330         20231016
PRIORITY APPLN. INFO.:                     IN 2022-41061823      A  20221031
PATENT STATUS PATENT INFORMATION:
     PATENT NO.           KIND  STATUS          STATUS DATE
     ---------------      ----  -------------   -----------
     US 20240156829        A1   Alive           20240523
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   The present invention relates to stable pharmaceutical compns. for
     parenteral administration comprising aprepitant.  The present invention
     further relates to a method for manufg. the compn. as well as to the use
     of these compns.  Also included are stable pharmaceutical compns. for
     parenteral administration comprising aprepitant and palonosetron.  The
     pharmaceutical compns. are stable oil-in-water emulsions for parenteral
     administration and are particularly useful for the prevention and control
     of acute and delayed chemotherapy-induced nausea and vomiting (CINV), for
     the prevention of postoperative nausea and vomiting (PONV), and/or for the
     prevention of radiation induced nausea and vomiting (RINV).
IPCI A61P0001-08 [ICM,7]; A61K0009-00 [ICS,7]; A61P0043-00 [ICS,7];
     A61K0031-5377 [ICS,7]; A61K0047-12 [ICS,7]
CC   63-6 (Pharmaceuticals)
IT   Egg yolk lecithins
     Oils
     Soybean oil
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (stable antiemetic emulsions for parenteral administration)
IT   57-50-1, biological studies   59-02-9   60-00-4, biological studies
     64-17-5, Ethanol, biological studies   69-65-8, D-Mannitol   128-37-0,
     biological studies   143-19-1   149-44-0   7732-18-5, Water, biological
     studies   10102-17-7   38098-46-3   135729-61-2   170729-80-3
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (stable antiemetic emulsions for parenteral administration)
IT   170729-80-3
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (stable antiemetic emulsions for parenteral administration)
RN   170729-80-3  CAPLUS
CN   3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro-  (CA INDEX
```

NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
IN 202241061823 A	IN 2022-41061823	Register
US 20240156829 A1	US 2023-18487330	Register|Global Dossier

L5 ANSWER 2 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2024:141628 CAPLUS Full-text
DOCUMENT NUMBER: 187:58792
TITLE: Aprepitant emulsion drug composition and preparation method thereof
INVENTOR(S): Chen, Xiangmei; Yu, Changhui; Wang, Xinlong; Lin, Liyang; Shen, Li; Zhao, Dong
PATENT ASSIGNEE(S): Sichuan Kelun Pharmaceutical Research Institute Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: SICHUAN KELUN PHARMACEUTICAL COMPANY LIMITED
ULTIMATE OWNER STANDARD: Sichuan KELUN
SOURCE: Faming Zhuanli Shenqing, 8pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

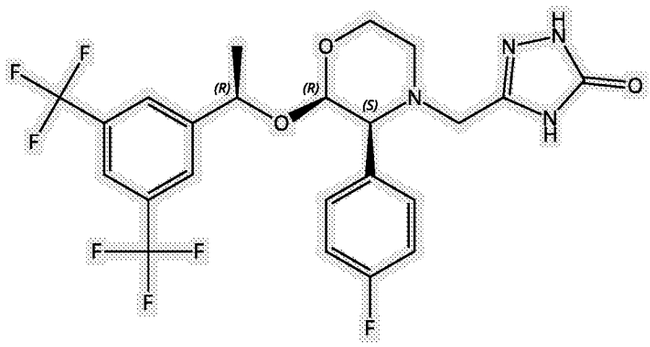
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 117414334	A	20240119	CN 2022-10811953	20220711

PRIORITY APPLN. INFO.: CN 2022-10811953 20220711
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 117414334	A	Alive	20240125

AB The present invention provides an aprepitant emulsion drug compn. and prepn. method thereof, which has the advantages of high quality and good stability. The method comprises the following steps: stirring and dissolving aprepitant, phospholipid, ethanol and soybean oil to obtain an oil phase, adding an isotonic regulator, the phospholipid and a pH regulator into water for injection, stirring uniformly to obtain a water phase, online shearing and mixing the oil phase and the water phase to prep. a primary emulsion, homogenizing by high-pressure microjet, sterilizing, filtering and filling.
IPCI A61K0009-107; A61K0031-5377; A61K0047-24; A61K0047-44; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
Soybean oil
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aprepitant emulsion drug compn. and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion drug compn. and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion drug compn. and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 117414334 A	CN 2022-10811953	Register|Global Dossier

L5 ANSWER 3 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2023:1752935 CAPLUS Full-text
DOCUMENT NUMBER: 184:181224
TITLE: Formulation and evaluation of lipid nanoparticulate drug delivery system of Aprepitant for the treatment of Cinv
AUTHOR(S): R., Joan Vijetha; Balamurugan, K.
CORPORATE SOURCE: College of Pharmacy, Sathyabama Institute of Science and Technology, Semmancheri, Chennai, 600119, India
SOURCE: Journal of Pharmaceutical Negative Results (2022), 13(Spec.Iss.10), 5114-5127
CODEN: JPNRBH; ISSN: 2229-7723
URL: https://www.pnrjournal.com/index.php/home/index
DIGITAL OBJECT ID: 10.47750/pnr.2022.13.s10.627
PUBLISHER: ResearchTrentz
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The present study was to formulate and evaluate the Aprepitant USP is a substance P/neurokinin 1 (NK1) receptor antagonist as nanoparticulate lipid carriers (AP-NLC) drug delivery systems and comparing with the marketed product. The formulations of AP-NLC were prepd. by the homogenization followed by ultrasonication method using the solid lipid as Glyceryl behenate, the liq. lipid Caprylocaproyl polyoxyglycerides and polysorbate 80 as hydrophilic surfactant. Based on the trial expts., the compn. of optimized formulation was AP-NLC blend consist of 125 mg of Aprepitant, 210 mg Glyceryl behenate, 90 mg Caprylocaproyl polyoxyglycerides, 36 mg polysorbate 80 and 20 mg soya lecithin. By liquisolid technique mesoporous silica gel taken was 160.4 mg was mixed with above AP-NLC blend to form from the optimized AP-NLC12 capsules. The AP NLC12 was found to be with mean particle size of mean av. of 200.6 nm with max. intensity of 541.0 nm particles, The dissoln. data demonstrates that the drug release was increased by 5-12% increase in drug release in initial time points upto 3 h as compared to the marketed product and the

release is sustained up to 30 h as compared to the 10 h for the marketed product. The drug release kinetics of AP NLC 12 was by Korsmeyer-Peppas model confirms the drug release from a polymeric system and release mechanisms was diffusion followed by erosion.This research is an attempt was made to design Aprepitant USP nanoparticulate lipid carrier drug delivery systems for sustained drug release in treatment chemotherapy induced nausea and vomiting (CINV).

CC 63-6 (Pharmaceuticals)

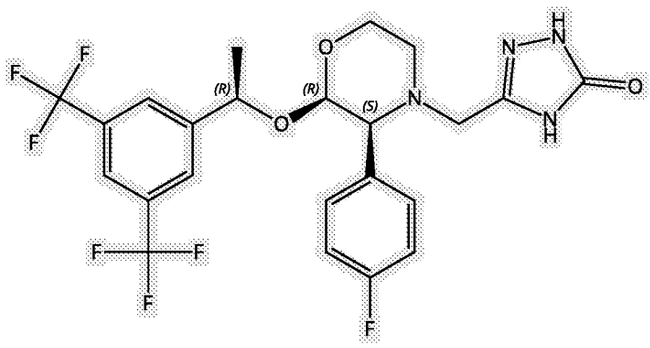
IT Soya lecithins
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and evaluation of lipid nanoparticulate drug delivery system of aprepitant for treatment of chemotherapy induced nausea and vomiting)

IT 9005-65-6 18641-57-1 170729-80-3
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and evaluation of lipid nanoparticulate drug delivery system of aprepitant for treatment of chemotherapy induced nausea and vomiting)

IT 170729-80-3
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and evaluation of lipid nanoparticulate drug delivery system of aprepitant for treatment of chemotherapy induced nausea and vomiting)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2023:1213332 CAPLUS Full-text
DOCUMENT NUMBER: 183:142125
TITLE: Personalized starvation therapy for cancer by administering an inhibitor of the mevalonate pathway with a diet low in cholesterol or lipids
INVENTOR(S): Maddocks, Oliver D. K.; Mishra, Swati
PATENT ASSIGNEE(S): Faeth Therapeutics, Inc., USA
ULTIMATE OWNER: FAETH THERAPEUTICS INC
ULTIMATE OWNER STANDARD: FAETH THERAPEUTICS INC
SOURCE: PCT Int. Appl., 210pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2023108146	A1	20230615	WO 2022-US81307		20221209
PRIORITY APPLN. INFO.:			US 2021-63288062	P	20211210

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2023108146	A1	Alive	20230629

AB Disclosed herein are methods of administering an inhibitor of the mevalonate pathway with a diet low in cholesterol or lipids. The methods of the present invention can be used to treat conditions such as cancer.

IPCI A61K0031-33 [I]; A61K0031-045 [I]; A61K0031-395 [I]; A61K0031-01 [N]

IPCR A61K0031-33 [I]; A61K0031-01 [N]; A61K0031-045 [I]; A61K0031-395 [I]

CC 1-6 (Pharmacology)
Section cross-reference(s): 18, 63

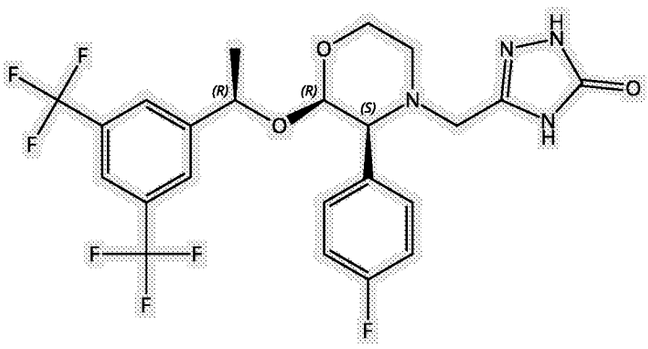
IT Castor oil
Lanolin
Lecithins
Tannins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(personalized starvation therapy for cancer by administering an inhibitor of mevalonate pathway with a diet low in cholesterol or lipids and combination with other agents)

IT 9031-14-5, Lecithin-cholesterol acyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; personalized starvation therapy for cancer by administering an inhibitor of mevalonate pathway with a diet low in cholesterol or lipids and combination with other agents)

IT 118292-40-3, Tazarotene 119169-78-7, Epristeride 119302-91-9, Rocuronium (Bromide) 119413-54-6, Topotecan (Hydrochloride) 119478-55-6, Danofloxacin (mesylate) 119478-56-7, Meropenem (trihydrate) 119615-63-3, Olprinone (Hydrochloride) 119637-67-1, Moguisteine 119793-66-7, Levocarnitine propionate (hydrochloride) 120011-70-3, Donepezil (Hydrochloride) 120014-06-4, Donepezil 120068-37-3, Fipronil 120202-66-6, Clopidogrel (hydrogen sulfate) 120410-24-4, Biapenem 120511-73-1, Anastrozole 120638-55-3 120685-11-2, Midostaurin 120876-23-5 121032-29-9, Nelarabine 121123-17-9, Cefprozil (monohydrate) 121268-17-5 121808-62-6, Pidotimod 122111-03-9, Gemcitabine (hydrochloride) 122320-73-4, Rosiglitazone 122341-38-2, Temoporfin 122547-49-3, Faropenem sodium 122647-32-9, Ibutilide (fumarate) 122841-12-7, Cefoselis (sulfate) 122852-69-1, Alosetron (Hydrochloride) 122892-31-3, Itopride (hydrochloride) 123040-16-4, Azasetron hydrochloride 123171-59-5, Cefepime (Dihydrochloride Monohydrate) 123318-82-1, Clofarabine 123441-03-2, Rivastigmine 123447-62-1, Prulifloxacin 123524-52-7, Azelnidipine 123663-49-0, Iguratimod 124750-99-8, Losartan (potassium) 124832-27-5, Valacyclovir (hydrochloride) 124858-35-1, Nadifloxacin 124937-51-5, Tolterodine 124937-52-6, Tolterodine (tartrate) 125572-93-2, Rotigotine (Hydrochloride) 125602-71-3, Bepotastine 126544-47-6, Ciclesonide 126784-99-4, Ulipristal acetate 127373-66-4, Sivelestat 127779-20-8, Saquinavir 127984-74-1, Lanreotide (acetate) 128607-22-7, Ospemifene 128794-94-5, Mycophenolate Mofetil 129101-54-8, Rivastigmine (tartrate) 129453-61-8, Fulvestrant 129497-78-5, Verteporfin 129618-40-2, Nevirapine 129722-12-9, Aripiprazole 129938-20-1, Dapoxetine (hydrochloride) 130018-87-0, Levocetirizine (dihydrochloride) 130209-82-4, Latanoprost 130693-82-2, Dorzolamide (hydrochloride) 130726-68-0, Neticonazole 130773-02-3, Neticonazole (hydrochloride) 130929-57-6, Entacapone 131410-48-5, Gadodiamide 131707-23-8, Umifenovir (hydrochloride) 132112-35-7, Ropivacaine (hydrochloride monohydrate) 132203-70-4, Cilnidipine 132539-06-1, Olanzapine 132810-10-7, Blonanserin 132866-11-6, Lercanidipine (hydrochloride) 132907-72-3, Ramosetron (Hydrochloride) 133033-93-9, (±)-Darifenacin 133099-07-7, Darifenacin (hydrobromide) 133454-47-4, Iloperidone 133865-89-1 134308-13-7, Tolcapone 134418-28-3, Dehydroandrographolide 134523-00-5, Atorvastatin 134523-03-8, Atorvastatin calcium 134678-17-4, Lamivudine 135062-02-1, Repaglinide 135159-51-2, Sarpogrelate (hydrochloride) 135326-22-6, Gadoxetate (Disodium) 135729-62-3, Palonosetron (Hydrochloride) 136087-85-9, Fidarestat 136310-93-5, Tiotropium (Bromide) 136434-34-9, Duloxetine (hydrochloride) 136470-78-5, Abacavir 136572-09-3, Irinotecan (hydrochloride trihydrate) 137071-32-0, Pimecrolimus 137234-62-9, Voriconazole 137281-23-3, Pemetrexed 137862-53-4, Valsartan

137975-06-5, Mozavaptan 138112-76-2, Agomelatine 138402-11-6, Irbesartan 138470-70-9, Mozavaptan (hydrochloride) 138530-94-6, (R)-Lansoprazole 138614-30-9, Icatibant (acetate) 138786-67-1, Pantoprazole (sodium) 138890-62-7, Brinzolamide 138926-19-9, Ibandronate (Sodium Monohydrate) 138982-67-9, Ziprasidone (hydrochloride monohydrate) 139110-80-8, Zanamivir 139481-59-7, Candesartan 139755-83-2, Sildenafil 139755-85-4, Lodenafil 140462-76-6, Olopatadine (hydrochloride) 140678-14-4, Mangafodipir (trisodium) 140898-91-5, Hexaminolevulinate (hydrochloride) 141396-28-3, Argatroban (monohydrate) 141433-60-5, Berberine (chloride hydrate) 141505-33-1, Levosimendan 141625-93-6, Dronedarone (Hydrochloride) 141626-36-0, Dronedarone 141702-36-5, Faropenem daloxate 142128-59-4, (+)-Ketoconazole 142340-99-6, Adefovir dipivoxil 143388-64-1, Naratriptan (hydrochloride) 143491-57-0, Emtricitabine 144060-53-7, Febuxostat 144143-96-4, Eprosartan (mesylate) 144481-98-1, Landiolol (hydrochloride) 144598-75-4, Paliperidone 144675-97-8, Pixantrone (dimaleate) 144689-24-7, Olmesartan 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan Cilexetil 145108-58-3, Dexmedetomidine (hydrochloride) 145202-66-0, Rizatriptan (benzoate) 145435-72-9, Gamithromycin 145525-41-3, Mitiglinide (Calcium) 145672-81-7, Cetrorelix (Acetate) 145781-92-6, Goserelin (acetate) 145821-59-6, Tiagabine (hydrochloride) 146464-95-1, Pralatrexate 146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 147084-10-4, Alcaftadine 147098-20-2, Rosuvastatin calcium 147127-20-6, Tenofovir 147221-93-0, Delavirdine (mesylate) 147403-03-0, Azilsartan 147511-69-1, Pitavastatin 147526-32-7, Pitavastatin calcium 147536-97-8, Bosentan 148408-66-6, Docetaxel (Trihydrate) 148849-67-6, Ivabradine (hydrochloride) 149003-01-0, Dexrazoxane (hydrochloride) 149647-78-9, Vorinostat 149709-62-6, Sacubitril 149845-06-7, Saquinavir (Mesylate) 150322-43-3, Prasugrel 150399-23-8, Pemetrexed (disodium) 150566-71-5, Levamlodipine besylate 150683-30-0, Tolvaptan 150821-03-7, Pranlukast (hemihydrate) 150915-40-5, Tirofiban (hydrochloride monohydrate) 150915-41-6, Perospirone 151767-02-1, Montelukast (sodium) 152459-95-5, Imatinib 152520-56-4, Nebivolol (hydrochloride) 152658-17-8, Nalfurafine (hydrochloride) 153439-40-8, Fexofenadine (hydrochloride) 153504-70-2, Cevimeline (hydrochloride hemihydrate) 153559-49-0, Bexarotene 154229-18-2, Abiraterone acetate 154229-19-3, Abiraterone 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155141-29-0, Rosiglitazone (maleate) 155148-31-5, Plerixafor (octahydrochloride) 155206-00-1, Bimatoprost 155213-67-5, Ritonavir 155270-99-8, Istradefylline 155558-32-0, Hydroxyfasudil (hydrochloride) 155569-91-8, Emamectin (Benzoate) 156137-99-4, Rapacuronium bromide 157212-55-0, Bosentan (hydrate) 157283-68-6, Travoprost 157810-81-6, Indinavir (sulfate) 158681-13-1, Rimonabant (Hydrochloride) 158930-17-7, Frovatriptan succinate hydrate 159351-69-6, Everolimus 159989-64-7, Nelfinavir 159989-65-8, Nelfinavir (Mesylate) 160970-54-7, Silodosin 161715-24-8, Tebipenem pivoxil 161735-79-1, Rasagiline (mesylate) 161804-20-2 161814-49-9, Amprenavir 161973-10-0, Esomeprazole magnesium 162011-90-7, Rofecoxib 162359-55-9, Fingolimod 162359-56-0, Fingolimod (hydrochloride) 162401-32-3, Roflumilast 162635-04-3, Temsirolimus 163222-33-1, Ezetimibe 163252-36-6, Clevudine 163253-37-0 163451-81-8, Teriflunomide 163521-08-2, Vilazodone (Hydrochloride) 163521-12-8, Vilazodone 163521-19-5 163680-77-1, Pazufloxacin (mesylate) 163706-36-3, Cangrelor (tetrasodium) 164650-44-6, Efinaconazole 164656-23-9, Dutasteride 165800-03-3, Linezolid 165800-06-6, Zoledronic acid (monohydrate) 166663-25-8, Anidulafungin 166734-83-4 167221-71-8, Clevidipine 167933-07-5, Flibanserin 168626-94-6, Conivaptan (hydrochloride) 169590-41-4, Deracoxib 169590-42-5, Celecoxib 170098-38-1, Alvimopan (dihydrate) 170105-16-5, Imidafenacin 170729-80-3, Aprepitant 171228-49-2, Posaconazole 171596-29-5, Tadalafil 171599-83-0, Sildenafil (citrate) 172152-36-2, Ilaprazole 172152-50-0, Ilaprazole (sodium) 173334-57-1, Aliskiren 173334-58-2, Aliskiren (hemifumarate) 173352-39-1 174484-41-4, Tipranavir 174671-46-6, Tavaborole 175865-59-5, Valganciclovir (hydrochloride) 177036-94-1, Ambrisentan 177834-92-3, Eletriptan (hydrobromide) 178307-42-1, Revaprazan (hydrochloride)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(personalized starvation therapy for cancer by administering an inhibitor of mevalonate pathway with a diet low in cholesterol or lipids and combination with other agents)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(personalized starvation therapy for cancer by administering an inhibitor of mevalonate pathway with a diet low in cholesterol or lipids and combination with other agents)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
WO 2023108146 A1	WO 2022-US81307	Register|Global Dossier

L5 ANSWER 5 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:2496852 CAPLUS Full-text
DOCUMENT NUMBER: 180:210930
TITLE: Compositions having improved bioavailability of therapeutics
INVENTOR(S): Brew, John; Gooding, Daniel; Bannister, Robin M.
PATENT ASSIGNEE(S): TRx Biosciences Limited, UK
ULTIMATE OWNER: TRX BIOSCIENCES; TRX BIOCIENCES
ULTIMATE OWNER STANDARD: TRX BIOSCIENCES; TRX BIOCIENCES
SOURCE: U.S. Pat. Appl. Publ., 202pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20220305125	A1	20220929	US 2022-17656702		20220328
CA 3212583	A1	20221006	CA 2022-3212583		20220328
WO 2022207580	A2	20221006	WO 2022-EP58180		20220328
WO 2022207580	A3	20221229			
AU 2022248850	A1	20231109	AU 2022-248850		20220328
EP 4312978	A2	20240207	EP 2022-718916		20220328
KR 2024021751	A	20240219	KR 2023-7037012		20220328
JP 2024511208	T	20240312	JP 2023-559684		20220328
WO 2023174948	A2	20230921	WO 2023-EP56506		20230314
WO 2023174948	A3	20231026			
US 20240075147	A1	20240307	US 2023-18487486		20231016
IN 202347072261	A	20231215	IN 2023-47072261		20231023
PRIORITY APPLN. INFO.:			US 2021-63166995	P	20210327
			US 2022-63269330	P	20220314
			US 2022-17656702	A1	20220328

WO 2022-EP58180 W 20220328

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20220305125	A1	Alive	20221006
CA 3212583	A1	Alive	20231005
WO 2022207580	A2	Alive	20221013
WO 2022207580	A3	Alive	20230112
AU 2022248850	A1	Alive	20231116
EP 4312978	A2	Alive	20240208
KR 2024021751	A	Alive	20240314
JP 2024511208	T	Alive	20240321
WO 2023174948	A2	Alive	20230928
US 20240075147	A1	Alive	20240314

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2022:2496852

AB The present specification discloses pharmaceutical compn. disclosed herein comprises one or more therapeutic compds., one or more glycerolipids, and one or more digestion enhancers. The disclosed glycerolipids comprise one or more hard fats and one or more liq. fats. The disclosed digestion enhancers comprise one or more bile acids, one or more phospholipids, one or more free C14-24 fatty acids, one or more free C14-24 fatty acid surfactants, or any combination thereof. The present specification also discloses methods and procedures to formulate the disclosed one or more therapeutic compds. into the disclosed pharmaceutical compns.

IPCI A61K0047-14 [I]; A61K0047-28 [I]; A61K0031-12 [I]; A61K0031-216 [I]; A61K0031-05 [I]; A61K0031-58 [I]; A61K0031-7135 [I]; A61K0031-192 [I]; A61K0031-553 [I]; A61K0031-4418 [I]; A61K0031-4453 [I]; A61K0031-196 [I]; A61K0031-44 [I]; A61K0031-4184 [I]; A61K0031-436 [I]; A61K0031-5377 [I]; A61K0031-502 [I]; A61K0031-496 [I]; A61K0031-4025 [I]; A61K0038-12 [I]

IPCR A61K0047-14 [I]; A61K0031-05 [I]; A61K0031-12 [I]; A61K0031-192 [I]; A61K0031-196 [I]; A61K0031-216 [I]; A61K0031-4025 [I]; A61K0031-4184 [I]; A61K0031-436 [I]; A61K0031-44 [I]; A61K0031-4418 [I]; A61K0031-4453 [I]; A61K0031-496 [I]; A61K0031-502 [I]; A61K0031-5377 [I]; A61K0031-553 [I]; A61K0031-58 [I]; A61K0031-7135 [I]; A61K0038-12 [I]; A61K0047-28 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

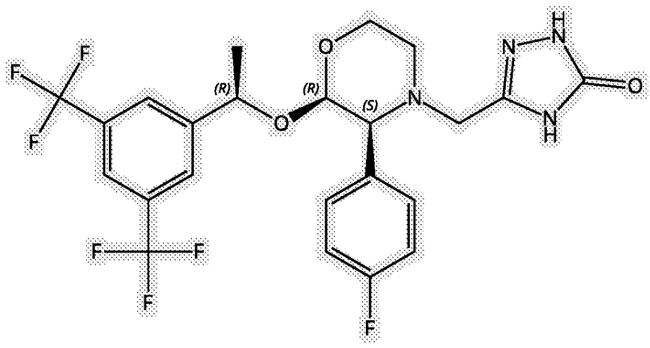
IT Bile acids
Fats and Glyceridic oils
Fatty acids
Glycerolipids
Lecithins
Monoglycerides
Phospholipids
Polyoxyalkylenes
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. having improved bioavailability of therapeutics)

IT 458-37-7, Curcumin 4394-00-7, Niflumic acid 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22204-53-1, Naproxen 31121-93-4 31431-39-7, Mebendazole 34031-32-8, Auranofin 53179-13-8, Pirfenidone 68302-57-8, Amlexanox 88170-10-9, Diclofenac calcium 120685-11-2, Midostaurin 130308-48-4, Icatibant 144701-48-4, Telmisartan 154229-19-3, Abiraterone 170729-80-3, Aprepitant 362665-56-3, Pitolisant 491833-29-5, Eliglustat 656247-17-5, Nintedanib 763113-22-0, Olaparib
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. having improved bioavailability of therapeutics)

IT 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. having improved bioavailability of therapeutics)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2022248850 A1	AU 2022-248850	Register
CA 3212583 A1	CA 2022-3212583	Register
EP 4312978 A2	EP 2022-718916	Register|Federated Reg.
IN 202347072261 A	IN 2023-47072261	Register
JP 2024511208 T	JP 2023-559684	Register|Global Dossier
KR 2024021751 A	KR 2023-7037012	Register|Global Dossier
US 20220305125 A1	US 2022-17656702	Register|Global Dossier
US 20240075147 A1	US 2023-18487486	Register|Global Dossier
WO 2022207580 A2	WO 2022-EP58180	Register|Global Dossier
WO 2022207580 A3	WO 2022-EP58180	Register|Global Dossier
WO 2023174948 A2	WO 2023-EP56506	Register|Global Dossier
WO 2023174948 A3	WO 2023-EP56506	Register|Global Dossier

L5 ANSWER 6 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:2221248 CAPLUS Full-text
DOCUMENT NUMBER: 181:431761
TITLE: Small scale in vitro method to determine a potential bioequivalent equilibrium solubility range for fed human intestinal fluid
AUTHOR(S): Ines Silva, Maria; Khadra, Ibrahim; Pyper, Kate; Halbert, Gavin W.
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, Glasgow, G4 0RE, UK
SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (2022), 177, 126-134
CODEN: EJPBEL; ISSN: 0939-6411
DIGITAL OBJECT ID: 10.1016/j.ejpb.2022.06.005
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Intestinal drug soly. is a key parameter controlling oral absorption but varies both intra and inter individuals and between the fasted and fed states, with food intake known to alter the bioavailability of many compds. Intestinal soly. can be measured in vitro either using sampled fed human intestinal fluid (FeHIF) or simulated fed intestinal fluid (SIF) but neither approach is optimal. FeHIF is difficult to obtain and variable, while for fed SIF multiple recipes are available with no consensus on the ideal version. A recent study characterised FeHIF aspirates using a multidimensional approach and calcd. nine simulated media recipes that covered over ninety percent of FeHIF compositional variability. In this study the equil. soly. of thirteen drugs have been measured using the nine simulated media recipes and compared to multiple previous design of expt. (DoE) studies, which have examd. the impact of fed SIF media components on soly. The measured nine media soly. data set

is only statistically equiv. to the large scale 92 media DoE in 4 out of 13 drug comparisons, but has improved equivalence against small scale DoEs (9 or 10 media) with 6 out of 9 or 10 out of 12 (9 and 10 media resp.) equiv. Selective removal of non-biorelevant compns. from the 92 media DoE improves statistical equivalence to 9 out of 13 comparisons. The results indicate that soly. equivalence is linked to media component concns. and compns., the nine media system is measuring a similar soly. space to previous systems, with a narrower soly. range than the 92 point DoE but equiv. to smaller DoE systems. Phenytoin and tadalafil display a narrow soly. range, a behavior consistent with previous studies in fed and fasted states and only revealed through the multiple media approach. Custom DoE anal. of the nine media results to det. the most statistically significant component influencing soly. does not detect significant components. Indicating that the approach has a low statistical resoln. and is not appropriate if detn. of media component significance is required. This study demonstrates that it is possible to assess the fed intestinal equil. soly. envelope using the nine media recipes obtained from a multi-dimensional anal. of fed HIF. The derivation of the nine media compns. coupled with the results in this study indicate that the soly. results are more likely to reflect the fed intestinal soly. envelope than previous DoE studies and highlight that the system is worthy of further investigation.

CC 63-6 (Pharmaceuticals)

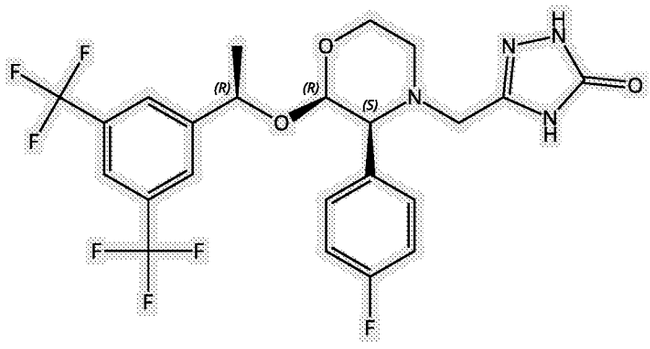
IT Lecithins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale in vitro method to det. potential bioequivalent equil. soly. range for fed human intestinal fluid)

IT 53-86-1 57-41-0 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies 110-16-7, 2-Butenedioic acid (2Z)-, biological studies 111-03-5 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 145-42-6 14265-44-2, Phosphate, biological studies 15687-27-1 23288-49-5 25614-03-3 49562-28-9 72509-76-3 72956-09-3 84625-61-6 107753-78-6 137862-53-4 170729-80-3 171596-29-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale in vitro method to det. potential bioequivalent equil. soly. range for fed human intestinal fluid)

IT 170729-80-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale in vitro method to det. potential bioequivalent equil. soly. range for fed human intestinal fluid)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

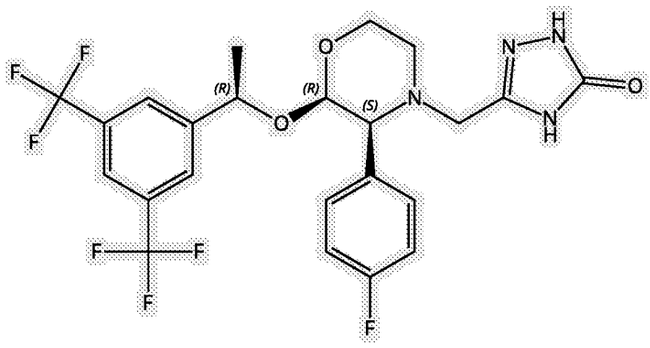
L5 ANSWER 7 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:1355958 CAPLUS Full-text
DOCUMENT NUMBER: 179:75293
TITLE: Stable antiemetic emulsions
INVENTOR(S): Bhagwatwar, Harshal Prabhakar; Nerurkar, Manoj
PATENT ASSIGNEE(S): Steps BioSciences, Inc., USA
ULTIMATE OWNER: STEPS BIOSCIENCES
ULTIMATE OWNER STANDARD: STEPS BIOSCIENCES
SOURCE: U.S. Pat. Appl. Publ., 11pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20220160722	A1	20220526	US 2021-17531216	20211119
PRIORITY APPLN. INFO.:			IN 2020-41050531 A	20201120

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20220160722	A1	Alive	20220609

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2022:1355958
AB Emulsion formulations and systems for the i.v. or parenteral administration. of neurokinin-1 (NK-1) receptor antagonists for treatment of emesis are provided. Methods for prepg. the stable NK-1 receptor antagonist emulsions and pharmaceutical formulations are further provided. The emulsion formulations are prepd. and characterized as a formulation and process that will allow an NK-1 receptor antagonist compd. to be incorporated into an emulsion for i.v. injection and remain stable during the shelf life of the formulation. Specifically, emulsion formulations have an oil phase that includes oil, ethanol, egg lecithin , and the further addn. of sodium oleate that is mixed with an aq. phase and processed to form the emulsion formulation.
IPCI A61K0031-5377 [I]; A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-24 [I]; A61K0047-12 [I]; A61K0047-10 [I]; A61K0047-44 [I]
IPCR A61K0031-5377 [I]; A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-44 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Castor oil
Coconut oil
Corn oil
Cottonseed oil
Egg yolk lecithins
Lecithins
Olive oil
Safflower oil
Sesame oil
Soybean oil
Triglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
IT 57-50-1, Sucrose, biological studies 64-17-5, Ethanol, biological studies 111-62-6, Ethyl oleate 143-19-1, Sodium oleate 303-43-5, Cholesteryl oleate 544-35-4, Ethyl linoleate 604-33-1, Cholesteryl linoleate 37220-82-9, Glyceryl oleate 37348-65-5, Glyceryl linoleate 136745-48-7, Octyl glycerate 152167-64-1, Decyl glycerate 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
US 20220160722 A1	US 2021-17531216	Register|Global Dossier

L5 ANSWER 8 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:139737 CAPLUS Full-text
DOCUMENT NUMBER: 177:284905
TITLE: Pharmaceutical emulsion comprising an aprepitant, pharmaceutical injections, and methods of preparing emulsions
INVENTOR(S): Amano, Yohei; Katagiri, Kazumi
PATENT ASSIGNEE(S): Kewpie Corporation, Japan; FBC (Shanghai) Pharmaceutical Technology Co., Ltd.
ULTIMATE OWNER: FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECH; KEWPIE CORPORATION; FUBICHENG SHANGHAI PHARMACEUTICAL TECH CO LTD ; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY; FBC SHANGHAI PHARMACEUTICAL TECH CO LTD
ULTIMATE OWNER STANDARD: FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECH; Kewpie Corp; FUBICHENG SHANGHAI PHARMACEUTICAL TECH CO LTD ; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY; FBC SHANGHAI PHARMACEUTICAL TECH CO LTD
SOURCE: PCT Int. Appl., 28pp.; Chemical Indexing Equivalent to 174:540291 (JP)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2022014113	A1	20220120	WO 2021-JP15552	20210415
JP 6832468	B1	20210224	JP 2020-121438	20200715
JP 2022018370	A	20220127		
CA 3187858	A1	20220120	CA 2021-3187858	20210415
KR 2023040956	A	20230323	KR 2022-7045138	20210415
EP 4169515	A1	20230426	EP 2021-843280	20210415
US 20230310443	A1	20231005	US 2023-18015492	20230110

PRIORITY APPLN. INFO.: JP 2020-121438 A 20200715
WO 2021-JP15552 W 20210415

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2022014113	A1	Alive	20220203
JP 6832468	B1	Alive	20210304
JP 2022018370	A	Alive	20220224
CA 3187858	A1	Alive	20230216
KR 2023040956	A	Alive	20230420

EP 4169515 A1 Alive 20230427
US 20230310443 A1 Alive 20231012

AB The present invention pertains to an emulsion which contains an aprepitant, an emulsifier, an oil, a polyethylene glycol having an av. mol. wt. of 260-1100, and water, and to which ethanol is substantially not added. The content of the aprepitant is 0.50-0.90 w/v% based on the total amt., and the content of the emulsifier is 12.0-18 w/v%. The content of oil is 7.0-12.0 w/v %, and the content of polyethylene glycol is 0.5-10.0 w/v %. The av. particle diam. of the emulsion is 60-140 nm. According to the present invention, provided is an aprepitant-contg. emulsion having excellent stability without substantially adding ethanol.

IPCI A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]

IPCR A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]

CC 63-6 (Pharmaceuticals)

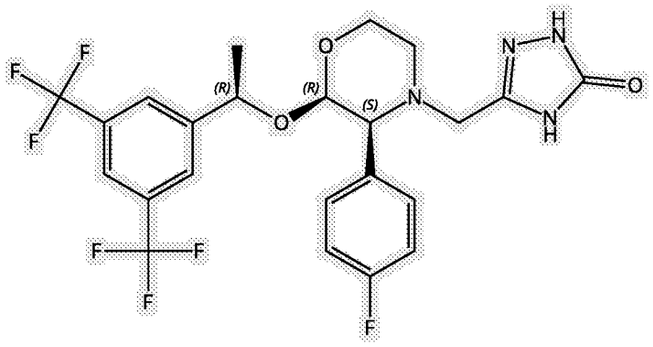
IT Egg yolk lecithins
Phospholipids
Polyoxyalkylenes
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CA 3187858 A1	CA 2021-3187858	Register
EP 4169515 A1	EP 2021-843280	Register|Federated Reg.
JP 2022018370 A	JP 2020-121438	Register|Global Dossier
JP 6832468 B1	JP 2020-121438	Register|Global Dossier
KR 2023040956 A	KR 2022-7045138	Register|Global Dossier
US 20230310443 A1	US 2023-18015492	Register|Global Dossier
WO 2022014113 A1	WO 2021-JP15552	Register|Global Dossier

L5 ANSWER 9 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN

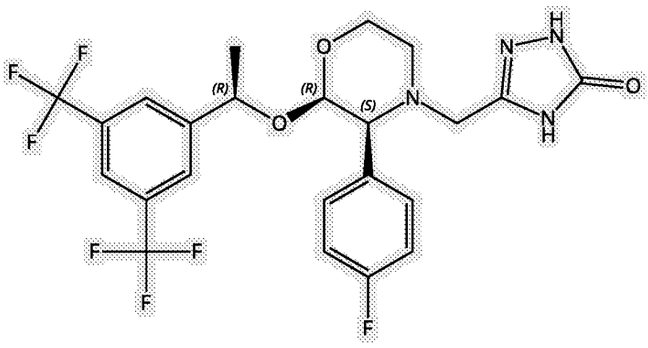
ACCESSION NUMBER: 2021:2591917 CAPLUS Full-text
DOCUMENT NUMBER: 177:123225
TITLE: Preparation method of aprepitant emulsion injection for preventing nausea and emesis
INVENTOR(S): Guo, Shuer; Qin, Zhijun
PATENT ASSIGNEE(S): Guangzhou Manxiang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU MAXENMED MEDICINE
ULTIMATE OWNER STANDARD: GUANGZHOU MAXENMED MEDICINE
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 113712915	A	20211130	CN 2021-10018100	20210107

PRIORITY APPLN. INFO.: CN 2021-10018100 20210107
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 113712915	A	Transitional	20240502

OTHER SOURCE(S): CASFORMULTNS 2021:2591917
AB The invention aprepitant emulsion injection is prepd. from (by wt%) aprepitant 0.2-1.2, pH regulator 0.25-0.75, permeation pressure regulator 3-8, injection water 56-75, emulsifier 12-15, cosolvent 2-5, and injection oil 5-15. The emulsifier is hydrogenated soybean lecithin or hydrogenated soybean phosphatidylcholine. The pH regulator is sodium hydroxide, sodium citrate, sodium dihydrogen phosphate or sodium oleate. The permeation pressure regulator is xylitol, sorbitol, mannitol or sucrose. The cosolvent is ethanol, glycerol, propylene glycol and polyethylene glycol. The injection oil is soybean oil, peanut oil, hydrogenated corn oil, triglyceride, medium-chain triglyceride, sesame oil and/or sunflower seed oil. By controlling content of emulsifier and shearing rotation speed, homogenization pressure and homogenization temp. in emulsion prepn. process, the invention preps. aprepitant emulsion injection with good oxidn. resistance and emulsification effect, and has operability, simple process and low device loss.
IPCI A61K0009-107; A61K0047-24; A61K0031-5377; A61P0001-08; A61P0035-00
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
IT Corn oil
Soya lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 113712915 A	CN 2021-10018100	Register|Global Dossier

L5 ANSWER 10 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:1541826 CAPLUS Full-text
DOCUMENT NUMBER: 175:329880
TITLE: Aprepitant ready-to-use injection emulsion compositions
INVENTOR(S): Akasapu, Prem Sagar; Subramanian, Veerappan; Subramanian, Ilango
PATENT ASSIGNEE(S): Somerset Therapeutics LLC, USA
ULTIMATE OWNER: SOMERSET THERAPEUTICS LLC
ULTIMATE OWNER STANDARD: SOMERSET THERAPEUTICS LLC
SOURCE: U.S. Pat. Appl. Publ., 8pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

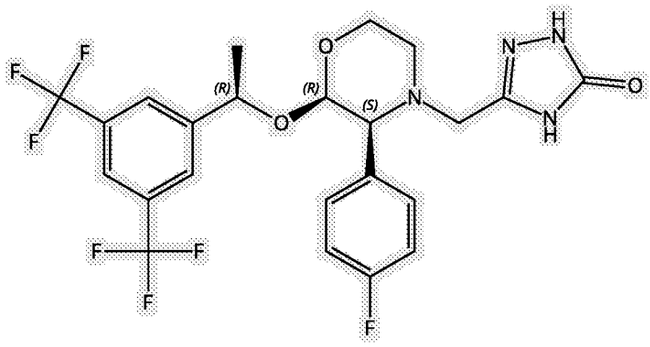
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20210212933	A1	20210715	US 2021-17147556	20210113
US 11517522	B2	20221206		

PRIORITY APPLN. INFO.: US 2020-62961039 P 20200114
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20210212933	A1	Alive	20210722
US 11517522	B2	Alive	20221215

OTHER SOURCE(S): CASFORMULTNS 2021:1541826
AB The present invention provides an emulsion compn. comprising aprepitant for treatment of emesis. Particularly, the invention is a ready-to-use emulsion compns. comprising aprepitant and medium chain triglycerides for administration by i.v. infusion, wherein the emulsion compn. is also free of ethanol. Further, the invention also provides processes of prepg. such compns. and their use for the prevention and control of acute and delayed chemotherapy-induced nausea and vomiting, and/or for prevention of postoperative nausea and vomiting.
IPCI A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-14 [I]; A61M0005-24 [I]; A61K0031-5377 [I]; A61K0009-00 [I]; A61K0047-14 [I]; A61K0009-107 [I]; A61K0031-5377 [I]; A61M0005-24 [I]
IPCR A61K0009-00 [I]; A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-14 [I]; A61M0005-24 [I]
CC 63-6 (Pharmaceuticals)
IT Lecithins
Medium-chain glycerides
Polyoxyalkylenes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aprepitant ready-to-use injection emulsion compns.)
IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)
IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
US 11517522 B2	US 2021-17147556	Register|Global Dossier
US 20210212933 A1	US 2021-17147556	Register|Global Dossier

L5 ANSWER 11 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:685825 CAPLUS Full-text
DOCUMENT NUMBER: 178:140851
TITLE: Aprepitant submicroemulsion injection capable of being autoclaved, and its preparation method
INVENTOR(S): Qin, Linghao; Li, Yusheng; Zhu, Wanye; Wang, Wanting
PATENT ASSIGNEE(S): Guangdong Pharmaceutical University, Peop. Rep. China
ULTIMATE OWNER: GUANGDONG PHARMACEUTICAL UNIVERSITY
ULTIMATE OWNER STANDARD: Guangdong Pharmaceutical University
SOURCE: Faming Zhuanli Shenqing, 19pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 112535661	A	20210323	CN 2020-11524237	20201222
CN 112535661	B	20230407		

PRIORITY APPLN. INFO.: CN 2020-11524237 20201222
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 112535661	A	Alive	20210408
CN 112535661	B	Alive	20230427

OTHER SOURCE(S): CASFORMULTNS 2021:685825
AB A safe aprepitant submicroemulsion injection capable of being autoclaved having high efficiency, good stability and sterilization effect, and wide application in medicine field is provided. The aprepitant submicroemulsion injection comprises: polyethylene glycol

15hydroxystearate, phospholipids, aprepitant, oil for injection, emulsifier, co-emulsifier, solubilizer, stabilizer, isotonic agent, pH regulator and water for injection. The prepn. method comprises the following steps: (1) mixing aprepitant, injection oil and solubilizer, dissolving and dispersing with alc., and removing the alc. to obtain an oil phase mixt.; (2) stirring and mixing the emulsifier, co-emulsifier, stabilizer, isotonic agent and water for injection, and heat to dissolve to obtain the water phase mixt.; and (3) adding the oil phase mixt. to the water phase mixt., prepg. the emulsion, and autoclaving to obtain the aprepitant submicroemulsion injection. The aprepitant submicroemulsion injection is used in the prepn. of a medicine for treating nausea and vomiting.

IPCI A61K0009-107; A61K0031-5377; A61K0047-24; A61K0047-14; A61K0047-18; A61P0001-08; A61L0002-07

IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-14 [I]; A61K0047-18 [I]; A61K0047-24 [I]; A61L0002-07 [I]; A61P0001-08 [I]

CC 63-6 (Pharmaceuticals)

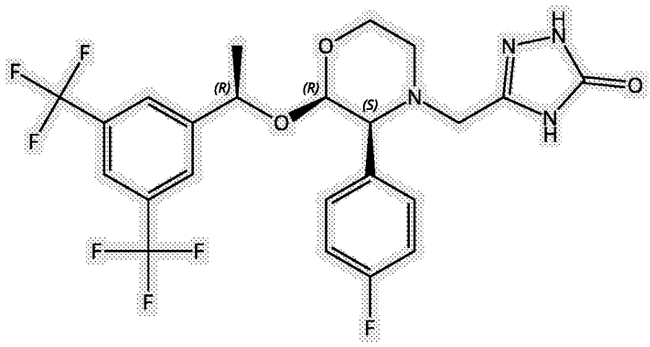
IT Amino acids
Egg yolk lecithins
Oils
Phospholipids
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)

IT 56-41-7, L-Alanine, biological studies 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 63-91-2, L-Phenylalanine, biological studies 73-32-5, L-Isoleucine, biological studies 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 112535661 A	CN 2020-11524237	Register|Global Dossier
CN 112535661 B	CN 2020-11524237	Register|Global Dossier

L5 ANSWER 12 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:481715 CAPLUS Full-text
DOCUMENT NUMBER: 174:540291

TITLE: Pharmaceutical emulsion comprising an aprepitant, pharmaceutical injections, and methods of preparing emulsions
INVENTOR(S): Amano, Yohei; Katagiri, Kazumi
PATENT ASSIGNEE(S): Kewpie Corporation, Japan; FBC (Shanghai) Pharmaceutical Technology Co., Ltd.
ULTIMATE OWNER: FBC SHANGHAI PHARMACEUTICAL TECH; KEWPIE CORPORATION; FBC SHANGHAI PHARMACEUTICAL TECH CO LTD ; FUBICHENG SHANGHAI PHARMACEUTICAL TECH CO LTD ; FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY
ULTIMATE OWNER STANDARD: FBC SHANGHAI PHARMACEUTICAL TECH; Kewpie Corp; FBC SHANGHAI PHARMACEUTICAL TECH CO LTD ; FUBICHENG SHANGHAI PHARMACEUTICAL TECH CO LTD ; FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY
SOURCE: Jpn. Tokkyo Koho, 15pp.; Chemical Indexing Equivalent to 177:284905 (WO)
CODEN: JTXXFF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 6832468	B1	20210224	JP 2020-121438	20200715
JP 2022018370	A	20220127		
CA 3187858	A1	20220120	CA 2021-3187858	20210415
WO 2022014113	A1	20220120	WO 2021-JP15552	20210415
KR 2023040956	A	20230323	KR 2022-7045138	20210415
EP 4169515	A1	20230426	EP 2021-843280	20210415
CN 113952299	A	20220121	CN 2021-10772526	20210708
CN 117017915	A	20231110	CN 2023-11089804	20210708
US 20230310443	A1	20231005	US 2023-18015492	20230110

PRIORITY APPLN. INFO.:

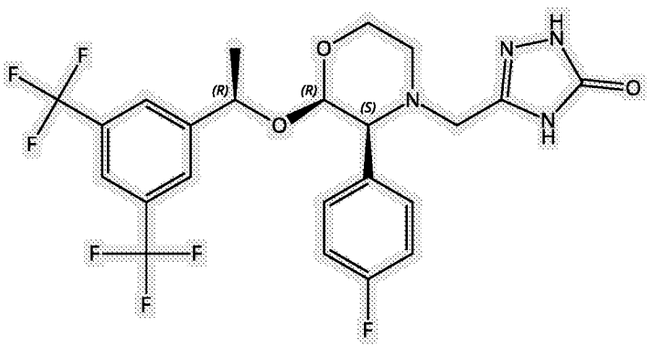
JP 2020-121438	A	20200715
WO 2021-JP15552	W	20210415
CN 2021-10772526	A3	20210708

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
JP 6832468	B1	Alive	20210304
JP 2022018370	A	Alive	20220224
CA 3187858	A1	Alive	20230216
WO 2022014113	A1	Alive	20220203
KR 2023040956	A	Alive	20230420
EP 4169515	A1	Alive	20230427
CN 113952299	A	Alive	20220203
CN 117017915	A	Alive	20231116
US 20230310443	A1	Alive	20231012

OTHER SOURCE(S): CASFORMULTNS 2021:481715
AB The emulsion comprises: an aprepitant, an emulsifier, an oil, polyethylene glycol and water, with substantially no addn. of ethanol. The emulsion comprises a pH regulator and having a pH of 8.0-9.0. The content of the aprepitant is 0.50 w/v% or more and 0.90 w/v% or less based on the total amt., and the content of the emulsifier is 12.0 w/v% or more and 12.0 w/v% or more based on the total amt. The emulsion is 0 w/v% or less, the emulsion in which the emulsifier is a phospholipid. According to the present invention, provided is an aprepitant-contg. emulsion having excellent stability without substantially adding ethanol.
IPCI A61K0031-5377 [I]; A61K0009-107 [I]; A61P0001-08 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0031-5377 [I]; A61P0001-08 [I]; A61K0047-24 [I]; A61K0047-44 [I]
IPCR A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
Phospholipids
Polyoxyalkylenes
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)
IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CA 3187858 A1	CA 2021-3187858	Register
CN 113952299 A	CN 2021-10772526	Register|Global Dossier
CN 117017915 A	CN 2023-11089804	Register|Global Dossier
EP 4169515 A1	EP 2021-843280	Register|Federated Reg.
JP 2022018370 A	JP 2020-121438	Register|Global Dossier
JP 6832468 B1	JP 2020-121438	Register|Global Dossier
KR 2023040956 A	KR 2022-7045138	Register|Global Dossier
US 20230310443 A1	US 2023-18015492	Register|Global Dossier
WO 2022014113 A1	WO 2021-JP15552	Register|Global Dossier

L5 ANSWER 13 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:2334591 CAPLUS Full-text
DOCUMENT NUMBER: 174:387650
TITLE: Enhanced transdermal permeation of BCS class IV aprepitant using binary ethosome: Optimization, characterization and ex vivo permeation
AUTHOR(S): Abouhussein, Dalia M. N.
CORPORATE SOURCE: Department of Pharmaceutics, Egyptian Drug Authority Formerly Known As National Organization for Drug Control and Research (NODCAR), Egypt
SOURCE: Journal of Drug Delivery Science and Technology (2021), 61, 102185
CODEN: JDDSAL; ISSN: 1773-2247
DIGITAL OBJECT ID: 10.1016/j.jddst.2020.102185
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Aprepitant (APR) belongs to the Biopharmaceutics Classification System (BCS) class IV that is characterized by both low soly. and permeability. This study aims to develop a new transdermal APR nanovesicle for

chemotherapy-induced nausea and vomiting. APR binary ethosomes (BEs) were developed using 32 factorial design where two independent variables namely; wt. of lecithin and propylene glycol were studied. The formulations were fully characterized through entrapment efficiency (EE), vesicle size (VS) and zeta potential (ZP). The optimized formulation was designated through the desirability value obtained by Design Expert program, visualized using transmission electron microscope (TEM) and studied for stability. Then the optimized formulation was incorporated in 0.8% carbopol 934 gel which was characterized and tested for in vitro and ex vivo release. F9 contg. 100 mg lecithin and 2.5 g propylene glycol was selected to be the optimum formulation. It showed desirability value of 0.958 as it displayed 89.6% EE, VS of 77 nm, -51.1 as ZP in addn. to adequate stability. The APR BE gel showed satisfactory phys., mech., rheol. and occlusive properties. The optimum formulation showed 4.9 folds higher permeation than APR suspension. BE gel exhibited a promising dosage form for the transdermal delivery of APR.

CC 63-5 (Pharmaceuticals)

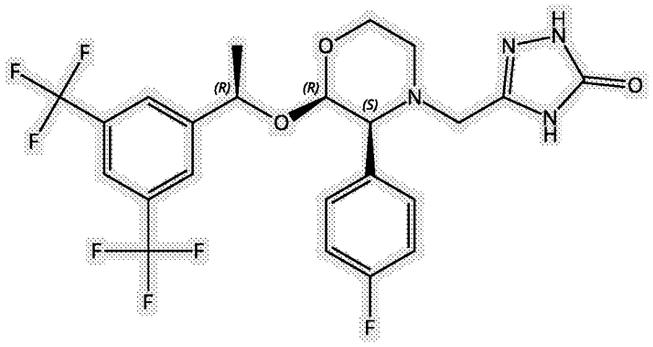
IT Lecithins
Phospholipids
RL: MOA (Modifier or additive use); USES (Uses)
(optimum formulation of aprepitant binary ethosomes gel showed satisfactory phys., mech., rheol. and occlusive properties for transdermal delivery)

IT 170729-80-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimum formulation of aprepitant binary ethosomes gel showed satisfactory phys., mech., rheol. and occlusive properties for transdermal delivery)

IT 170729-80-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimum formulation of aprepitant binary ethosomes gel showed satisfactory phys., mech., rheol. and occlusive properties for transdermal delivery)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)

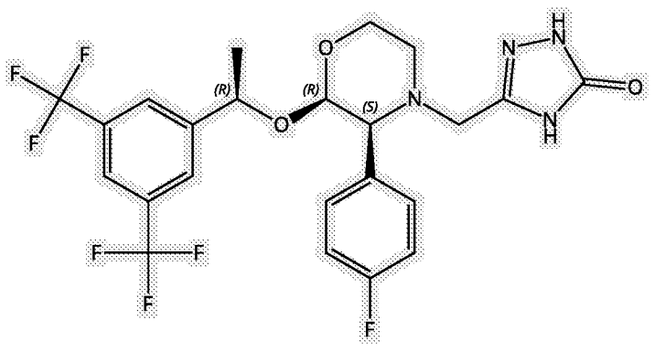


Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:485442 CAPLUS Full-text
DOCUMENT NUMBER: 177:51750
TITLE: Aprepitant Intravenous Emulsion Based on Ion Pairing/Phospholipid Complex for Improving Physical and Chemical Stability During Thermal Sterilization
AUTHOR(S): Zhang, Xinyu; Wei, Ying; Cao, Zhijun; Xu, Ying; Lu, Cong; Zhao, Meiqi; Gou, Jingxin; Yin, Tian; Zhang, Yu;

He, Haibing; Wang, Yanjiao; Tang, Xing
CORPORATE SOURCE: Department of Pharmaceutics, Shenyang Pharmaceutical University, Shenyang, Peop. Rep. China
SOURCE: AAPS PharmSciTech (2020), 21(3), 75
CODEN: AAPHFZ; ISSN: 1530-9932
DIGITAL OBJECT ID: 10.1208/s12249-019-1605-7
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB An aprepitant (APT) cholesteryl hemisuccinate (CHEMS) ion pair complex emulsion (AIPE) with high lecithin content was prepd. to improve sterilization stability through the film dispersion homogenization method; therefore, it could be a promising delivery system of APT. Medium-chain triglycerides (MCT) was selected as the oil phase to improve the soly. and stability of APT in oil phase. DSC, XRD, FT-IR, and 1H-NMR spectroscopies confirmed that the APT-CHEMS ion pair (AIP) was formed between CHEMS and APT. The formation of AIP significantly increased the hydrophobicity of APT, allowing it to be completely embedded in the oil phase core to improve chem. stability and decrease hydrolysis of APT in the water phase. Also, CHEMS had a strong affinity with lecithin and could stabilize lipid membranes, forming a stronger and thicker interface membrane to increase the phys. stability of AIPE. As a result, AIPE could withstand autoclaving at 120°C for 8 min without any change of particle size or content. Furthermore, AIPE with a potential of - 53.4 mV remained stable through spatial repulsion during sterilization. The encapsulation efficiency of AIPE was over 90% and the particle size was 106.8 ± 65.62 nm(0.286). Pharmacokinetic study in rats was comparable with that of CINVANTI which yielded a relative bioavailability of 114.31% indicating that the AIPE had similar pharmacokinetic processes in vivo with the analog of CINVANTI. The AUC0-t of the AIPE was 4.31-fold that of the APT soln.
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Egg yolk lecithins
Medium-chain glycerides
Soya lecithins
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)
IT 170729-80-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)
IT 170729-80-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

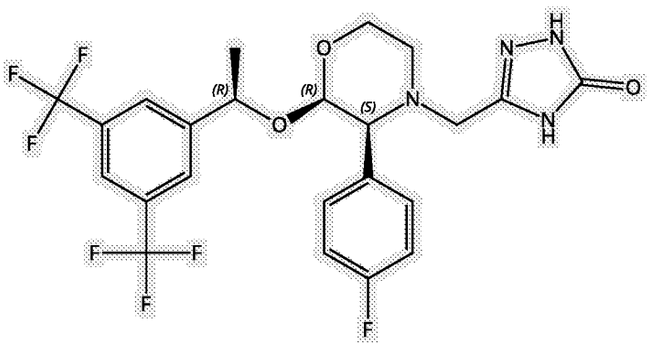
L5 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:456048 CAPLUS Full-text
DOCUMENT NUMBER: 177:51649
TITLE: Small scale design of experiment investigation of equilibrium solubility in simulated fasted and fed intestinal fluid
AUTHOR(S): McPherson, Stephanie; Perrier, Jeremy; Dunn, Claire; Khadra, Ibrahim; Davidson, Scott; Ainousah, Bayan; Wilson, Clive G.; Halbert, Gavin
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK
SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (2020), 150, 14-23
CODEN: EJPBEL; ISSN: 0939-6411
DIGITAL OBJECT ID: 10.1016/j.ejpb.2020.01.016
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB It is widely recognized that drug soly. within the gastrointestinal tract (GIT) differs from values detd. in a simple aq. buffer and to circumvent this problem measurement in biorelevant fluids is detd. Biorelevant fluids are complex mixts. of components (sodium taurocholate, lecithin, sodium phosphate, sodium chloride, pancreatin and sodium oleate) at various concns. and pH levels to provide systems simulating fasted (FaSSIF) or fed (FeSSIF) intestinal media. Design of Expt. (DoE) studies have been applied to investigate FaSSIF and FeSSIF and indicate that a drugs equil. soly. varies over orders of magnitude, is influenced by the drug type and individual or combinations of media components, with some of these interactions being drug specific. Although providing great detail on the drug media interactions these studies are resource intensive requiring up to ninety individual expts. for FeSSIF. In this paper a low sample no. or reduced DoE system has been investigated by restricting components with minimal soly. impact to a single value and only investigating variations in the concns. of sodium taurocholate, lecithin, sodium oleate, pH and addnl. in the case of fed media, monoglyceride. This reduces the expts. required to ten (FaSSIF) and nine (FeSSIF). Twelve poorly sol. drugs (Ibuprofen, Valsartan, Zafirlukast, Indomethacin, Fenofibrate, Felodipine, Probucol, Tadalafil, Carvedilol, Aprepitant, Bromocriptine and Itraconazole) were investigated and the results compared to published DoE studies and literature soly. values in human intestinal fluid (HIF), FaSSIF or FeSSIF. The soly. range detd. by the reduced DoE is statistically equiv. to the larger scale published DoE results in over eighty five percent of the cases. The reduced DoE range also covers HIF, FaSSIF or FeSSIF literature soly. values. In addn. the reduced DoE provides lowest measured soly. values that agree with the published DoE values in ninety percent of the cases. However, the reduced DoE only identified single and in some cases none of the major components influencing soly. in contrast to the larger published DoE studies which identified multiple individual components and component interactions. The identification of significant components within the reduced DoE was also dependent upon the drug and system under investigation. The study demonstrates that the lower exptl. no. reduces statistical power of the DoE to resolve the impact of media components on soly. However, in a situation where only the soly. range is required the reduced DoE can provide the desired information, which will be of benefit during in vitro development studies. Further refinements are possible to extend the reduced DoE protocol to improve biorelevance and application into areas such as PBPK modeling.
CC 63-5 (Pharmaceuticals)
IT Lecithins
Monoglycerides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(small scale design of expt. investigation of equil. soly. in simulated fasted and fed intestinal fluid)
IT 53-86-1 143-19-1 145-42-6 15687-27-1 23288-49-5 25614-03-3

49562-28-9 72509-76-3 72956-09-3 84625-61-6 107753-78-6
137862-53-4 170729-80-3 171596-29-5
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale design of expt. investigation of equil. soly. in simulated fasted and fed intestinal fluid)

IT 170729-80-3
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale design of expt. investigation of equil. soly. in simulated fasted and fed intestinal fluid)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:418384 CAPLUS Full-text
DOCUMENT NUMBER: 172:285814
TITLE: Preparation of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents
INVENTOR(S): Martin, Brice; Mignet, Nathalie; Corvis, Yohann
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique (CNRS), Fr.; Universite Paris Descartes; Institut National de la Sante et de la Recherche Medicale (INSERM); Ecole Nat Superieure de Chimie Paris
ULTIMATE OWNER: PARIS CITE UNIVERSITY; CHIMIE PARISTECH (ECOLE NATIONALE SUPERIEURE DE CHIMIE DE PARIS); NATIONAL INSTITUTE OF HEALTH AND MEDICAL RESEARCH; CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE
ULTIMATE OWNER STANDARD: Paris Cit3 University; Chimie ParisTech; Inserm; CNRS
SOURCE: PCT Int. Appl., 66pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2020043735	A1	20200305	WO 2019-EP72873	20190827
EP 3616688	A1	20200304	EP 2018-306138	20180827
EP 3843705	A1	20210707	EP 2019-756406	20190827
EP 3843705	B1	20231129		
EP 3843705	C0	20231129		
US 20210315831	A1	20211014	US 2021-17269802	20210219

PRIORITY APPLN. INFO.: EP 2018-306138 A 20180827
WO 2019-EP72873 W 20190827

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2020043735	A1	Dead	20230427
EP 3616688	A1	Dead	20210909
EP 3843705	A1	Indeterminate	20240418
EP 3843705	B1	Indeterminate	20240418
EP 3843705	C0	Alive	20240215
US 20210315831	A1	Alive	20211121

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to a method for manufg. a nanostructured powder comprising nanocryst. agglomerates contg. active pharmaceutical ingredient (API) in its cryst. form, said method comprising (i) Prepg. a first soln. comprising API and an API solvent; (ii) Mixing the first soln. with a second soln. comprising an API antisolvent and optionally a stabilizing agent P1 to obtain a third mixt.; (iii) Evapg. the third mixt. until both the API solvent and the API antisolvent are evapd., advantageously under vacuum; characterized in that when the stabilizing agent P1 is present, the third mixt. has a stabilizing agent P1 to API wt. ratio equal or less than 5, preferably less than 2. The invention also concerns a nanostructured powder and a nanosuspension.

IPCI A61K0009-14 [I]; A61K0009-51 [I]; A61K0031-365 [I]; A61K0031-7048 [I]; A61P0035-00 [I]

IPCR A61K0009-14 [I]; A61K0009-51 [I]; A61K0031-365 [I]; A61K0031-7048 [I]; A61P0035-00 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT Albumins
Asialofetuins
Egg yolk lecithins
Lecithins
Soya phosphatidylcholines
Transferrins
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents)

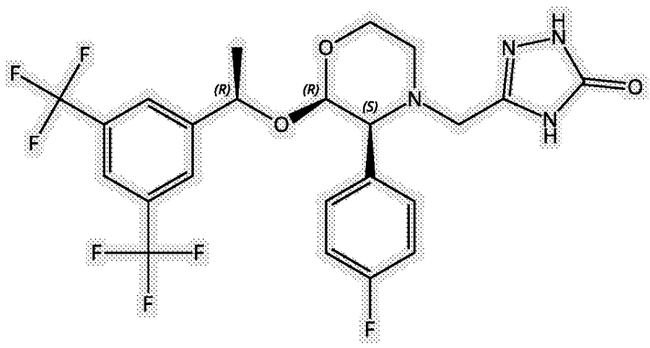
IT 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 50-24-8, Prednisolone 52-01-7, Spironolactone 53-86-1, Indometacin 61-68-7, Mefenamic acid 126-07-8, Griseofulvin 127-40-2, Lutein 137-66-6, Ascorbyl palmitate 153-18-4, Rutin 458-37-7, Curcumin 501-36-0, Resveratrol 520-33-2, Hesperetin 528-48-3, Fisetin 1198-77-2, Monosodium urate 1397-89-3, Amphotericin B 2030-63-9, Clofazimine 2608-24-4, Piposulfan 3681-99-0, Puerarin 7689-03-4, Camptothecin 10238-21-8, Glibenclamide 15307-86-5, Diclofenac acid 15687-27-1, Ibuprofen 17230-88-5, Danazol 19685-09-7, Hydroxycamptothecin 21967-41-9, Baicalin 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22888-70-6, Silybin 22916-47-8, Miconazole 23214-92-8, Doxorubicin 28957-04-2, Oridonin 29990-52-1, Methyltryptophan 31431-39-7, Mebendazole 33069-62-4, Paclitaxel 49562-28-9, Fenofibrate 54965-21-8, Albendazole 59865-13-3, Cyclosporine 63675-72-9, Nisoldipine 66085-59-4, Nimodipine 71125-38-7, Meloxicam 73590-58-6, Omeprazole 73963-72-1, Cilostazole 79902-63-9, Simvastatin 80841-47-0, Asulacrine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 88426-33-9, Buparvaquone 98093-93-7, Riccardin D 114977-28-5, Docetaxel 116122-36-2, Breviscapine 129722-12-9, Aripiprazole 141374-81-4, Tarazepide 145040-37-5, Candesartan cilexetil 146939-27-7, Ziprasidone 147362-57-0, Loviride 153559-49-0, Bexarotene 154598-52-4, Efavirenz 169590-42-5, Celecoxib 170729-80-3, Aprepitant 183133-96-2, Cabazitaxel 206361-99-1, Darunavir 330784-47-9, Avanafil 1257228-26-4, Amoitone B
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen

yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
EP 3616688 A1	EP 2018-306138	Register|Federated Reg.
EP 3843705 A1	EP 2019-756406	Register|Federated Reg.
EP 3843705 B1	EP 2019-756406	Register|Federated Reg.
EP 3843705 C0	EP 2019-756406	Register|Federated Reg.
US 20210315831 A1	US 2021-17269802	Register|Global Dossier
WO 2020043735 A1	WO 2019-EP72873	Register|Global Dossier

L5 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:245679 CAPLUS Full-text
DOCUMENT NUMBER: 172:258881
TITLE: Emulsion containing high proportion emulsifier and preparation method thereof
INVENTOR(S): Niu, Yawei; Xu, Wendong; Tang, Shunzhi; Yuan, Cheng; Fu, Yuping; Guan, Weijian; Wang, Guocai; Mou, Xiaonan; Li, Jirong; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

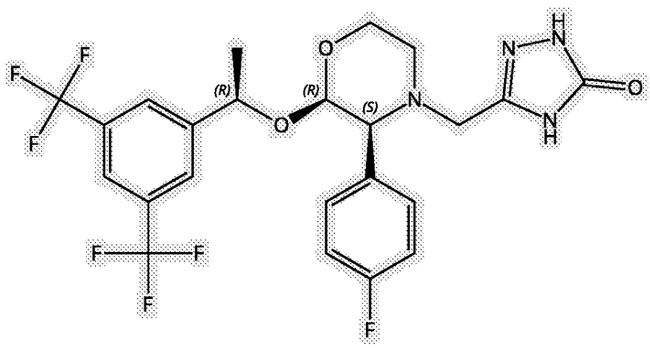
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 110772482	A	20200211	CN 2019-11215436	20191202

PRIORITY APPLN. INFO.: CN 2019-11215436 20191202
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 110772482	A	Dead	20230511

AB The invention discloses an emulsion contg. high proportion emulsifier and prepn. method thereof, which has the advantages of high drug loading and high bioavailability. The emulsion contg. high proportion emulsifier comprises the following raw materials in percentage by wt.: oil phase solvent 10-30%, emulsifier 10-30%, co-emulsifier 1-5%, volatile assistant 1-5%, stabilizer 0.05-0.6%, isoosmotic adjusting agent 1-5%, viscosity regulator 1-10%, active pharmaceutical ingredient 1-5%, and the balance of injection water.
IPCI A61K0009-107; A61K0047-26; A61K0047-44; A61K0047-14; A61K0047-10;

A61K0031-5377
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-10 [I]; A61K0047-14 [I]; A61K0047-26 [I]; A61K0047-44 [I]
CC 63-7 (Pharmaceuticals)
IT Carbohydrates
Castor oil
Egg yolk lecithins
Fish oil
Fructooligosaccharides
Olive oil
Phosphatidylcholines
Phosphatidylglycerols
Soya lecithins
Soybean oil
Triglycerides
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 170729-80-3, Aprepitant 552292-08-7, Rolapitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 110772482 A	CN 2019-11215436	Register|Global Dossier

L5 ANSWER 18 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:1744396 CAPLUS Full-text
DOCUMENT NUMBER: 171:388517
TITLE: Aqueous formulations for insoluble drugs
INVENTOR(S): Chen, Andrew Xian; Islam, Mohammad Saiful; Chu, Jan-Jon; Xu, Jianmin
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2019173526	A1	20190912	WO 2019-US21029		20190306
CA 3088017	A1	20190912	CA 2019-3088017		20190306
AU 2019231699	A1	20200716	AU 2019-231699		20190306
AU 2019231699	B2	20230309			
CN 111867562	A	20201030	CN 2019-80017435		20190306
CN 111867562	B	20230707			
EP 3761961	A1	20210113	EP 2019-764228		20190306
JP 2021515048	T	20210617	JP 2020-570411		20190306
US 20200368159	A1	20201126	US 2020-16993017		20200813
US 11541006	B2	20230103			
PRIORITY APPLN. INFO.:			US 2018-62639710	P	20180307
			WO 2019-US21029	W	20190306

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2019173526	A1	Dead	20221110
CA 3088017	A1	Alive	20201121
AU 2019231699	A1	Alive	20201121
AU 2019231699	B2	Alive	20230316
CN 111867562	A	Alive	20201120
CN 111867562	B	Alive	20230720
EP 3761961	A1	Alive	20210118
JP 2021515048	T	Alive	20210624
US 20200368159	A1	Alive	20221020
US 11541006	B2	Alive	20230119

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2019:1744396

AB This invention relates to clear one-phase liq. formulation vehicles comprising lecithin , MCT, bile salt and water. In an aspect, this invention provides a clear and one-phase aq. liq. compn. comprising: a lecithin , MCT, bile salt, and water, in a four-component LMBW compn., their prepn. and applications in drug formulations.

IPCI A61K0009-08 [I]; A61K0009-00 [I]; A61K0047-14 [I]; A61K0047-54 [I]

IPCR A61K0009-08 [I]; A61K0009-00 [I]; A61K0047-14 [I]; A61K0047-54 [I]

CC 63-6 (Pharmaceuticals)

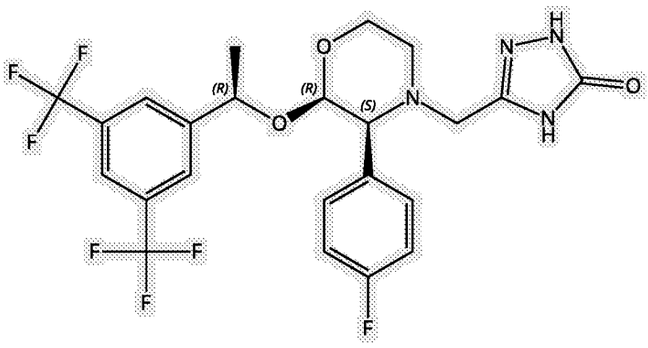
IT Bile salts
Egg yolk lecithins
Lecithins
Medium-chain glycerides
Polyoxyalkylenes
Sesame oil
Soya phosphatidylcholines
Soybean oil
Tocopherols
RL: MOA (Modifier or additive use); USES (Uses)
(aq. formulations for insol. drugs)

IT 52-21-1, Prednisolone Acetate 57-83-0, Progesterone, biological studies 59-92-7, Levodopa, biological studies 60-18-4, L-Tyrosine, biological studies 84-80-0, Phytonadione 501-36-0, Resveratrol 1951-25-3, Amiodarone 2078-54-8, Propofol 7553-56-2, Iodine, biological studies 7689-03-4, Camptothecin 12633-72-6, Amphotericin 15687-27-1, Ibuprofen 33069-62-4, Paclitaxel 59865-13-3, Cyclosporine 81103-11-9, Clarithromycin 84625-61-6, Itraconazole 100286-90-6, Irinotecan hydrochloride 169590-42-5, Celecoxib 170729-80-3, Aprepitant 171228-49-2, Posaconazole
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aq. formulations for insol. drugs)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aq. formulations for insol. drugs)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2019231699 A1	AU 2019-231699	Register
AU 2019231699 B2	AU 2019-231699	Register
CA 3088017 A1	CA 2019-3088017	Register
CN 111867562 A	CN 2019-80017435	Register|Global Dossier
CN 111867562 B	CN 2019-80017435	Register|Global Dossier
EP 3761961 A1	EP 2019-764228	Register|Federated Reg.
JP 2021515048 T	JP 2020-570411	Register|Global Dossier
US 11541006 B2	US 2020-16993017	Register|Global Dossier
US 20200368159 A1	US 2020-16993017	Register|Global Dossier
WO 2019173526 A1	WO 2019-US21029	Register|Global Dossier

L5 ANSWER 19 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:1475315 CAPLUS Full-text
DOCUMENT NUMBER: 171:221789
TITLE: Method of administering emulsion formulations of an NK-1 receptor antagonist
INVENTOR(S): Ottoboni, Thomas B.; Quart, Barry D.
PATENT ASSIGNEE(S): Heron Therapeutics, Inc., USA
ULTIMATE OWNER: HERON THERAPEUTICS, INC.
ULTIMATE OWNER STANDARD: HERON THERAPEUTICS, INC.
SOURCE: U.S. Pat. Appl. Publ., 23pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

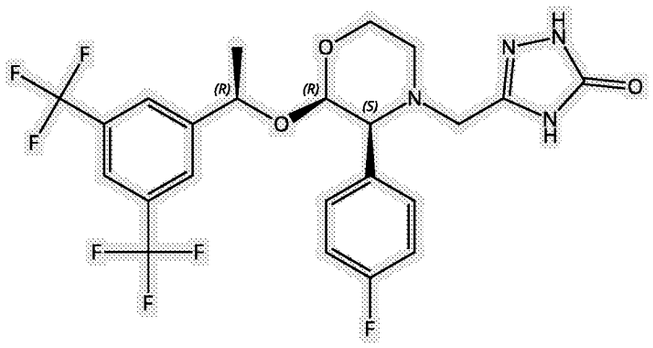
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20190231688	A1	20190801	US 2019-16261459		20190129
WO 2019152430	A1	20190808	WO 2019-US15708		20190129
AU 2019214872	A1	20200806	AU 2019-214872		20190129
EP 3746051	A1	20201209	EP 2019-705044		20190129
JP 2021512091	T	20210513	JP 2020-541556		20190129
PRIORITY APPLN. INFO.:			US 2018-62624050	P	20180130
			WO 2019-US15708	W	20190129

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20190231688	A1	Alive	20230914
WO 2019152430	A1	Dead	20220929
AU 2019214872	A1	Dead	20230803
EP 3746051	A1	Dead	20211117
JP 2021512091	T	Alive	20210520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2019:1475315
AB Disclosed herein are methods of administering pharmaceutical formulations of a neurokinin-1 (NK-1) receptor antagonist to a subject in need of

treatment of emesis.
IPCI A61K0009-107 [I]; A61K0031-5377 [I]; A61K0009-00 [I]; A61K0047-24 [I];
A61K0031-573 [I]; A61K0047-44 [I]; A61K0047-10 [I]; A61K0047-12 [I];
A61K0047-26 [I]; A61K0031-496 [I]
IPCR A61K0009-107 [I]; A61K0009-00 [I]; A61K0031-496 [I]; A61K0031-5377 [I];
A61K0031-573 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I];
A61K0047-26 [I]; A61K0047-44 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
IT Alcohols
Egg yolk lecithins
Phospholipids
Soybean oil
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor
antagonist)
IT 2392-39-4, Dexamethasone sodium phosphate 147116-64-1, Ezlopitant
147116-67-4, Maropitant 170729-80-3, Aprepitant 290296-68-3,
Befetupitant 290297-26-6, Netupitant 334476-46-9, Vestipitant
414910-27-3, Casopitant 552292-08-7, Rolapitant 579475-18-6,
Orvepitant 860642-69-9, Ser-lopitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor
antagonist)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor
antagonist)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2019214872 A1	AU 2019-214872	Register
EP 3746051 A1	EP 2019-705044	Register|Federated Reg.
JP 2021512091 T	JP 2020-541556	Register|Global Dossier
US 20190231688 A1	US 2019-16261459	Register|Global Dossier
WO 2019152430 A1	WO 2019-US15708	Register|Global Dossier

L5 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:425605 CAPLUS Full-text
DOCUMENT NUMBER: 170:406568
TITLE: Aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its preparation method and application
INVENTOR(S): Xu, Wendong; Tang, Shunzhi; Yuan, Cheng; Niu, Yawei;

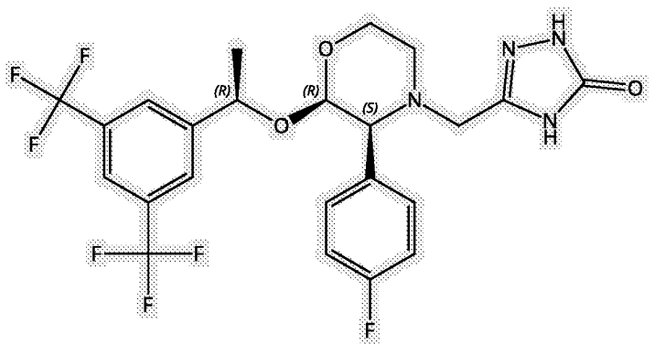
Fu, Yuping; Wang, Guocai; Guan, Weijian; Mou, Xiaonan; He, Jie; Li, Jirong; Yang, Yuqiong; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109432002	A	20190308	CN 2018-11587906	20181225

PRIORITY APPLN. INFO.: CN 2018-11587906 20181225
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109432002	A	Dead	20220825

OTHER SOURCE(S): CASFORMULTNS 2019:425605
AB An aprepitant emulsion useful for reducing nausea and vomiting in the pre and post-chemotherapy of the tumor, improving immunity and nutritional support of the tumor patient, and reducing acute and delayed nausea and vomiting in high-dose cisplatin combined with high-dose sensitized cancer chemotherapy is provided. The aprepitant emulsion comprises the following components in mass %: 0.05-2.5 of aprepitant, 10-30 of oil phase solvent, 0.8-18 of emulsifier, 0.03-0.6 of stabilizer, 1-5 of isotonicity regulator, and further comprising a pH regulator, balance being purified water, where the pH of the emulsion is 5.5-8. The prepn. method comprises the following steps: (1) weighing the oil phase solvent, emulsifier and antioxidant, heating in a water bath, dissolving all the emulsifiers, and adding aprepitant and dissolving well to obtain an oil phase; (2) weighing stabilizer, isotonicity regulator, pH regulator, adding to purified water, and heating in water bath to obtain water phase; (3) slowly adding the oil phase to the water phase, shearing at high speed under stirring, adding the remaining purified water with high speed stirring to obtain colostrum; (4) subjecting obtained colostrum to microfluidization to obtain a final emulsion; and (5) filling the colostrum with nitrogen, sealing and sterilizing in a rotary sterilizing pot to obtain an aprepitant emulsion.
IPCI A61K0009-107; A61K0031-5377; A23L0033-10; A23P0010-00; A61P0001-08; A61P0035-00
IPCR A61K0009-107 [I]; A23L0033-10 [I]; A23P0010-00 [I]; A61K0031-5377 [I]; A61P0001-08 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Egg yolk lecithins
Fatty acids
Phosphatidylcholines
Phosphatidylglycerols
Soya lecithins
Tocopherols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)
IT 50-99-7, D-Glucose, biological studies 56-81-5, Glycerin, biological studies 69-65-8, D-Mannitol 112-80-1, Oleic acid, biological studies 143-19-1, Sodium oleate 7631-90-5, Sodium bisulfite 7647-14-5, Sodium chloride, biological studies 7681-57-4, Sodium metabisulfite 7772-98-7, Sodium thiosulfate 9005-65-6, Polysorbate 80 106392-12-5, Poloxamer 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109432002 A	CN 2018-11587906	Register|Global Dossier

L5 ANSWER 21 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:340286 CAPLUS Full-text
DOCUMENT NUMBER: 170:348016
TITLE: Aprepitant intravenous emulsion for treating chemotherapy-induced nausea and vomiting, and its preparation method
INVENTOR(S): Yuan, Cheng; Xu, Wendong; Tang, Shunzhi; He, Jie; Niu, Yawei; Fu, Yuping; Wang, Guocai; Guan, Weijian; Mou, Xiaonan; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109364023	A	20190222	CN 2018-11588409	20181225

PRIORITY APPLN. INFO.: CN 2018-11588409 20181225
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109364023	A	Transitional	20240222

OTHER SOURCE(S): CASFORMULTNS 2019:340286
AB The present invention relates to an i.v. emulsion contg. the following components by mass percentage: 0.05-3% of aprepitant, 5-30% of oil phase solvent, 1.2-18% of emulsifier, 0.03-0.6% of stabilizer, 1-5% of isotonicity adjusting agent, and 0.02-0.5% of antioxidant. The i.v. emulsion further contains a pH adjusting agent and water for injection, where the pH of the i.v. emulsion is 5.5-8.0. The i.v. emulsion has greatly improved the clin. safety, and is utilized for treating acute and delayed nausea and vomiting caused by high-dose cisplatin combined with high-dose sensitizing cancer chemotherapy and reducing nausea and vomiting in the early and middle stages of tumor chemotherapy.
IPCI A61K0009-107; A61K0047-24; A61K0047-12; A61K0031-5377; A61P0035-00; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
IT Castor oil

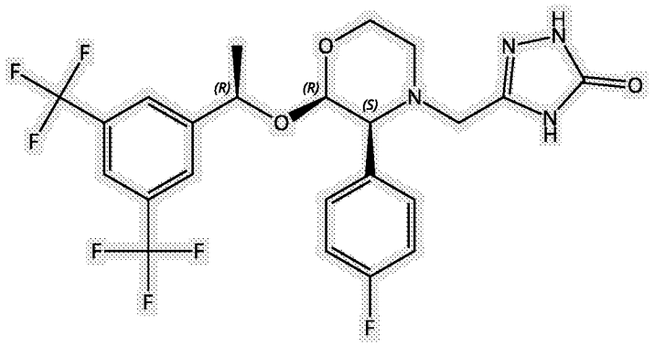
Egg yolk lecithins
Fish oil
Olive oil
Phosphatidylcholines
Phosphatidylglycerols
Soya phospholipids
Soybean oil
Teaseed oil
Tocopherols
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109364023 A	CN 2018-11588409	Register|Global Dossier

L5 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:2521745 CAPLUS Full-text
DOCUMENT NUMBER: 170:140265
TITLE: High stability aprepitant nano-emulsion and preparation method thereof
INVENTOR(S): Fu, Jifeng; Wang, Wenjuan; Guo, Jia; Zhang, Liancheng
PATENT ASSIGNEE(S): Beijing Ruiyue Biomedical Technology Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: BEIJING RUIYUE BIOLOGY MEDICAL TECH
ULTIMATE OWNER STANDARD: BEIJING RUIYUE BIOLOGY MEDICAL TECH
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109010272	A	20181218	CN 2018-11133738	20180927

PRIORITY APPLN. INFO.: CN 2018-11133738 20180927
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109010272	A	Dead	20230323

OTHER SOURCE(S): CASFORMULTNS 2018:2521745

AB The invention discloses a nano-emulsion of aprepitant as shown in structure I and prepn. method thereof. The nano-emulsion is prepd. with the following components in percentage by wt.: aprepitant 0.05-1.5%, soybean oil 2-20%, egg yolk lecithin 5-20%, ethanol 0.5-5%, sodium oleate 0.05-2%, sucrose 2-10%, and water for injection 40-80%. The sodium oleate is added into the oil phase to rapidly stabilize the oil droplets when contacts with the aq. phase, thereby increasing the stability of the nano-emulsion.

IPCI A61K0009-107; A61K0047-12; A61K0047-44; A61K0047-24; A61K0047-10; A61K0047-26; A61K0031-5377; A61P0001-08

IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]; A61P0001-08 [I]

CC 63-6 (Pharmaceuticals)

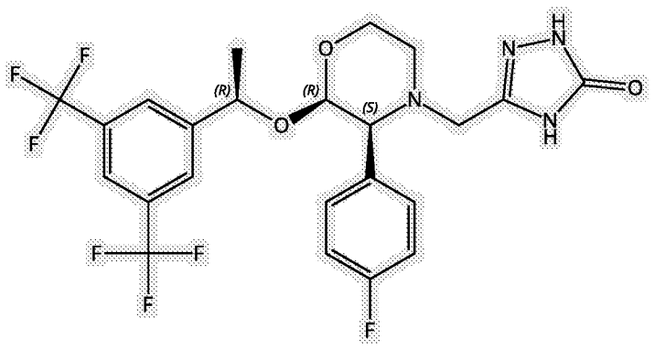
IT Egg yolk lecithins
Soybean oil
RL: MOA (Modifier or additive use); NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)

IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)

IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109010272 A	CN 2018-11133738	Register|Global Dossier

L5 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:2521716 CAPLUS Full-text
DOCUMENT NUMBER: 170:154781
TITLE: Fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting
INVENTOR(S): Liu, Jie; Liu, Yun; Zhou, Lili
PATENT ASSIGNEE(S): Fubicheng (Shanghai) Pharmaceutical Technology Co.,

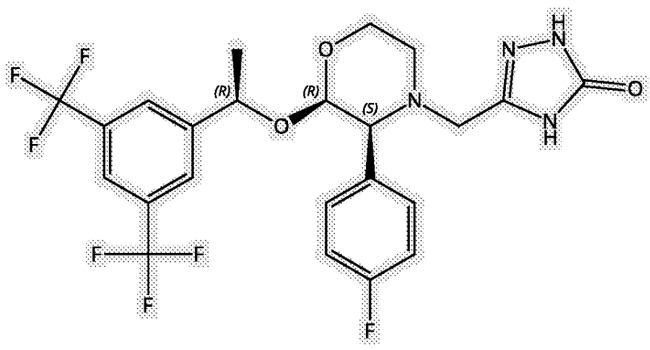
Ltd., Peop. Rep. China
ULTIMATE OWNER: FUBICHENG SHANGHAI MEDICINE TECH
ULTIMATE OWNER STANDARD: FUBICHENG SHANGHAI MEDICINE TECH
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109010269	A	20181218	CN 2018-10979074	20180827
CN 109010269	B	20210420		

PRIORITY APPLN. INFO.: CN 2018-10979074 20180827
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109010269	A	Alive	20201121
CN 109010269	B	Alive	20210430

OTHER SOURCE(S): CASFORMULTNS 2018:2521716
AB The title fat emulsion injection of aprepitant for treating chemotherapy-induced nausea and vomiting is prepd. from aprepitant, egg yolk lecithin , oil for injection (coconut oil, soybean oil, or olive oil), glycine, polyvinylpyrrolidone, water for injection, sodium oleate, and C1-5 short-chain alc. (ethanol or propanediol). The inventive prepn. has improved stability and reduced vascular irritation.
IPCI A61K0009-107; A61K0031-5377; A61K0047-18; A61K0047-32; A61K0031-439; A61K0009-08; A61P0001-08
IPCR A61K0009-107 [I]; A61K0009-08 [I]; A61K0031-439 [I]; A61K0031-5377 [I]; A61K0047-18 [I]; A61K0047-32 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Lipoid E 80; fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109010269 A	CN 2018-10979074	Register|Global Dossier
CN 109010269 B	CN 2018-10979074	Register|Global Dossier

L5 ANSWER 24 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:1210583 CAPLUS Full-text
DOCUMENT NUMBER: 169:118657
TITLE: Novel formulations of aprepitant
INVENTOR(S): Titley, Paul Charlton
PATENT ASSIGNEE(S): N4 Pharma UK Limited, UK
ULTIMATE OWNER: N4 PHARMA UK; N4 PHARMA
ULTIMATE OWNER STANDARD: N4 PHARMA UK; N4 PHARMA
SOURCE: PCT Int. Appl., 85pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2018115888	A1	20180628	WO 2017-GB53864		20171221
PRIORITY APPLN. INFO.:			GB 2016-21867	A	20161221
			GB 2017-16293	A	20171005

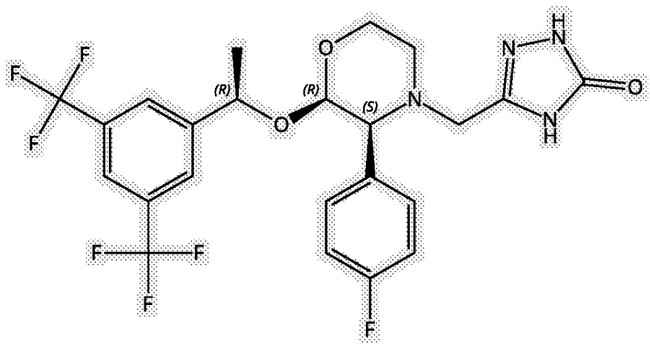
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2018115888	A1	Dead	20210826

OTHER SOURCE(S): CASFORMULTNS 2018:1210583
AB The invention provides a pharmaceutical compn. which comprises: a first fraction comprising aprepitant; and a controlled-release fraction comprising aprepitant.
IPCI A61K0009-20 [I]; A61K0009-24 [I]; A61K0031-00 [I]
IPCR A61K0009-20 [I]; A61K0009-24 [I]; A61K0031-00 [I]
CC 63-1 (Pharmaceuticals)
IT Acrylic polymers
Activated charcoal
Alkali metal bicarbonates
Alkali metal carbonates
Carnauba wax
Fatty acids
Gelatins
Hydrogenated vegetable oils
Lecithins
Paraffin waxes
Polyoxyalkylenes
Polysaccharides
Shellac
Silica gel
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel formulations of aprepitant)
IT 50-02-2, Dexamethasone 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-35-1, Synovir 50-44-2, Mercaptopurine 50-69-1, Ribose 50-76-0, Dactinomycin 52-24-4, Thiotepa 53-03-2, Prednisone 55-86-7, Mechlorethamine hydrochloride 56-40-6, Glycine, biological studies 57-11-4, Stearic acid, biological studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-88-5, Cholesterol, biological studies 59-23-4, Galactose, biological studies 61-90-5, Leucine, biological studies 63-42-3, Lactose 67-68-5, Sclerosol, biological studies 69-65-8, Mannitol 69-79-4, Maltose 70-00-8, Trifluridine 77-92-9, Citric acid, biological studies 79-41-4, biological studies 106-60-5, Aminolevulinic acid 112-92-5, Stearyl alcohol 127-07-1, Hydrea 134-62-3, OFF 143-67-9, Vinblastine sulfate 144-55-8, Sodium bicarbonate, biological studies 147-81-9, Arabinose 148-82-3, Alkeran 151-21-3, Sodium lauryl sulphate, biological studies 154-42-7, Tabloid 154-93-8, Carmustine 305-03-3, Ambochlorin 320-67-2, Azacitidine 366-70-1, Procarbazine hydrochloride 555-44-2, Glyceryl tripalmitate 557-04-0, Magnesium stearate 585-88-6, Maltitol 595-33-5, Megestrol acetate 1323-83-7, Glyceryl distearate 1327-43-1, Aluminum Magnesium silicon oxide 1327-53-3, Arsenic Trioxide 1492-18-8, Leucovorin calcium 2068-78-2, Vincristine sulfate 2068-78-2D, Vincristine sulfate, liposomes 2353-33-5, Dacogen

2921-88-2, Cyfos 3543-75-7, Treanda 4105-38-8, Uridine triacetate 4342-03-4, Dacarbazine 7447-40-7, Potassium chloride, biological studies 7447-41-8, Lithium chloride, biological studies 7487-88-9, Magnesium sulphate, biological studies 7631-86-9, Silica, biological studies 7647-14-5, Sodium chloride, biological studies 7757-82-6, Sodium sulphate, biological studies 7778-80-5, Potassium sulphate, biological studies 7786-30-3, Magnesium chloride, biological studies 9000-30-0, Guar gum 9000-69-5, Pectin 9000-92-4, Amylase 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Carboxymethylcellulose 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, ethers 9004-35-7 9004-38-0, Cellulose acetate phthalate 9004-57-3, Ethyl cellulose 9004-62-0, Hydroxyethylcellulose 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9004-67-5, Methylcellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-38-3, Sodium alginate 9032-42-2, Hydroxyethyl-methylcellulose 9050-04-8 9050-31-1, Hydroxypropylmethylcellulose phthalate 9063-38-1, Sodium starch glycolate 10377-48-7, Lithium sulphate 11056-06-7, Bleomycin 11138-66-2, Xanthan gum 13010-47-4, Lomustine 13311-84-7, Flutamide 14807-96-6, Talc, biological studies 18641-57-1 19171-19-8, Pomalidomide 19767-45-4, Mesna 20830-81-3, Rubidomycin 23214-92-8, Doxil 24584-09-6, Totect 25086-15-1, Methacrylic acid-methyl methacrylate co-polymer 25212-88-8, Methacrylic acid-ethyl acrylate copolymer 25316-40-9, Doxorubicin hydrochloride 25322-68-3, Polyethylene glycol 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26833-87-4, Omacetaxine mepesuccinate 31566-31-1, Glyceryl monostearate 33419-42-0, Etoposide 37380-42-0, Amberlite XAD 4 37380-43-1, Amberlite XAD 7 41575-94-4, Carboplatin 50935-57-4, Methyl vinyl ether-maleic acid copolymer ethyl ester 53237-50-6 54182-62-6, Polacrilin potassium 54578-91-5, Methyl vinyl ether-maleic acid copolymer butyl ester 56038-13-2, Sucralose 56390-09-1, Ellence 57248-88-1, Aredia 57852-57-0, Idamycin 61825-94-3, Eloxatin 64519-82-0, Isomalt 70476-82-3, Mitoxantrone hydrochloride 70535-77-2, Hydroxypropylmethylcellulose acetate succinate 74381-53-6, Leuprolide acetate 74811-65-7, Croscarmellose sodium 75607-67-9, Fludara 82640-04-8, Evista 83712-60-1, Defibrotide Sodium 84449-90-1, Keoxifene 85622-93-1, Methazolastone 89778-26-7, Fareston 90357-06-5, Bicalutamide 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 98530-12-2, Interferon Alfa-2b 99011-02-6, Aldara 99614-01-4, Ondansetron hydrochloride 100286-90-6, Camptosar 100286-90-6D, Irinotecan hydrochloride, liposomes 104219-63-8, Amberlite XAD 16 108736-35-2, Somatuline Depot 110942-02-4, Aldesleukin 112809-51-5, Femara 114899-77-3, Trabectedin 114977-28-5, Docetaxel 117091-64-2, Etopophos 118072-93-8, Zoledronic acid 119413-54-6, Hycamtin 120511-73-1, Anastrozole 121181-53-1, Filgrastim 122111-03-9, Gemcitabine hydrochloride 122312-54-3 123119-31-3 123318-82-1, Clofarabine 125317-39-7, Navelbine 127984-74-1, Lanreotide acetate 128517-07-7, Istodax 129453-61-8, Faslodex 130167-69-0, Oncaspar 134774-45-1, Elitek 135729-62-3, Palonosetron hydrochloride 145781-92-6, Goserelin acetate 146464-95-1, Folotyn 148618-33-1, Ambersorb 572 148879-45-2, Ambersorb 563 149003-01-0, Dexrazoxane hydrochloride 149647-78-9, Vorinostat 150399-23-8, Alimta 153559-49-0, Bexarotene 154229-18-2, Abiraterone Acetate 154361-50-9, Capecitabine 159351-69-6, Everolimus 162394-19-6, Kepivance 162635-04-3, Temsirolimus 170729-80-3, Aprepitant 173146-27-5, Denileukin Diftitox 179324-69-7, Bortezomib 180288-69-1, Herceptin 183133-96-2, Cabazitaxel 183204-72-0, Tipiracil hydrochloride 183319-69-9, Erlotinib hydrochloride 184475-35-2, Gefitinib 191732-72-6, Lenalidomide 192391-48-3, Bexxar 205923-56-4, Cetuximab 206181-63-7, Ibritumomab Tiuxetan 208921-02-2, Tositumomab 208921-02-2D, Tositumomab, Iodine I-131 214766-78-6, Degarelix 215647-85-1, Peginterferon Alfa-2b 216503-57-0, Alemtuzumab 216974-75-3, Avastin 219989-84-1, Ixabepilone 220127-57-1, Gleevec 220578-59-6, Gemtuzumab 290297-26-6, Akynzeo 302962-49-8, Dasatinib 319460-85-0, Axitinib 339177-26-3, Panitumumab 341031-54-7, Sunitinib malate 380610-27-5, Perjeta 380843-75-4, Bosulif 388082-77-7, Lapatinib ditosylate 400046-53-9, Ozogamicin 404950-80-7, Farydak 417716-92-8, Lenvima 441045-17-6, Eribulin mesylate 443913-73-3, Vandetanib 477202-00-9, Ipilimumab 496775-62-3, Eltrombopag Olamine 541502-14-1, Siltuximab 571190-30-2, Ibrance 615258-40-7, Denosumab 635702-64-6, Pazopanib hydrochloride 641571-10-0, Nilotinib 679818-59-8, Arzerra 733030-01-8, Lonsurf 755037-03-7, Regorafenib 763113-22-0, Lynparza 843613-19-4, Ambersorb 348F 849217-68-1,

Cabometyx 850140-72-6, Gilotrif 850140-73-7, Afatinib dimaleate
853426-35-4, Blinatumomab 857890-39-2, Lenvatinib mesylate
858102-79-1, Rolapitant hydrochloride 866323-14-0, Beleodaq
868540-17-4, Carfilzomib 870281-82-6, Idelalisib 871700-17-3, Mekinist
877399-52-5, Crizotinib 879085-55-9, Erivedge 906805-06-9, Necitumumab
910046-32-1, Gardasil 912337-47-4, Cervarix 914088-09-8, Adcetris
915087-33-1, Enzalutamide 915296-00-3, Elotuzumab 917381-47-6,
Provenge 918504-65-1, Vemurafenib 930113-49-8, CAPOX
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel formulations of aprepitant)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel formulations of aprepitant)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
WO 2018115888 A1	WO 2017-GB53864	Register|Global Dossier

L5 ANSWER 25 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2017:1728289 CAPLUS Full-text
DOCUMENT NUMBER: 168:9512
TITLE: Nanocrystal composition for improving oral absorption of insoluble drug
INVENTOR(S): Liu, Yan; Li, Xueping; Li, Xinru; Zhou, Yanxia
PATENT ASSIGNEE(S): Peking University, Peop. Rep. China
ULTIMATE OWNER: PEKING UNIVERSITY
ULTIMATE OWNER STANDARD: Peking University
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 107303272	A	20171031	CN 2016-10239333	20160418

PRIORITY APPLN. INFO.: CN 2016-10239333 20160418
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 107303272	A	Dead	20220527

OTHER SOURCE(S): CASFORMULTNS 2017:1728289
AB The title compn. is composed of an insol. drug, a stabilizer, the ligand of the specific receptor expressed by intestinal epithelial cell and/or substrate of transporter and optional pharmaceutically acceptable

auxiliary, and is prepd. by prepg. into a suspension and lyophilizing. The expt. proves that the compn. can remarkably improve the oral absorption of the insol. drug so as to provide the prepn. strategy for insol. drug oral administration.

IPCI A61K0009-10; A61K0009-19; A61K0047-10; A61K0047-42; A61K0047-22; A61K0047-26; A61K0047-18; A61K0047-24; A61K0047-38; A61K0047-32; A61K0031-4745; A61K0031-337; A61K0031-7048; A61K0031-436; A61K0031-5377; A61K0031-357

IPCR A61K0009-10 [I]; A61K0009-19 [I]; A61K0031-337 [I]; A61K0031-357 [I]; A61K0031-436 [I]; A61K0031-4745 [I]; A61K0031-5377 [I]; A61K0031-7048 [I]; A61K0047-10 [I]; A61K0047-18 [I]; A61K0047-22 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-32 [I]; A61K0047-38 [I]; A61K0047-42 [I]

CC 63-6 (Pharmaceuticals)

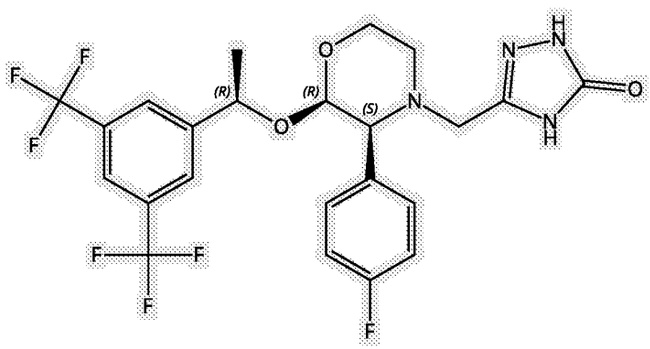
IT Amino acids
Dipeptides
Ethoxylated hydrogenated castor oil
Lecithins
Polyoxyalkylenes
Soya phospholipids
Transferrins
Tripeptides
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanocrystal compn. for improving oral absorption of insol. drug)

IT 50-02-2, Dexamethasone 50-04-4, Cortisone acetate 426-13-1, Fluorometholone 458-37-7, Curcumin 15687-27-1, Ibuprofen 19685-09-7, 10-Hydroxycamptothecin 22888-70-6, Silibinin 25316-40-9, Adriamycin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34368-04-2, Dobutamine 35354-74-6, Honokiol 49562-28-9, Fenofibrate 51333-22-3, Budesonide 59865-13-3, Cyclosporin A 65666-07-1, Silymarin 80474-14-2, Fluticasone propionate 84625-61-6, Itraconazole 91421-42-0, 9-Nitrocamptothecin 104987-11-3, Tacrolimus 114977-28-5, Docetaxel 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanocrystal compn. for improving oral absorption of insol. drug)

IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanocrystal compn. for improving oral absorption of insol. drug)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

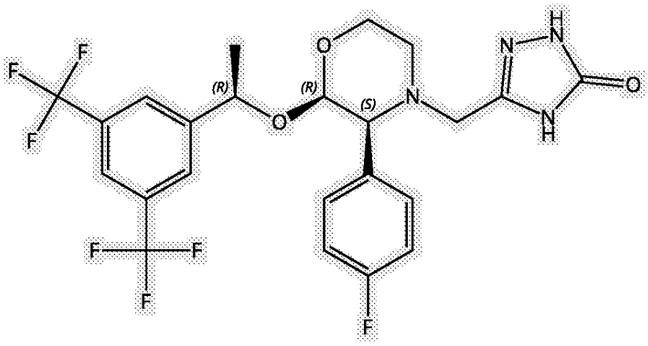
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER

L5 ANSWER 26 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2017:1554024 CAPLUS Full-text
DOCUMENT NUMBER: 168:18112
TITLE: Biorelevant Drug Solubility Enhancement Modeled by a Linear Solvation Energy Relationship
AUTHOR(S): Niederquell, Andreas; Kuentz, Martin
CORPORATE SOURCE: Institute of Pharma Technology, University of Applied Sciences and Arts Northwestern Switzerland, Muttenz, 4132, Switz.
SOURCE: Journal of Pharmaceutical Sciences (Philadelphia, PA, United States) (2018), 107(1), 503-506
CODEN: JPMSAE; ISSN: 0022-3549
DIGITAL OBJECT ID: 10.1016/j.xphs.2017.08.017
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB It is for the pharmaceutical sciences of vital importance to understand how drugs are solubilized in biorelevant media. However, the complexity of fasted state simulated intestinal fluid (FaSSIF) has so far hampered adequate soly. modeling. The present study focuses on apparently neutral compds. at physiol. pH and a linear free energy relationship is introduced for biorelevant drug solubilization. Based on literature data of 40 compds., the Abraham solvation descriptors were calcd. from chem. structure to then predict the ratio of soly. enhancement log(SE) in FaSSIF compared to aq. buffer soly. at pH 6.5. A suitable model was obtained with R2 of 0.810 and notable were esp. the pos. effect of McGowan's characteristic vol. and the neg. effect of drug basicity. A neg. influence on log(SE) was further evidenced for dipolarity/polarizability and for the excess molar refraction descriptor. A pos. solubilization effect was obtained for drug acidity and hence the tendency for proton donation, which was likely due to the different proton-accepting moieties of taurocholic acid and lecithin that are both present in the mixed colloids of FaSSIF. Overall, an improved understanding was achieved regarding the mol. features that are driving drug solubilization in biorelevant media.
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Lecithins
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biorelevant drug soly. enhancement modeled by a linear solvation energy relationship)
IT 50-02-2, Dexamethasone 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies 52-01-7, Spironolactone 53-03-2, Prednisone 53-16-7, Estrone, biological studies 57-41-0, Phenytoin 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 58-32-2, Dipyridamole 58-94-6, Chlorothiazide 81-24-3, Taurocholic acid 81-81-2, Warfarin 84-17-3, Dienestrol 126-07-8, Griseofulvin 298-46-4, Carbamazepine 439-14-5, Diazepam 846-49-1, Lorazepam 17230-88-5 23288-49-5, Probucol 39562-70-4, Nitrendipine 49562-28-9, Fenofibrate 51803-78-2, Nimesulide 54965-21-8, Albendazole 55268-74-1 59865-13-3, Cyclosporine 65646-68-6, Fenretinide 70288-86-7, Ivermectin 72509-76-3 73963-72-1, Cilostazole 75330-75-5, Lovastatin 95233-18-4, Atovaquone 103577-45-3, Lansoprazole 124423-84-3, Panadiplon 138402-11-6 154598-52-4 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 170729-80-3, Aprepitant 192725-17-0, Lopinavir 262352-17-0, Torcetrapib
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biorelevant drug soly. enhancement modeled by a linear solvation energy relationship)
IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biorelevant drug soly. enhancement modeled by a linear solvation energy relationship)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX

NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2017:1232902 CAPLUS Full-text
DOCUMENT NUMBER: 167:591636
TITLE: Influence of Physiological Gastrointestinal Surfactant Ratio on the Equilibrium Solubility of BCS Class II Drugs Investigated Using a Four Component Mixture Design
AUTHOR(S): Zhou, Zhou; Dunn, Claire; Khadra, Ibrahim; Wilson, Clive G.; Halbert, Gavin W.
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK
SOURCE: Molecular Pharmaceutics (2017), 14(12), 4132-4144
CODEN: MPOHBP; ISSN: 1543-8384
DIGITAL OBJECT ID: 10.1021/acs.molpharmaceut.7b00354
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The absorption of poorly water-sol. drugs is influenced by the luminal gastrointestinal fluid content and compn. which controls soly. Simulated intestinal fluids have been introduced into dissoln. testing including endogenous amphiphiles and digested lipids at physiol. levels; however, in vivo individual variation exists in the concns. of these components, which will alter drug absorption through an effect on soly. The use of a factorial design of expt. and varying media by introducing different levels of bile, lecithin and digested lipids has been previously reported, but here we investigate the soly. variation of poorly-sol. drugs through more complex biorelevant amphiphile interactions. A four component mixt. design was conducted to understand the solubilization capacity and interactions of bile salt, lecithin, oleate and monoglyceride with a const. total concn. (11.7 mM) but varying molar ratios. The equil. soly. of seven low soly. acidic (zafirlukast), basic (aprepitant, carvedilol) and neutral (fenofibrate, felodipine, griseofulvin and spironolactone) drugs was investigated. Soly. results are comparable with literature values and also our own previously published design of expt. studies. Results indicate that solubilization is not a sum accumulation of individual amphiphile concns., but a drug specific effect through interactions of mixed amphiphile compns. with the drug. This is probably due to a combined interaction of drug characteristics for example lipophilicity, mol. shape and ionization with amphiphile components, which can generate specific drug-micelle affinities. The proportion of each component can have a remarkable influence on soly. with in some cases the highest and lowest points close to each other. A single point soly. measurement in a fixed compn.

simulated media or human intestinal fluid sample will therefore provide a value without knowledge of the surrounding soly. topog. meaning that variability may be overlooked. This study has demonstrated how the amphiphile ratios influence drug soly. and highlights the importance of the envelope of physiol. variation when simulating in vivo drug behavior.

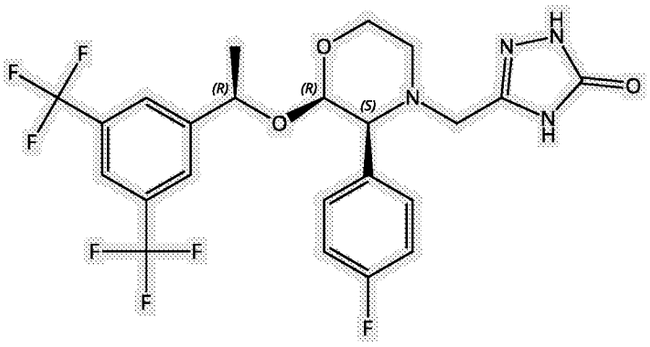
CC 63-6 (Pharmaceuticals)

IT 52-01-7, Spironolactone 126-07-8, Griseofulvin 49562-28-9, Fenofibrate 72509-76-3, Felodipine 72956-09-3, Carvedilol 107753-78-6, Zafirlukast 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of physiol. gastrointestinal surfactant ratio on equil. soly. of BCS class II drugs investigated using a four component mixt. design)

IT 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of physiol. gastrointestinal surfactant ratio on equil. soly. of BCS class II drugs investigated using a four component mixt. design)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 28 THERE ARE 28 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN

ACCESSION NUMBER: 2016:2157637 CAPLUS Full-text

DOCUMENT NUMBER: 166:118691

TITLE: Cosmeceutical compositions comprising polyalkylene glycols

INVENTOR(S): Schmaus, Gerhard; Lange, Sabine

PATENT ASSIGNEE(S): Symrise AG, Germany

ULTIMATE OWNER: SYMRISE AG

ULTIMATE OWNER STANDARD: Symrise

SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016207084	A1	20161229	WO 2016-EP64109	20160619
EP 3108941	A1	20161228	EP 2015-173373	20150623
EP 3108941	B1	20180509		
KR 2018015265	A	20180212	KR 2018-7002058	20160619

KR 2117171	B1	20200601			
MX 2017016226	A	20180223	MX 2017-16226		20160619
CN 107847772	A	20180327	CN 2016-80045857		20160619
CN 107847772	B	20220104			
JP 2018518496	T	20180712	JP 2017-565942		20160619
JP 6945458	B2	20211006			
BR 112017027546	A2	20180821	BR 2017-112017027546		20160619
BR 112017027546	B1	20220426			
IN 201717044256	A	20180105	IN 2017-17044256		20171208
US 20180185301	A1	20180705	US 2017-15736494		20171214
PRIORITY APPLN. INFO.:			EP 2015-173373	A	20150623
			WO 2016-EP64109	W	20160619

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2016207084	A1	Dead	20201201
EP 3108941	A1	Indeterminate	20201106
EP 3108941	B1	Indeterminate	20201107
KR 2018015265	A	Alive	20201121
KR 2117171	B1	Alive	20201121
MX 2017016226	A	Alive	20201121
CN 107847772	A	Alive	20201121
CN 107847772	B	Alive	20220120
JP 2018518496	T	Alive	20201120
JP 6945458	B2	Alive	20211118
BR 112017027546	A2	Alive	20220519
BR 112017027546	B1	Alive	20220519
US 20180185301	A1	Dead	20220818

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2016:2157637

AB Suggested are compns. comprising or consisting of specific polyalkylene glycol deriv. as pharmaceutical actives for preventing, treating and/or curing itchy conditions of human skin and scalp, and/or providing a PAR-2 antagonistic effect to human skin and scalp.

IPCI A61Q0019-00 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]; A61Q0015-00 [I]; A61K0008-39 [I]; A61K0008-33 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]

IPCR A61K0008-33 [I]; A61Q0019-00 [I]; A61K0008-39 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0015-00 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]

CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 63

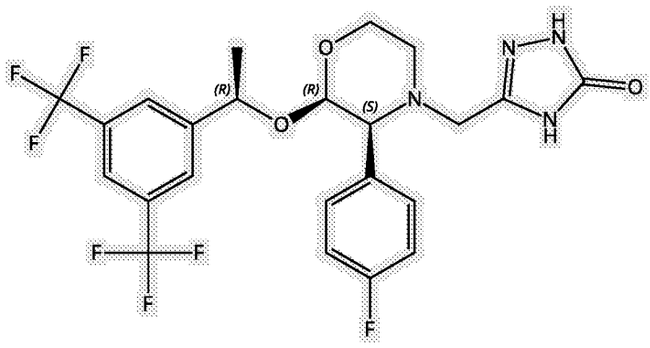
IT Amino acids
Cannabinoids
Carbohydrates
Ceramides
Collagens
Corticosteroids
Disaccharides
Elastins
Glycosphingolipids
Hydroxy fatty acids
Hydroxycarboxylic acids
Lanolin
Lecithins
Oligosaccharides
Petrolatum
Phytosterols
Polyoxyalkylenes
Pyrazoles
Steroids
Tocopherols
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

IT 50-02-2 50-21-5, biological studies 50-23-7 50-33-9, biological studies 50-78-2 50-99-7, D-Glucose, biological studies 53-06-5 53-86-1 56-81-5, 1,2,3-Propanetriol, biological studies 57-13-6, Urea, biological studies 57-48-7, D-Fructose, biological studies 57-55-6, 1,2-Propanediol, biological studies 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies 58-95-7 59-23-4, D-Galactose, biological studies 61-68-7 63-42-3 69-46-5 72-17-3 77-52-1

77-92-9, biological studies 81-13-0 83-43-2 89-78-1 89-79-2
97-59-6 98-52-2 104-98-3 124-04-9D, Hexanedioic acid, acyl derivs.
129-20-4 312-93-6 472-15-1 502-65-8, ψ,ψ-Carotene 515-69-5
520-36-5 530-78-9 544-31-0 552-94-3 555-66-8 578-74-5 644-62-2
873-94-9 1117-77-7 1117-86-8, 1,2-Octanediol 1405-86-3, Glycyrrhizin
1406-18-4, Vitamin E 2304-80-5 3458-28-4, D-Mannose 3804-01-1
4394-00-7 5343-92-0, 1,2-Pentanediol 6915-15-7 6920-22-5,
1,2-Hexanediol 9004-61-9, Hyaluronic acid 9007-28-7 9012-76-4,
Chitosan 9041-22-9, β-D-Glucan 13539-59-8 13609-67-1
15307-86-5 15687-27-1 22204-53-1 24938-91-8 26171-23-3
27113-22-0 30748-29-9 34645-84-6 36322-90-4 36945-98-9
38194-50-2 41736-92-9 51115-67-4 51234-28-7 53254-77-6
53597-27-6 55965-23-6 58253-27-3, Gingerol 58749-22-7 59804-37-4
59870-68-7 61723-78-2 63187-91-7 74563-64-7 77341-67-4
106729-72-0 108766-16-1 110483-07-3 170729-80-3
185740-18-5 185915-25-7 189128-20-9 207792-35-6 211184-47-3
220621-22-7 381224-15-3 506412-91-5 521981-60-2 637336-79-9
697235-49-7 857557-19-8 1122460-01-8
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

IT 170729-80-3
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
BR 112017027546 A2	BR 2017-112017027546	Register
BR 112017027546 B1	BR 2017-112017027546	Register
CN 107847772 A	CN 2016-80045857	Register|Global Dossier
CN 107847772 B	CN 2016-80045857	Register|Global Dossier
EP 3108941 A1	EP 2015-173373	Register|Federated Reg.
EP 3108941 B1	EP 2015-173373	Register|Federated Reg.
IN 201717044256 A	IN 2017-17044256	Register
JP 2018518496 T	JP 2017-565942	Register|Global Dossier
JP 6945458 B2	JP 2017-565942	Register|Global Dossier
KR 2018015265 A	KR 2018-7002058	Register|Global Dossier
KR 2117171 B1	KR 2018-7002058	Register|Global Dossier
MX 2017016226 A	MX 2017-16226	Register
US 20180185301 A1	US 2017-15736494	Register|Global Dossier
WO 2016207084 A1	WO 2016-EP64109	Register|Global Dossier

L5 ANSWER 29 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:2152998 CAPLUS Full-text
DOCUMENT NUMBER: 166:112176
TITLE: Cosmeceutical compositions comprising polyalkylene glycols
INVENTOR(S): Schmaus, Gerhard; Lange, Sabine
PATENT ASSIGNEE(S): Symrise AG, Germany
ULTIMATE OWNER: SYMRISE AG
ULTIMATE OWNER STANDARD: Symrise
SOURCE: Eur. Pat. Appl., 46pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 3108941	A1	20161228	EP 2015-173373	20150623
EP 3108941	B1	20180509		
WO 2016207084	A1	20161229	WO 2016-EP64109	20160619
KR 2018015265	A	20180212	KR 2018-7002058	20160619
KR 2117171	B1	20200601		
MX 2017016226	A	20180223	MX 2017-16226	20160619
CN 107847772	A	20180327	CN 2016-80045857	20160619
CN 107847772	B	20220104		
JP 2018518496	T	20180712	JP 2017-565942	20160619
JP 6945458	B2	20211006		
BR 112017027546	A2	20180821	BR 2017-112017027546	20160619
BR 112017027546	B1	20220426		
IN 201717044256	A	20180105	IN 2017-17044256	20171208
US 20180185301	A1	20180705	US 2017-15736494	20171214

PRIORITY APPLN. INFO.: EP 2015-173373 A 20150623
WO 2016-EP64109 W 20160619

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
EP 3108941	A1	Indeterminate	20201106
EP 3108941	B1	Indeterminate	20201107
WO 2016207084	A1	Dead	20201201
KR 2018015265	A	Alive	20201121
KR 2117171	B1	Alive	20201121
MX 2017016226	A	Alive	20201121
CN 107847772	A	Alive	20201121
CN 107847772	B	Alive	20220120
JP 2018518496	T	Alive	20201120
JP 6945458	B2	Alive	20211118
BR 112017027546	A2	Alive	20220519
BR 112017027546	B1	Alive	20220519
US 20180185301	A1	Dead	20220818

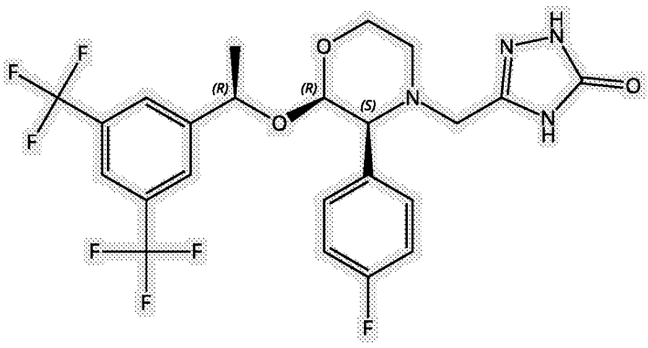
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2016:2152998
AB Suggested are compns. comprising or consisting of specific polyalkylene glycol deriv. as pharmaceutical actives for preventing, treating and/or curing itchy conditions of human skin and scalp, and/or providing a PAR-2 antagonistic effect to human skin and scalp.
IPCI A61Q0019-00 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]; A61Q0015-00 [I]; A61K0008-39 [I]; A61K0008-33 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]
IPCR A61Q0019-00 [I]; A61K0008-33 [I]; A61K0008-39 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0015-00 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 63
IT Amino acids
Cannabinoids
Carbohydrates
Ceramides
Collagens
Corticosteroids
Disaccharides
Elastins
Glycosphingolipids

Hydroxy fatty acids
Hydroxycarboxylic acids
Lanolin
Lecithins
Oligosaccharides
Petrolatum
Phytosterols
Polyoxyalkylenes
Pyrazoles
Steroids
Tocopherols
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

IT 50-02-2, Dexamethasone 50-21-5, Lactic acid, biological studies
50-23-7, Hydrocortisone 50-33-9, Phenylbutazone, biological studies
50-78-2, Aspirin 50-99-7, D-Glucose, biological studies 53-06-5,
Cortisone 53-86-1, Indomethacin 56-81-5, Glycerol, biological studies
57-13-6, Urea, biological studies 57-48-7, D-Fructose, biological
studies 57-55-6, Propylene glycol, biological studies 57-88-5,
Cholesterol, biological studies 58-95-7, Tocopheryl acetate 59-23-4,
D-Galactose, biological studies 61-68-7, Mefenamic acid 63-42-3,
Lactose 69-46-5, Solprin 72-17-3, Sodium lactate 77-52-1, Ursolic
acid 77-92-9, Citric acid, biological studies 81-13-0 83-43-2,
Methylprednisolone 89-78-1, Menthol 89-79-2 97-59-6 98-52-2
104-98-3 124-04-9D, Adipic acid, acyl derivs. 129-20-4,
Oxyphenylbutazone 312-93-6, Dexamethasone phosphate 472-15-1, Betulic
acid 502-65-8, ψ,ψ-Carotene 515-69-5, α-Bisabolol
520-36-5, Apigenin 530-78-9, Flufenamic acid 544-31-0, N-Palmitoyl
Ethanolamine 552-94-3, Disalcid 555-66-8 578-74-5 629-54-9,
Hexadecanamide 644-62-2, Meclofenamic acid 873-94-9 1117-77-7
1117-86-8, 1,2-Octanediol 1405-86-3, Glycyrrhizin 1406-18-4, Vitamin E
2304-80-5 3458-28-4, D-Mannose 3804-01-1 4394-00-7, Niflumic acid
5343-92-0, 1,2-Pentanediol 6915-15-7, Malic acid 6920-22-5,
1,2-Hexanediol 9004-61-9, Hyaluronic acid 9007-28-7, Chondroitin
sulfate 9012-76-4, Chitosan 9041-22-9, β-Glucan 13539-59-8
13609-67-1, Hydrocortisone 17-butyrate 15307-86-5, Diclofenac
15687-27-1, Ibuprofen 22204-53-1, Naproxen 24938-91-8, Polyethylene
glycol Tridecyl ether 26171-23-3, Tolmetin 27113-22-0 30748-29-9,
Feprazone 34645-84-6, Fenclofenac 36322-90-4, Piroxicam 36945-98-9,
Icilin 38194-50-2, Sulindac 41736-92-9 51115-67-4,
2-Isopropyl-N-2,3-trimethylbutanamide 51234-28-7, Benoxaprofen
53254-77-6 53597-27-6, Fendosal 55965-23-6 58253-27-3, Gingerol
58749-22-7 59804-37-4, Tenoxicam 59870-68-7 61723-78-2 63187-91-7
74563-64-7 77341-67-4 106729-72-0 108766-16-1 170729-80-3
185740-18-5 185915-25-7, L-Menthyl lactate 189128-20-9 207792-35-6,
3-Menthoxypropane-1,2-diol 211184-47-3 220621-22-7 381224-15-3
506412-91-5 521981-60-2 637336-79-9 697235-49-7 857557-19-8
1122460-01-8
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

IT 170729-80-3
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
BR 112017027546 A2	BR 2017-112017027546	Register
BR 112017027546 B1	BR 2017-112017027546	Register
CN 107847772 A	CN 2016-80045857	Register|Global Dossier
CN 107847772 B	CN 2016-80045857	Register|Global Dossier
EP 3108941 A1	EP 2015-173373	Register|Federated Reg.
EP 3108941 B1	EP 2015-173373	Register|Federated Reg.
IN 201717044256 A	IN 2017-17044256	Register
JP 2018518496 T	JP 2017-565942	Register|Global Dossier
JP 6945458 B2	JP 2017-565942	Register|Global Dossier
KR 2018015265 A	KR 2018-7002058	Register|Global Dossier
KR 2117171 B1	KR 2018-7002058	Register|Global Dossier
MX 2017016226 A	MX 2017-16226	Register
US 20180185301 A1	US 2017-15736494	Register|Global Dossier
WO 2016207084 A1	WO 2016-EP64109	Register|Global Dossier

L5 ANSWER 30 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:2116494 CAPLUS Full-text
DOCUMENT NUMBER: 172:545657
TITLE: Statistical investigation of simulated fed intestinal media composition on the equilibrium solubility of oral drugs
AUTHOR(S): Zhou, Zhou; Dunn, Claire; Khadra, Ibrahim; Wilson, Clive G.; Halbert, Gavin W.
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK
SOURCE: European Journal of Pharmaceutical Sciences (2017), 99, 95-104
CODEN: EPSCED; ISSN: 0928-0987
DIGITAL OBJECT ID: 10.1016/j.ejps.2016.12.008
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Gastrointestinal fluid is a complex milieu and it is recognized that gut drug soly. is different to that obsd. in simple aq. buffers. Simulated gastrointestinal media have been developed covering fasted and fed states to facilitate in vitro prediction of gut soly. and product dissoln. However, the combination of bile salts, phospholipids, fatty acids and proteins in an aq. buffered system creates multiple phases and drug soly. is therefore a complex interaction between these components, which may create unique environments for each API. The impact on soly. can be assessed through a statistical design of expt. (DoE) approach, to det. the influence and relationships between factors. In this paper DoE has been

applied to fed simulated gastrointestinal media consisting of eight components (pH, bile salt, lecithin, sodium oleate, monoglyceride, buffer, salt and pancreatin) using a two level D-optimal design with forty-four duplicate measurements and four center points. The equil. soly. of a range of poorly sol. acidic (indomethacin, ibuprofen, phenytoin, valsartan, zafirlukast), basic (aprepitant, carvedilol, tadalafil, bromocriptine) and neutral (fenofibrate, felodipine, probucol, itraconazole) drugs was investigated. Results indicate that the DoE provides equil. soly. values that are comparable to literature results for other simulated fed gastrointestinal media systems or human intestinal fluid samples. For acidic drugs the influence of pH predominates but other significant factors related to oleate and bile salt or interactions between them are present. For basic drugs pH, oleate and bile salt have equal significance along with interactions between pH and oleate and lecithin and oleate. Neutral drugs show diverse effects of the media components particularly with regard to oleate, bile salt, pH and lecithin but the presence of monoglyceride, pancreatin and buffer have significant but smaller effects on soly. There are fourteen significant interactions between factors mainly related to the surfactant components and pH, indicating that the soly. of neutral drugs in fed simulated media is complex. The results also indicate that the equil. soly. of each drug can exhibit individualistic behavior assocd. with the drug's chem. structure, physicochem. properties and interaction with media components. The utility of DoE for fed simulated media has been demonstrated providing equil. soly. values comparable with similar in vitro systems while also providing greater information on the influence of media factors and their interactions. The detn. of a drug's gastrointestinal soly. envelope provides useful limits that can potentially be applied to in silico modeling and in vivo expts.

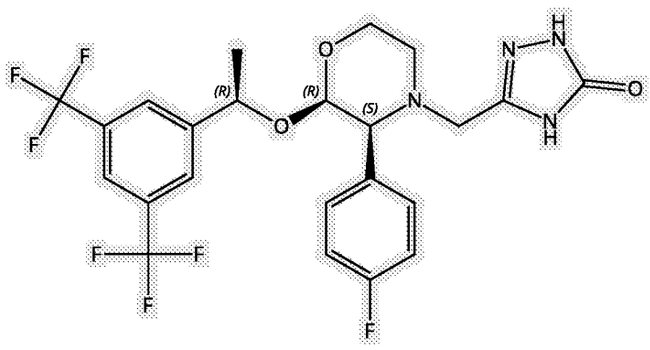
CC 63-5 (Pharmaceuticals)

IT 53-86-1, Indomethacin 57-41-0, Phenytoin 15687-27-1, Ibuprofen 23288-49-5, Probucol 25614-03-3, Bromocriptine 49562-28-9, Fenofibrate 72509-76-3, Felodipine 72956-09-3, Carvedilol 84625-61-6, Itraconazole 107753-78-6, Zafirlukast 137862-53-4, Valsartan 170729-80-3, Aprepitant 171596-29-5, Tadalafil
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated fed intestinal media compn. effect on equil. soly. of oral drugs)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated fed intestinal media compn. effect on equil. soly. of oral drugs)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 31 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:2039523 CAPLUS Full-text
DOCUMENT NUMBER: 167:295158
TITLE: Stable injectable pharmaceutical composition of neurokinin 1 receptor antagonist and process for preparation thereof
INVENTOR(S): Karavas, Evangelos; Koutris, Efthimios; Bikiaris, Dimitrios; Chatidou, Sotiria; Diakidou, Amalia; Barmpalexis, Panagiotis; Konstanti, Louiza; Minioti, Katerina
PATENT ASSIGNEE(S): Pharmathen S.A., Greece
ULTIMATE OWNER: PARTNERS GROUP HOLDING AG
ULTIMATE OWNER STANDARD: Partners Group
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150165045	A1	20150618	US 2014-14412147	20141230
WO 2014005606	A1	20140109	WO 2012-EP2854	20120706
US 20200237920	A1	20200730	US 2020-16851779	20200417

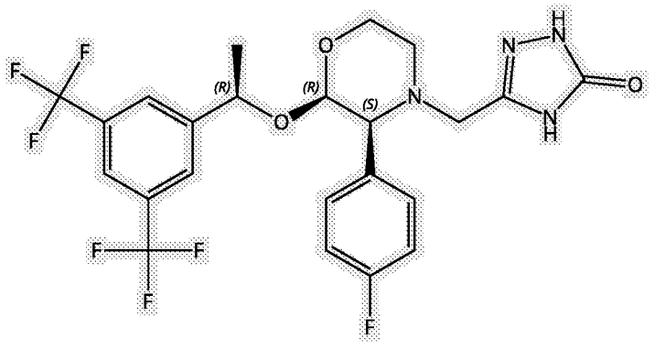
PRIORITY APPLN. INFO.: WO 2012-EP2854 W 20120706
US 2014-14412147 A1 20141230

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20150165045	A1	Dead	20220105
WO 2014005606	A1	Dead	20201202
US 20200237920	A1	Dead	20231109

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2016:2039523
AB The present invention relates to a controlled release sterile injectable formulation in the form of soln., suspension or sol-gel formulation for i.m. or s.c. administration comprising a therapeutically effective amt. of a neurokinin 1 receptor antagonist, in particular Aprepitant or Fosaprepitant or pharmaceutical acceptable salt, deriv. or metabolite thereof. It also relates to a process for developing such formulations.
IPCI A61K0047-38 [I]; A61K0031-675 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0047-14 [I]; A61K0047-46 [I]; A61K0031-5377 [I]; A61K0009-00 [I]
IPCR A61K0047-38 [I]; A61K0009-00 [I]; A61K0031-5377 [I]; A61K0031-675 [I]; A61K0047-14 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0047-46 [I]
NCL 514/090.000; 514/230.800
CC 63-6 (Pharmaceuticals)
IT Castor oil
Cottonseed oil
Gelatins
Lecithins
Polymers
Polyoxyalkylenes
Sesame oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)
IT 170729-80-3 172673-20-0 265121-04-8
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)
IT 170729-80-3
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX

NAME)



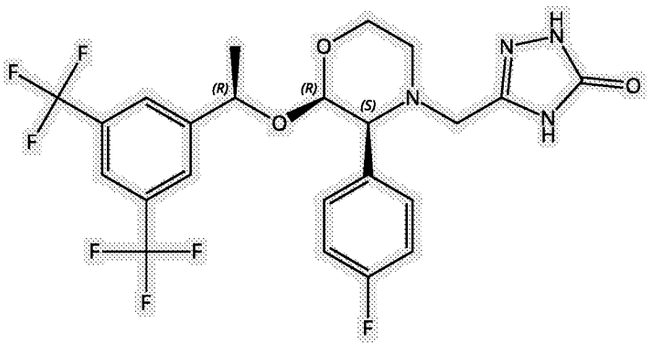
Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
US 20150165045 A1	US 2014-14412147	Register|Global Dossier
US 20200237920 A1	US 2020-16851779	Register|Global Dossier
WO 2014005606 A1	WO 2012-EP2854	Register|Global Dossier

L5 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:1859837 CAPLUS Full-text
DOCUMENT NUMBER: 166:232413
TITLE: Evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital
AUTHOR(S): Bourdon, F.; Lecoeur, M.; Leconte, L.; Ultre, V.; Kouach, M.; Odou, P.; Vaccher, C.; Foulon, C.
CORPORATE SOURCE: EA GRITA-7365-Groupe de Recherche sur les formes Injectables et les Technologies Associees, Univ. Lille, Lille, F-59000, Fr.
SOURCE: International Journal of Pharmaceutics (Amsterdam, Netherlands) (2016), 515(1-2), 774-787
CODEN: IJPHDE; ISSN: 0378-5173
DIGITAL OBJECT ID: 10.1016/j.ijpharm.2016.11.014
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASFORMULTNS 2016:1859837
AB The objective of this study was to evaluate five com. ready-to-use transdermal vehicles (Phytobase, Lipovan, Pentravan, Pentravan Plus and Pluronic Lecithin Organogel (PLO)), for the compounding of three antiemetic drugs (ondansetron, dexamethasone and aprepitant) and their administration in combination to treat chemotherapy-induced nausea and vomiting (CINV) at the hospital. Drugs were individually formulated in these vehicles and in mixt. in Pentravan Plus using different penetration enhancers. Quality control of the forms has demonstrated that formulation process was mastered and convenient for the hospital (time required: 20 min). Diffusion expts. through synthetic membranes and pig ear epidermis performed using Franz-type diffusion cells, have shown that the release and permeation process were greater for ondansetron than for dexamethasone and aprepitant, with a release step not limiting. As permeation of aprepitant was too low, it was discarded of the study. When ondansetron and dexamethasone were compounded in combination in Pentravan Plus, the most efficient vehicle, a permeation decrease was obsd. Finally, the use of tween 20 instead of EtOH as chem. enhancer has led to 2-fold factor increase in the flux of dexamethasone, resulting in fluxes convenient for transdermal administration of ondansetron to a child, but insufficient for an adult and for dexamethasone.

CC 63-6 (Pharmaceuticals)
ST antiemitic Pentravan Plus Phytobase Lipovan Pluronic Lecithin Organogel skin
IT Antiemetics
Biological permeation
Chemotherapy
Child
Combination chemotherapy
Drug delivery systems
Drug toxicity
Homo sapiens
Human
Nausea
Organogels
Permeation enhancers
Skin
Solubility
Transdermal drug delivery systems
Vomiting
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)
IT 1610779-74-2, Pentravan 1610779-77-5, Pluronic Lecithin Organogel 2074721-57-4, Pentravan Plus 2074721-58-5, Phytobase 2074721-59-6, Lipovan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)
IT 50-02-2, Dexamethasone 99614-01-4, Ondansetron hydrochloride 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)
IT 9005-64-5, Tween 20
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)
IT 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)

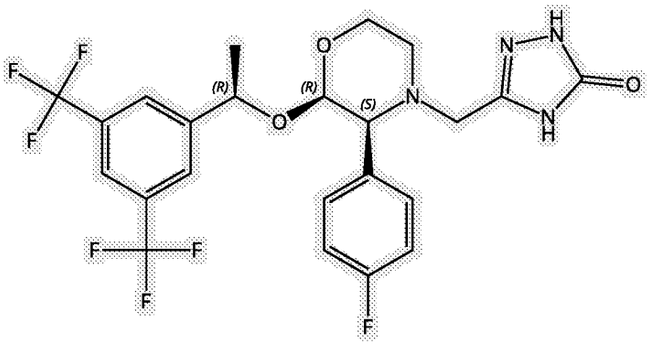


Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:1723954 CAPLUS Full-text
DOCUMENT NUMBER: 172:411315
TITLE: Optimization of the Ussing chamber setup with excised rat intestinal segments for dissolution/permeation experiments of poorly soluble drugs
AUTHOR(S): Forner, Kristin; Roos, Carl; Dahlgren, David; Kesisoglou, Filippos; Konerding, Moritz A.; Mazur, Johanna; Lennernaes, Hans; Langguth, Peter
CORPORATE SOURCE: Department of Pharmaceutical Technology and Biopharmaceutics, Johannes Gutenberg University, Mainz, Germany
SOURCE: Drug Development and Industrial Pharmacy (2017), 43(2), 338-346
CODEN: DDIPD8; ISSN: 0363-9045
DIGITAL OBJECT ID: 10.1080/03639045.2016.1251449
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Prediction of the in vivo absorption of poorly sol. drugs may require simultaneous dissoln./permeation expts. In vivo predictive media have been modified for permeation expts. with Caco-2 cells, but not for excised rat intestinal segments. The present study aimed at improving the setup of dissoln./permeation expts. with excised rat intestinal segments by assessing suitable donor and receiver media. The regional compatibility of rat intestine in Ussing chambers with modified Fasted and Fed State Simulated Intestinal Fluids (Fa/FeSSIFmod) as donor media was evaluated via several parameters that reflect the viability of the excised intestinal segments. Receiver media that establish sink conditions were investigated for their foaming potential and toxicity. Dissoln./permeation expts. with the optimized conditions were then tested for two particle sizes of the BCS class II drug aprepitant. Fa/FeSSIFmod were toxic for excised rat ileal sheets but not duodenal sheets, the compatibility with jejunal segments depended on the bile salt concn. A non-foaming receiver medium contg. bovine serum albumin (BSA) and Antifoam B was nontoxic. With these conditions, the permeation of nanosized aprepitant was higher than of the unmilled drug formulations. The compatibility of Fa/FeSSIFmod depends on the excised intestinal region. The chosen conditions enable dissoln./permeation expts. with excised rat duodenal segments. The expts. correctly predicted the superior permeation of nanosized over unmilled aprepitant that is obsd. in vivo. The optimized setup uses FaSSIFmod as donor medium, excised rat duodenal sheets as permeation membrane and a receiver medium contg. BSA and Antifoam B.
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 9

IT Lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)
IT 81-81-2, Warfarin 15307-86-5, Diclofenac 29122-68-7, Atenolol 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:1057307 CAPLUS Full-text
DOCUMENT NUMBER: 165:169358
TITLE: Difficultly-soluble drug-containing nanostructure lipid carrier pharmaceutical composition with good solubility and high bioavailability and preparation method thereof
INVENTOR(S): Jin, Yinxiu; Wang, Yuxin; Tao, Xuefen; Shi, Lei; Shen, Peipei; Xia, Nianyou
PATENT ASSIGNEE(S): Taizhou Vocational & Technical College, Peop. Rep. China
ULTIMATE OWNER: TAIZHOU VOCATIONAL AND TECHNICALl COLLEGE
ULTIMATE OWNER STANDARD: Taizhou Vocational and Technical College
SOURCE: Faming Zhuanli Shenqing, 21pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105708799	A	20160629	CN 2016-10056874	20160127

PRIORITY APPLN. INFO.: CN 2016-10056874 20160127
PATENT STATUS PATENT INFORMATION:

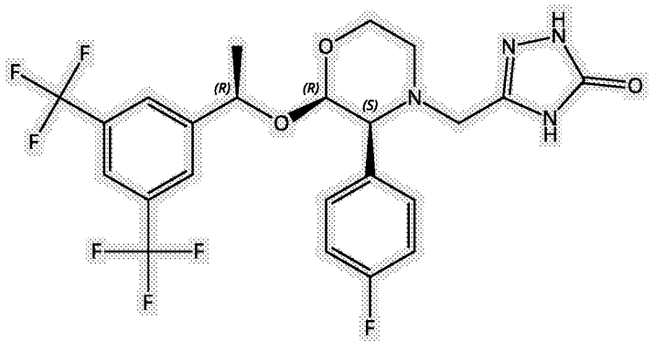
PATENT NO.	KIND	STATUS	STATUS DATE
CN 105708799	A	Dead	20201120

OTHER SOURCE(S): CASFORMULTNS 2016:1057307
AB The title nanostructure lipid carrier pharmaceutical compn. is prepd. from (by wt.%) difficultly-sol. drug (bezafibrate, oxcarbazepine, etc.) 0.02-1, solid lipid material (glyceryl monostearate, etc.) 0.3-15, liq. lipid material (soybean oil, etc.) 0.5-20, lipid-sol. emulsifier (lecithin and/or soybean phospholipid) 0.8-10, water-sol. emulsifier (Tween-20, etc.) 1-15 and water-sol. solvent (water, phosphate buffer soln., etc.) 39-97.38. The invention also provides a prepn. method of the nanostructure lipid carrier pharmaceutical compn. The inventive prepn. method has simple process, and good controllability and repeatability; and the inventive nanostructure lipid carrier pharmaceutical compn. contains difficultly-sol. drug, has good soly., degradability, physiol. compatibility and stability, and high bioavailability and entrapment rate, and no org. solvent residues, and can be used as drug delivery system for difficultly-sol. drug.
IPCI A61K0009-127; A61K0009-19; A61K0047-44; A61K0031-192; A61K0031-55; A61P0003-06; A61P0009-10
IPCR A61K0009-127 [I]; A61K0009-19 [I]; A61K0031-192 [I]; A61K0031-55 [I]; A61K0047-44 [I]; A61P0003-06 [I]; A61P0009-10 [I]
CC 63-6 (Pharmaceuticals)
IT Corn oil
Lecithins
Lipids
Peanut oil
Soya phospholipids
Soybean oil
Sunflower oil
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(difficultly-sol. drug-contg. nanostructure lipid carrier pharmaceutical compn. with good soly. and high bioavailability and prepn. method thereof)
IT 50-14-6, Ergocalciferol 50-24-8, Prednisolone 50-28-2, Oestradiol, biological studies 51-48-9, L-Thyroxine, biological studies 52-01-7, Spironolactone 52-86-8, Haloperidol 53-43-0, Dehydroepiandrosterone 53-86-1, Indomethacin 55-98-1, Busulfan 57-83-0, Progesterone, biological studies 66-76-2, Bishydroxycoumarin 67-20-9, Furadantin 67-45-8, Furazolidone 67-96-9, Dihydrotachysterol 67-97-0, Cholecalciferol 68-26-8, Vitamin A 76-57-3, Codeine 76-99-3, Methadone 90-82-4, Pseudoephedrine 104-31-4, Benzonatate 113-15-5, Ergotamine 113-92-8 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 127-40-2, Xanthophyll 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-57-7, Cinnarizine 298-81-7, Methoxsalen 300-62-9, Amfetamine 302-79-4, Tretinoin 303-49-1, Clomipramine 303-53-7, Cyclobenzaprine 303-98-0, Coenzyme Q10 303-98-0D, Ubidecarenone, salt deriv. 321-64-2, Tacrine 359-83-1, Pentazocine 378-44-9, Betamethasone 404-86-4, Capsaicin 437-38-7, Fentanyl 443-48-1, Metronidazole 502-65-8, Lycopene 511-12-6, Dihydroergotamine 520-85-4, Medroxyprogesterone 652-67-5, Isosorbitol 911-45-5, Clomifene 1134-47-0, Baclofen 1397-89-3, Amphotericin B 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1665-48-1, Metaxalone 1951-25-3, Amiodarone 1972-08-3, Tetrahydrocannabinol 3562-63-8 4419-39-0, Beclomethasone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 7261-97-4, Dantrolene 7689-03-4, Camptothecin 10238-21-8, Glibenclamide 10238-21-8D, Glibenclamide, salt deriv. 10540-29-1, Tamoxifen 12001-79-5, Vitamin K 15307-86-5, Diclofenac 15574-96-6, Pizotifen 15686-51-8, Clemastine 17230-88-5, Danazol 17230-88-5D, Danazol, salt deriv. 18559-94-9, Salbutamol 19356-17-3, Calcifediol 20594-83-6, Nalbuphine 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22916-47-8, Miconazole 23288-49-5, Probucol 25523-97-1, Dexchlorpheniramine 25812-30-0, Gemfibrozil 27203-92-5, Tramadol 28721-07-5, Oxcarbazepine 29094-61-9, Glipizide 29767-20-2, Teniposide 32222-06-3, Calcitriol 33069-62-4, Taxol 33419-42-0, Etoposide 34911-55-2, Bupropion 38304-91-5, Minoxidil 41340-25-4, Etodolac 41859-67-0, Bezafibrate 42924-53-8, Nabumetone 43200-80-2, Zopiclone 49562-28-9, Fenofibrate 49697-38-3, Rimexolone 51322-75-9, Tizanidine 51333-22-3, Budesonide 51481-61-9, Cimetidine 53123-88-9, Sirolimus 53179-11-6, Loperamide 53230-10-7, Mefloquine 54965-21-8, Albendazole 55079-83-9, Acitretin 55142-85-3, Ticlopidine 57469-82-6, Ibuprofen arginine 59467-70-8, Midazolam 59865-13-3, Cyclosporine 60142-96-3, Gabapentin 61379-65-5, Rifapentine 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 63590-64-7, Terazosin

63612-50-0, Nilutamide 63675-72-9, Nisoldipine 65271-80-9,
Mitoxantrone 65277-42-1, Ketoconazole 68506-86-5, Vigabatrin
69756-53-2, Halofantrine 70288-86-7, Ivermectin 72432-03-2, Miglitol
72559-06-9, Rifabutine 73590-58-6, Omeprazole 73963-72-1, Cilostazol
74103-06-3, Ketorolac 75330-75-5, Lovastatin 75706-12-6, Leflunomide
76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine
79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin
80621-81-4, Rifaximin 81093-37-0, Pravastatin 81098-60-4, Cisapride
81103-11-9, Clarithromycin 82626-48-0, Zolpidem 83799-24-0,
Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin
84057-84-1, Lamotrigine 84371-65-3, Mifepristone 84449-90-1,
Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin
86386-73-4, Fluconazole 86541-75-5, Benazepril 88150-42-9, Amlodipine
89778-26-7, Toremifene 90357-06-5, Bicalutamide 91161-71-6,
Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine
93479-97-1, Glimepiride 93957-54-1, Fluvastatin 95233-18-4, Atovaquone
97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan
98319-26-7, Finasteride 101828-21-1, Butenafine 103577-45-3,
Lansoprazole 103628-46-2, Sumatriptan 104987-11-3, Tacrolimus
106133-20-4, Tamsulosin 106650-56-0, Sibutramine 107753-78-6,
Zafirlukast 111025-46-8, Pioglitazone 111406-87-2, Zileuton
112965-21-6, Calcipotriene 113665-84-2, Clopidogrel 114977-28-5,
Docetaxel 115103-54-3, Tiagabine 117976-89-3, Rabeprazole
118292-40-3, Tazarotene 120014-06-4, Donepezil 121679-13-8,
Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan
127779-20-8, Saquinavir 129497-78-5, Verteporfin 131918-61-1,
Paricalcitol 133040-01-4, Eprosartan 134523-00-5, Atorvastatin
135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6,
Irbesartan 139264-17-8, Zolmitriptan 139481-59-7, Candesartan
139755-83-2, Sildenafil 144034-80-0, Rizatriptan 144494-65-5,
Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin
145941-26-0, Oprevelkin 146939-27-7, Ziprasidone 147059-72-1,
Trovafloxacin 153559-49-0, Targretin 154229-19-3, Abiraterone
154598-52-4, Efavirenz 155213-67-5, Ritonavir 158747-02-5,
Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir
162011-90-7, Rofecoxib 169590-42-5, Celecoxib 170729-80-3,
Aprepitant 290297-26-6, Netupitant 366789-02-8, Rivaroxaban
394730-60-0, Boceprevir 402957-28-2, Telaprevir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(difficultly-sol. drug-contg. nanostructure lipid carrier
pharmaceutical compn. with good soly. and high bioavailability and
prepn. method thereof)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(difficultly-sol. drug-contg. nanostructure lipid carrier
pharmaceutical compn. with good soly. and high bioavailability and
prepn. method thereof)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105708799 A	CN 2016-10056874	Register|Global Dossier

L5 ANSWER 35 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:725430 CAPLUS Full-text
DOCUMENT NUMBER: 164:573948
TITLE: Self-microemulsifying drug delivery system for improving bioavailability of poorly soluble drug and its application
INVENTOR(S): Li, Suhua; Li, Jixi
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 23pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105535979	A	20160504	CN 2015-10819197	20151122
CN 105535979	B	20190625		

PRIORITY APPLN. INFO.: CN 2015-10819197 20151122
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 105535979	A	Alive	20201121
CN 105535979	B	Alive	20201121

AB The present invention provides a novel self-microemulsifying drug delivery system (SEDDS), wherein the SEDDS carrier material comprises Capmul MCMs and medium-chain fatty acid-contg. oil phase and surfactant. It is suitable for loading two classes of poorly sol. drugs, including pH-dependent (weak acid, weak base drug) and non-pH-dependent (neutral drugs), greatly increases the soly. of the drug to achieve the optimal bioavailability, and has important application value in the formulation development of insol. drugs.
IPCI A61K0047-14 [I]; A61K0047-12 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0031-405 [I]; A61K0031-4515 [I]; A61K0031-58 [I]; A61K0047-14; A61K0047-12; A61K0047-10; A61K0047-44; A61K0031-405; A61K0031-4515; A61K0031-58
IPCR A61K0047-14 [I]; A61K0031-405 [I]; A61K0031-4515 [I]; A61K0031-58 [I]; A61K0047-12 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0047-14 [I]; A61K0047-10 [I]; A61K0047-44 [I]
CC 63-6 (Pharmaceuticals)
IT Acylcarnitines
Alcohols
Amino acids
Bile acids
Bile salts
Cephalins
Ceramides
Dipeptides
Ethoxylated hydrogenated castor oil
Gangliosides
Glycerides
Glycerophospholipids
Glycosphingolipids
Lecithins
Lysophosphatides
Lysophosphatidylcholines
Lysophosphatidylserines
Medium-chain fatty acids
Monoglycerides
Phosphatidic acids
Phosphatidylcholines
Phosphatidylserines
Phospholipids
Polyoxyalkylenes

Pyranosides
Sphingomyelins
Tripeptides
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self-microemulsifying drug delivery system for improving bioavailability of poorly sol. drug and its application)

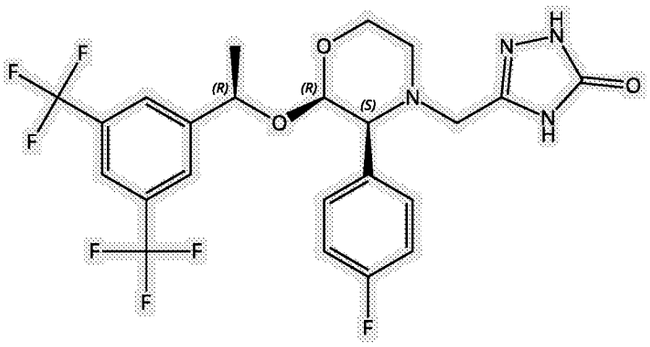
IT 50-14-6, Ergocalciferol 50-24-8, Prednisolone 50-28-2, Oestradiol, biological studies 51-48-9, L-Thyroxine, biological studies 52-01-7, Spironolactone 52-86-8, Haloperidol 53-43-0, Dehydroepiandrosterone 53-86-1, Indomethacin 55-98-1, Busulfan 57-83-0, Progestin, biological studies 66-76-2, Dicoumarol 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-96-9, Dihydrotachysterol 67-97-0, Cholecal ciferol 68-26-8, Vitamin A 76-57-3, Codeine 76-99-3, Methadone 83-43-2, Methylprednisolone 90-82-4, Pseudoephedrine 104-31-4, Benzonatate 113-15-5, Ergotamine 113-92-8, Chlorphenamine maleate 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 127-40-2 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-57-7, Cinnarizine 298-81-7, Methoxsalen 300-62-9, Amphetamine 302-79-4, Retinoic acid 303-49-1, Clomipramine 303-53-7, Cyclobenzaprine 303-98-0, Coenzyme Q10 321-64-2, Tacrine 359-83-1, Pentazocine 378-44-9, Betamethasone 404-86-4, Capsaicin 437-38-7, Fentanyl 443-48-1, Metronidazole 502-65-8, Lycopene 511-12-6, Dihydroergotamine 652-67-5, Isosorbitol 911-45-5, Clomifene 1134-47-0, Baclofen 1397-89-3, Amphotericin B 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1665-48-1, Metaxalone 1951-25-3, Amiodarone 1972-08-3, Tetrahydrocannabinol 3562-63-8 4419-39-0, Beclomethasone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 7261-97-4, Dantrolene 7689-03-4, Camptothecin 10238-21-8, Glyburide 10540-29-1, Tamoxifen 12001-79-5, Vitamin K 15307-86-5, Diclofenac 15574-96-6, Pizotifen 15686-51-8, Clemastine 15687-27-1, Ibuprofen 17230-88-5, Danazol 18559-94-9, Salbutamol 19356-17-3, Calcifediol 20594-83-6, Nalbuphine 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22916-47-8, Miconazole 23288-49-5, Probucol 25523-97-1, Dexchlorpheniramine 25812-30-0, Gemfibrozil 27203-92-5, Tramadol 29094-61-9, Glipizide 29767-20-2, Teniposide 32222-06-3, Calcitriol 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34911-55-2, Bupropion 38304-91-5, Minoxidil 41340-25-4, Etodolac 42924-53-8, Nabumetone 43200-80-2, Zopiclone 49562-28-9, Fenofibrate 49697-38-3, Rimexolone 51322-75-9, Tizanidine 51333-22-3, Budesonide 51481-61-9, Cimetidine 53123-88-9, Sirolimus 53179-11-6, Loperamide 53230-10-7, Mefloquine 54965-21-8, Albendazole 55079-83-9, Acitretin 55142-85-3, Ticlopidine 59467-70-8, Midazolam 60142-96-3, Gabapentin 61379-65-5, Rifapentine 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 63590-64-7, Terazosin 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 68506-86-5, Vigabatrin 69756-53-2, Halofantrine 70288-86-7, Ivermectin 72432-03-2, Miglitol 72559-06-9, Rifabutine 73590-58-6, Omeprazole 73963-72-1, Cilostazole 74103-06-3, Ketorolac 75330-75-5, Lovastatin 75706-12-6, Leflunomide 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 79217-60-0, Cyclosporin 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 80621-81-4, Rifaximin 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82626-48-0, Zolpidem 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84371-65-3, Mifepristone 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 88150-42-9, Amlodipine 89778-26-7, Toremifene 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan 98319-26-7, Finasteride 101828-21-1, Butenafine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104987-11-3, Tacrolimus 106133-20-4, Tamsulosin 106650-56-0, Sibutramine 107753-78-6, Zafirlukast 111025-46-8, Pioglitazone 111406-87-2, Zileuton 112965-21-6, Calcipotriene 113665-84-2, Clopidogrel 114977-28-5, Docetaxel 115103-54-3, Tiagabine 117976-89-3, Rabeprazole 118292-40-3, Tazarotene 120014-06-4, Donepezil 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan 127779-20-8, Saquinavir 129497-78-5, Verteporfin 131918-61-1, Paricalcitol 133040-01-4, Eprosartan 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6,

Irbesartan 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 139755-83-2, Sildenafil 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 153559-49-0, Targretin 154229-19-3, Abiraterone 154598-52-4, Efavirenz 155213-67-5, Ritonavir 158747-02-5, Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 170729-80-3, Aprepitant 290297-26-6, Netupitant 366789-02-8, Rivaroxaban 394730-60-0, Boceprevir 402957-28-2, Telaprevir
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self-microemulsifying drug delivery system for improving bioavailability of poorly sol. drug and its application)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self-microemulsifying drug delivery system for improving bioavailability of poorly sol. drug and its application)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105535979 A	CN 2015-10819197	Register|Global Dossier
CN 105535979 B	CN 2015-10819197	Register|Global Dossier

L5 ANSWER 36 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:535017 CAPLUS Full-text
DOCUMENT NUMBER: 164:512967
TITLE: Aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy
INVENTOR(S): Zhu, Songlin; Xiao, Yan; Meng, Qingyue; Zhao, Yongxing; Cui, Hao; Chen, Yongqiang; Fang, Shuixia; Pan, Na; Chen, Shuiku; Liang, Qian; Luo, Feng; Liu, Jinxia; Yue, Xiaohui
PATENT ASSIGNEE(S): Furen Medicines Group Co., Ltd., Peop. Rep. China; Kaifeng Pharmaceutical (Group) Co., Ltd.; Henan Furen Pharmaceutical Technology Development Co., Ltd.
ULTIMATE OWNER: HENAN FUREN MEDICAL TECH DEV; KAIFENG PHARMACEUTICAL GROUP; FUREN MEDICINE GROUP
ULTIMATE OWNER STANDARD: HENAN FUREN MEDICAL TECH DEV; KAIFENG PHARMACEUTICAL GROUP; FUREN MEDICINE GROUP
SOURCE: Faming Zhuanli Shenqing, 7pp.
CODEN: CNXXEV

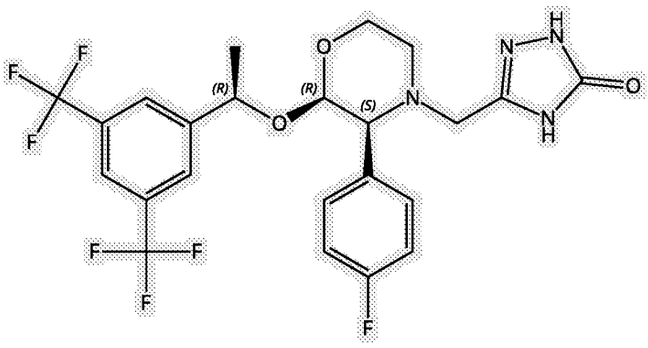
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105456228	A	20160406	CN 2015-10928963	20151211
CN 105456228	B	20180605		

PRIORITY APPLN. INFO.: CN 2014-10814246 A 20141224
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 105456228	A	Alive	20201121
CN 105456228	B	Alive	20201121

OTHER SOURCE(S): CASFORMULTNS 2016:535017
AB The present invention provides an aprepitant loaded nanocrystal lipid microcapsule, and its prepn. method is as follows: prepg. aprepitant nanocrystals with av. particle size ranging from 50 nm to 400 nm with aprepitant and stabilizer through grinding, high-speed air-jet milling or high-pressure homogenization, dispersing in water and forming a suspension; after then, after dissolving phospholipid in an org. solvent, mixing and emulsifying with the aprepitant nanocrystals suspension, subsequently removing liq. phase, drying and obtaining prepd. the aprepitant nanocrystal lipid microcapsule; wherein the particle size distribution of aprepitant nanocrystal lipid microcapsules is 10-500 μm; the stabilizer is a mixt. of one or two and more of polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft copolymer, polyvinyl pyrrolidone, hydroxypropylmethyl cellulose, poloxamer and the like; the phospholipid is a mixt. of one or two and more of soybean phospholipid, lecithin and hydrogenated phospholipid. The above-mentioned aprepitant nanocrystal lipid microcapsule has stable properties, good in vivo absorption, high bioavailability and rapid drug efficacy functions; it can be used for treating nausea and vomiting after chemotherapy.
IPCI A61K0009-50; A61K0031-5377; A61K0047-24; A61P0001-08; A61P0025-24
IPCR A61K0009-50 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0025-24 [I]
CC 63-6 (Pharmaceuticals)
IT Lecithins
Phospholipids
Soya phospholipids
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105456228 A	CN 2015-10928963	Register|Global Dossier
CN 105456228 B	CN 2015-10928963	Register|Global Dossier

L5 ANSWER 37 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:473657 CAPLUS Full-text
DOCUMENT NUMBER: 164:387016
TITLE: Emulsion formulations of aprepitant
INVENTOR(S): Ottoboni, Thomas B.; Han, Han
PATENT ASSIGNEE(S): Heron Therapeutics, Inc., USA
ULTIMATE OWNER: HERON THERAPEUTICS, INC.
ULTIMATE OWNER STANDARD: HERON THERAPEUTICS, INC.
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016044784	A1	20160324	WO 2015-US51050	20150918
US 20160082013	A1	20160324	US 2015-14859013	20150918
US 9808465	B2	20171107		
KR 2017056575	A	20170523	KR 2017-7008598	20150918
KR 2424837	B1	20220725		
CN 106852118	A	20170613	CN 2015-80050449	20150918
EP 3193830	A1	20170726	EP 2015-772163	20150918
EP 3193830	B1	20231101		
EP 3193830	C0	20231101		
JP 2017533183	T	20171109	JP 2017-514863	20150918
JP 6741655	B2	20200819		
US 20160206622	A1	20160721	US 2016-15083071	20160328
US 9561229	B2	20170207		
US 20170112847	A1	20170427	US 2017-15398928	20170105
US 10500208	B2	20191210		
US 20180000828	A1	20180104	US 2017-15705201	20170914
US 9974793	B2	20180522		
US 20180000829	A1	20180104	US 2017-15705208	20170914
US 9974794	B2	20180522		
JP 2019196398	A	20191114	JP 2019-137539	20190726
US 20200197404	A1	20200625	US 2019-16669262	20191030
US 10953018	B2	20210323		
US 20210186981	A1	20210624	US 2021-17194114	20210305
JP 2022092040	A	20220621	JP 2022-66236	20220413
US 20240139201	A1	20240502	US 2024-18408463	20240109

PRIORITY APPLN. INFO.:

US 2014-62052948	P	20140919
JP 2017-514863	A3	20150918
US 2015-14859013	A1	20150918

		WO 2015-US51050	W 20150918
		US 2016-15083071	A1 20160328
		US 2017-15398928	A1 20170105
		JP 2019-137539	A3 20190726
		US 2019-16669262	A1 20191030
		US 2021-17194114	A1 20210305

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2016044784	A1	Dead	20201202
US 20160082013	A1	Alive	20201121
US 9808465	B2	Alive	20201120
KR 2017056575	A	Alive	20220602
KR 2424837	B1	Alive	20220811
CN 106852118	A	Transitional	20240307
EP 3193830	A1	Indeterminate	20240418
EP 3193830	B1	Indeterminate	20240418
EP 3193830	C0	Alive	20240104
JP 2017533183	T	Alive	20201121
JP 6741655	B2	Alive	20201121
US 20160206622	A1	Alive	20201120
US 9561229	B2	Alive	20201120
US 20170112847	A1	Alive	20201120
US 10500208	B2	Alive	20201120
US 20180000828	A1	Alive	20201121
US 9974793	B2	Alive	20201120
US 20180000829	A1	Alive	20201121
US 9974794	B2	Alive	20201120
JP 2019196398	A	Dead	20231026
US 20200197404	A1	Alive	20201121
US 10953018	B2	Alive	20210401
US 20210186981	A1	Transitional	20240321
JP 2022092040	A	Dead	20231207
US 20240139201	A1	Alive	20240509

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2016:473657

AB Disclosed herein are novel pharmaceutical formulations of aprepitant suitable for parenteral administration including i.v. administration. Also included are formulations including both aprepitant and dexamethasone sodium phosphate. The pharmaceutical formulations are stable oil-in-water emulsions for non-oral treatment of emesis and are particularly useful for treatment of subjects undergoing cancer chemotherapy.

IPCI A61K0009-00 [I]; A61K0047-10 [I]; A61K0047-44 [I]; A61K0047-24 [I]; A61K0047-12 [I]; A61K0047-26 [I]

IPCR A61K0009-00 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]

CC 63-6 (Pharmaceuticals)

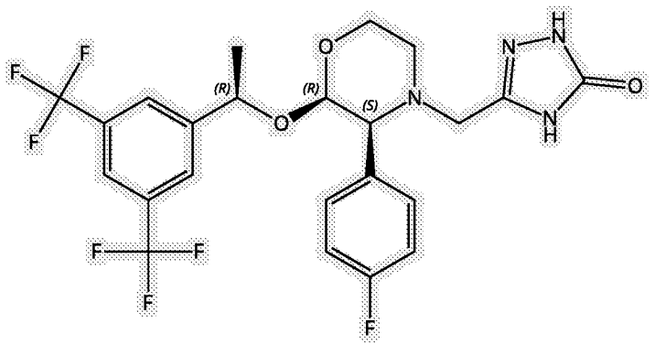
IT Alcohols
Egg yolk lecithins
Phospholipids
Soybean oil
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

IT 2392-39-4 170729-80-3
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

IT 170729-80-3
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 106852118 A	CN 2015-80050449	Register|Global Dossier
EP 3193830 A1	EP 2015-772163	Register|Federated Reg.
EP 3193830 B1	EP 2015-772163	Register|Federated Reg.
EP 3193830 C0	EP 2015-772163	Register|Federated Reg.
JP 2017533183 T	JP 2017-514863	Register|Global Dossier
JP 6741655 B2	JP 2017-514863	Register|Global Dossier
JP 2019196398 A	JP 2019-137539	Register|Global Dossier
JP 2022092040 A	JP 2022-66236	Register|Global Dossier
KR 2017056575 A	KR 2017-7008598	Register|Global Dossier
KR 2424837 B1	KR 2017-7008598	Register|Global Dossier
US 20160082013 A1	US 2015-14859013	Register|Global Dossier
US 9808465 B2	US 2015-14859013	Register|Global Dossier
US 20160206622 A1	US 2016-15083071	Register|Global Dossier
US 9561229 B2	US 2016-15083071	Register|Global Dossier
US 10500208 B2	US 2017-15398928	Register|Global Dossier
US 20170112847 A1	US 2017-15398928	Register|Global Dossier
US 20180000828 A1	US 2017-15705201	Register|Global Dossier
US 9974793 B2	US 2017-15705201	Register|Global Dossier
US 20180000829 A1	US 2017-15705208	Register|Global Dossier
US 9974794 B2	US 2017-15705208	Register|Global Dossier
US 10953018 B2	US 2019-16669262	Register|Global Dossier
US 20200197404 A1	US 2019-16669262	Register|Global Dossier
US 20210186981 A1	US 2021-17194114	Register|Global Dossier
US 20240139201 A1	US 2024-18408463	Register|Global Dossier
WO 2016044784 A1	WO 2015-US51050	Register|Global Dossier

L5 ANSWER 38 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2015:1470836 CAPLUS Full-text
DOCUMENT NUMBER: 163:403366
TITLE: Method for manufacture of nano suspension
INVENTOR(S): Wang, Yongjun; Han, Xiangfei; Xue, Peng; Wang, Jing; Jiang, Mengjuan; He, Zhonggui
PATENT ASSIGNEE(S): Shenyang Pharmaceutical University, Peop. Rep. China
ULTIMATE OWNER: SHENYANG PHARMACEUTICAL UNIVERSITY
ULTIMATE OWNER STANDARD: Shenyang Pharmaceutical University
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

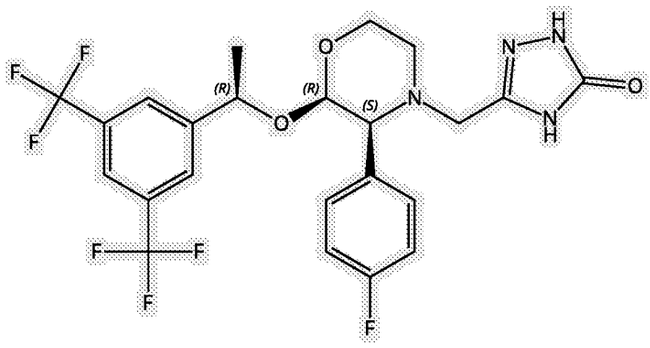
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CN 104887626 A 20150909 CN 2015-10287997 20150529
PRIORITY APPLN. INFO.: CN 2015-10287997 20150529
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 104887626	A	Dead	20201120

AB The present invention relates to a method for manuf. of nano suspension, belonging to the field of pharmaceutical prepns. The present invention utilizes an effervescent method to generate bubbles for dispersion and mixing to obtain nano-suspensions, and includes the following specific steps : mixing drug, stabilizer, the org. acid and other pharmaceutically acceptable excipients as org. phase, dissolving carbonate and other pharmaceutically acceptable excipients in water as carbonate phase, mixing the two phases, or shaking or vortex, to obtain nano suspension. The drug contg. prescription comprises drugs 1, stabilizer 0. 01-20, org. acids 0. 01 -10, carbonate 0. 01 -10 wt. parts. The carbonate is sodium carbonate, potassium carbonate, KHCO3, CaCO3, calcium bicarbonate, ammonium carbonate, etc. The org. acid is malic acid, citric acid, succinic acid, sorbic acid, formic acid, acetic acid, propionic acid. The stabilizer is PEG 1000 vitamin E succinate, Tween, Span, poloxamer, etc. The drug is insol. anticancer drug, insol. antifungal drug, insol. antimicrobial agent, hypotensive drug, etc. The present invention significantly improves the soly. and dissoln. rate of poorly sol. drugs, thereby increases the bioavailability of poorly sol. drugs.

IPCI A61K0009-10 [I]; A61K0047-12 [I]; A61K0047-04 [I]; A61K0045-00 [I]
IPCR A61K0009-10 [I]; A61K0045-00 [I]; A61K0047-04 [I]; A61K0047-12 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Amino acids
Carbonates
Ethoxylated hydrogenated castor oil
Fatty acids
Fatty alcohols
Gelatins
Lecithins
Organic acids
Phospholipids
Polyoxyalkylenes
Taxanes
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for manuf. of pharmaceutical nano suspension)
IT 50-02-2, Dexamethasone 52-01-7, Spirolactone 443-48-1, Metronidazole 595-33-5, Megestrol acetate 1397-89-3, Amphotericin B 7689-03-4, Camptothecin 9002-96-4, TPGS 10238-21-8, Glibenclamide 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16773-42-5, Ornidazole 23593-75-1, Clotrimazole 29767-20-2, Teniposide 33069-62-4, Taxol 33419-42-0, Etoposide 39562-70-4, Nitrendipine 53123-88-9, Sirolimus 55985-32-5, Nicardipine 66085-59-4, Nimodipine 79794-75-5, Loratadine 84625-61-6, Itraconazole 93479-97-1, Glimepiride 103577-45-3, Lansoprazole 104987-11-3, Tacrolimus 170729-80-3, Aprepitant 183133-96-2, Cabazitaxel 199739-10-1, Paliperidone palmitate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for manuf. of pharmaceutical nano suspension)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for manuf. of pharmaceutical nano suspension)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 104887626 A	CN 2015-10287997	Register|Global Dossier

L5 ANSWER 39 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2015:1390403 CAPLUS Full-text
DOCUMENT NUMBER: 163:369597
TITLE: Compositions of pentosan polysulfate salts for oral administration and methods of use
INVENTOR(S): Parsons, C. Lowell; Goldberg, Michael; Meenan, Christopher P.
PATENT ASSIGNEE(S): Urigen Pharmaceuticals, Inc., USA
ULTIMATE OWNER: PLATINUM MONTAUR LIFE SCIENCES
ULTIMATE OWNER STANDARD: PLATINUM MONTAUR LIFE SCIENCES
SOURCE: PCT Int. Appl., 248pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015127416	A1	20150827	WO 2015-US17205	20150224
CA 2949480	A1	20150827	CA 2015-2949480	20150224
AU 2015218642	A1	20161006	AU 2015-218642	20150224
EP 3110427	A1	20170104	EP 2015-751441	20150224
KR 2017003527	A	20170109	KR 2016-7026610	20150224
CN 106456662	A	20170222	CN 2015-80022057	20150224
JP 2017512757	T	20170525	JP 2016-554267	20150224
US 20170189443	A1	20170706	US 2016-15121312	20160824
PRIORITY APPLN. INFO.:			US 2014-61943824 P	20140224
			WO 2015-US17205 W	20150224

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2015127416	A1	Dead	20201201
CA 2949480	A1	Dead	20220428
AU 2015218642	A1	Dead	20210318
EP 3110427	A1	Dead	20210729
KR 2017003527	A	Alive	20201121
CN 106456662	A	Dead	20201121
JP 2017512757	T	Alive	20201120
US 20170189443	A1	Dead	20210324

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 163:369597; CASFORMULTNS 2015:1390403
AB The invention is directed to a pharmaceutical compn. comprising: (1) a therapeutically effective quantity of sodium pentosan polysulfate; (2) a quantity of a penetration enhancer sufficient to improve the bioavailability of the sodium pentosan polysulfate; and (3) optionally, a

pharmaceutically acceptable carrier and to methods for the oral administration of sodium pentosan polysulfate with improved bioavailability for the treatment of interstitial cystitis and other urinary tract diseases and conditions. Such compns. and methods allow the administration of sodium pentosan polysulfate at lower dosages to reduce the frequency and severity of side effects.

IPCI A61K0031-715 [I]; C07H0005-10 [I]; A61K0047-14 [I]; A61P0019-02 [I]

IPCR A61K0031-715 [I]; A61K0047-14 [I]; A61P0019-02 [I]; C07H0005-10 [I]

CC 1-12 (Pharmacology)

IT Acrylic polymers
Acylcarnitines
Amino acids
Bile salts
Bone morphogenetic protein 7
Bone sialoproteins
Cartilage oligomeric matrix protein
Collagen type I
Collagen type II
Collagen type IX
Collagen type XI
Collagens
Crown compounds
Dendrimers
Diglycerides
Estrogens
Fatty acids
Insulin-like growth factor-binding protein 3
Lecithins
Matrix proteins
Medium-chain fatty acids
Monoclonal antibodies
Monoglycerides
Opioids
Osteocalcins
Osteonectin
Osteopontin
Peptides
Polyanhydrides
Polyoxyalkylenes
Proteins
Salicylates
Steroidal hormones
Sulfonanilides
Terpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and methods of use)

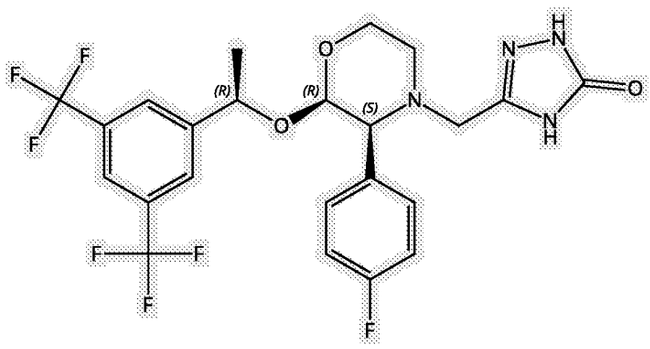
IT 15866-90-7, Metastat 15880-03-2 16011-96-4, 2-Iminopiperidine hydrochloride 16067-69-9, Strontium benzenesulfonate 16088-89-4, Strontium maleate 16139-18-7, Aminoguanidine hydrochloride 18847-18-2 19767-45-4, Mesna 19878-22-9 19982-08-2, Memantine 20093-91-8 20594-83-6, Nalbuphine 21084-57-1, 8-(Phthalimido)caprylic acid 21256-18-8, Oxaprozin 21463-31-0, 2-Amino-5,6-dihydro-6-methyl-4H-1,3-thiazine hydrochloride 22059-21-8, 1-Aminocyclopropane-1-carboxylic acid 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22410-94-2 22494-42-4, Diflunisal 22834-47-5 24314-23-6 24339-95-5 25087-26-7 25087-26-7D, derivs. 25322-68-3 25496-72-4 25518-54-1 25587-34-2 26009-03-0, Poly[oxy(1-oxo-1,2-ethanediyl)] 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26171-23-3, Tolmetin 26615-21-4, Zotepine 26864-56-2, Penfluridol 27203-92-5, Tramadol 27261-86-5 27540-07-4 27638-00-2 28945-89-3, 3-(3-Ethoxyphenyl)propanoic acid 28945-91-7, 3-(3-Butoxyphenyl)propanoic acid 29679-58-1, Fenoprofen 30762-02-8, 4-(Cyclopentyloxy)benzoic acid 31477-60-8, Ormeloxifene 33369-31-2, Zomepirac 34346-01-5 34816-55-2, Moxestrol 35197-20-7 36322-90-4, Piroxicam 36330-86-6 36440-58-1 36978-49-1 38194-50-2, Sulindac 39860-99-6, Pipotiazine 40182-75-0, Strontium citrate 40391-99-9 40472-00-2, Strontium succinate 41340-25-4, Etodolac 41839-80-9 42408-82-2, Butorphanol 42907-92-6 42907-93-7 43218-50-4 47739-98-0, Clocapramine 49594-75-4 50700-72-6,

Vecuronium 51036-98-7 51333-22-3, Budesonide 51803-78-2, Nimesulide
52240-14-9 52349-26-5 52485-79-7, Buprenorphine 52888-70-7,
3-(3-Phenoxyphenyl)propanoic acid 53583-79-2, Sultopride 53597-27-6,
Fendosal 53648-55-8, Dezocine 53716-49-7, Carprofen 53772-83-1,
Zuclopenthixol 57648-21-2, Timiperone 57821-78-0 59122-46-2,
Misoprostol 59227-89-3 59804-37-4, Tenoxicam 59865-13-3,
Cyclosporine 60118-07-2, Endorphin 61126-74-7 61126-76-9
63471-88-5 64228-79-1, Atracurium 64779-07-3 64779-14-2
65576-45-6, Asenapine 66644-81-3, Veralipride 67763-96-6, Insulin like
growth factor-1 68047-06-3, 4-Hydroxy-tamoxifen 68134-81-6,
Gacyclidine 71125-38-7, Meloxicam 71675-85-9, Amisulpride
74103-06-3, Ketorolac 75221-40-8, [4-(Cyclohexylmethoxy)phenyl]acetic
acid 75221-43-1 75272-39-8, Nemonapride 75706-12-6, Leflunomide
77086-21-6, Dizocilpine 77599-17-8, Panomifene 78994-23-7,
Levormeloxifene 79055-68-8 79669-11-7, 3-(4-Isopropoxyphenyl)propanoic
acid 79778-41-9, Neridronate 80125-14-0, Remoxipride 81093-37-0,
Pravastatin 81109-85-5 82413-20-5, Droloxifene 83015-26-3,
Atomoxetine 84449-90-1, Raloxifene 86111-26-4, Zindoxifene
89326-69-2, 5-(4-Ethylphenyl)pentanoic acid 89419-40-9, Mosapramine
89750-15-2, Glucagon like peptide-2 89778-26-7, Toremifene 89987-06-4,
Tiludronate 93957-54-1, Fluvastatin 98007-99-9 98774-23-3,
Tesmilifene 100759-29-3 100944-08-9 101253-68-3 102676-47-1,
Fadrozole 103735-76-8, erythro-MEA 103987-16-2 105462-24-6,
Risedronate 106266-06-2, Risperidone 106516-24-9, Sertindole
107868-30-4, Exemestane 108179-99-3 110347-85-8, Selfotel
110931-77-6 111974-69-7, Quetiapine 112809-51-5, Letrozole
114084-78-5, Ibandronate 115767-74-3, TAT-59 116057-68-2
116057-75-1, Idoxifene 117910-70-0 117928-94-6, Rapastinel
118072-93-8, Zoledronic acid 119431-25-3, Eliprodil 120511-73-1,
Anastrozole 121368-58-9, Olpadronate 122004-99-3 123663-49-0, T-614
124937-51-5, Tolterodine 124937-52-6, Detrol 128298-28-2, Remacemide
128607-22-7, Ospemifene 129318-43-0 129453-61-8, Fulvestrant
129612-87-9, Miproxifene 129722-12-9, Aripiprazole 129731-10-8,
Vorozole 129948-69-2 130370-59-1, GI-129471 130370-60-4, Batimastat
131123-76-7, 5,7-Dichlorokynurenic acid 131692-21-2 132539-06-1,
Olanzapine 132810-10-7, Blonanserin 133454-47-4, Iloperidone
133814-18-3, Doxacurium 134523-00-5, Atorvastatin 135459-87-9,
Strontium ranelate 136013-76-8, 2-(Cyclopropylmethoxy)benzoic acid
136553-81-6, BQ-123 136982-36-0, CP-99994 137159-92-3, Aptiganel
137945-48-3, CT-3 138330-18-4, Incadronate 141620-66-8 142880-36-2,
Ilomastat 144598-75-4, Paliperidone 145599-86-6, Cerivastatin
146490-38-2 146939-27-7, Ziprasidone 147536-97-8, Bosentan
148215-77-4, 2-(Cyclopentyloxy)benzoic acid 148700-85-0, L-733060
150403-89-7 150915-41-6, Perospirone 153322-05-5, Lanicemine
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893 156161-89-6, BQ-788 156806-79-0 157116-68-2 157116-71-7
158089-95-3, S-2474 158860-95-8, 3-(Cyclohexylmethoxy)benzoic acid
158860-99-2, 3-(Cyclopentyloxy)benzoic acid 159190-44-0 162011-90-7,
Rofecoxib 162752-13-8, 3-(4-Propylphenyl)propanoic acid 165536-41-4,
MDL-103323 168158-16-5, KB-R-7785 168266-90-8, Vofopitant
168980-06-1 168980-07-2 168980-08-3 168980-09-4 168980-10-7
168980-12-9 168980-13-0 169590-41-4, Deracoxib 169590-42-5,
Celecoxib 169799-04-6, MMI-270 169799-44-4, Keratin sulfate
170277-31-3, Infliximab 170566-84-4, Lanepitant 170713-75-4
170729-80-3, Aprepitant 172673-20-0, Fosaprepitant
173937-91-2, Atrasentan 175033-36-0, NCX4016 177036-94-1, Ambrisentan
177172-49-5 177653-18-8 177653-31-5 177653-36-0 177653-53-1
177653-62-2 177653-65-5 179545-77-8, Tanomastat 180064-38-4
180384-57-0, Tezosentan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and
methods of use)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and
methods of use)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2015218642 A1	AU 2015-218642	Register
CA 2949480 A1	CA 2015-2949480	Register
CN 106456662 A	CN 2015-80022057	Register|Global Dossier
EP 3110427 A1	EP 2015-751441	Register|Federated Reg.
JP 2017512757 T	JP 2016-554267	Register|Global Dossier
KR 2017003527 A	KR 2016-7026610	Register|Global Dossier
US 20170189443 A1	US 2016-15121312	Register|Global Dossier
WO 2015127416 A1	WO 2015-US17205	Register|Global Dossier

L5 ANSWER 40 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2015:865407 CAPLUS Full-text
DOCUMENT NUMBER: 162:663467
TITLE: Orally disintegrating porous film comprising pharmacological active ingredient and method for preparing the same
INVENTOR(S): Oh, Dong Hoon; Lee, Jin Hoo; Lee, So Yi; Kang, Jun Hyuk; Lim, Chae Yun; Jung, Kyung Tae; Yeon, Kyu Jeong; Park, Jin Gyu
PATENT ASSIGNEE(S): Seoul Pharma. Co., Ltd., S. Korea
ULTIMATE OWNER: SEOUL PHARMA. CO., LTD.
ULTIMATE OWNER STANDARD: SEOUL PHARMA. CO., LTD.
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

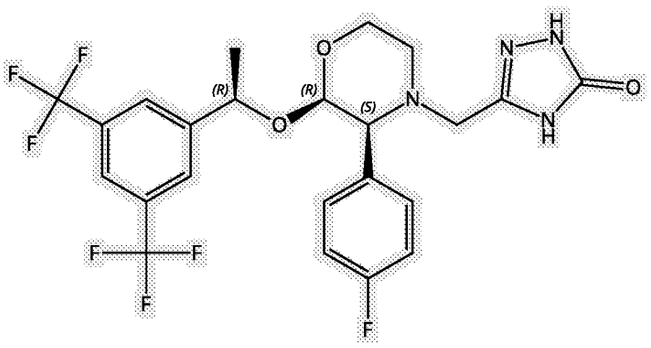
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015072684	A1	20150521	WO 2014-KR10293	20141030
KR 1407922	B1	20140617	KR 2013-138040	20131114
CN 105873572	A	20160817	CN 2014-80071821	20141030
EP 3069716	A1	20160921	EP 2014-861454	20141030
US 20160279071	A1	20160929	US 2016-15036784	20160513
PRIORITY APPLN. INFO.:			KR 2013-138040 A	20131114
			WO 2014-KR10293 W	20141030

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2015072684	A1	Dead	20201202
KR 1407922	B1	Dead	20201121
CN 105873572	A	Dead	20201121

EP 3069716 A1 Dead 20201203
US 20160279071 A1 Dead 20201121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2015:865407
AB The present invention relates to an orally disintegrating porous film and a method for prepg. the same, the film comprising a foaming agent, a foam stabilizing agent, a plasticizer, and pharmacol. active ingredient. The orally disintegrating porous film according to the present invention has micropores within the film and phys. properties suitable for a film, so that the film has an effect of significantly improving the dissoln. rate of a drug and has good processability since the film can be easily prepd. at low cost and through a simplified prepn. method.
IPCI A61K0009-70 [I]; A61P0003-10 [I]; A61P0003-04 [I]
IPCR A61K0009-70 [I]; A61P0003-04 [I]; A61P0003-10 [I]
CC 63-6 (Pharmaceuticals)
IT Alditols
Enzymes
Hormones, animal
Lecithins
Medium-chain fatty acids
Polyoxyalkylenes
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active substance and its manufg. method)
IT 50-02-2, Dexamethasone 50-58-8, Phendimetrazine tartrate 50-81-7, L-Ascorbic acid, biological studies 54-11-5, Nicotine 55-63-0, Nitroglycerin 56-81-5, Glycerin, biological studies 56-81-5D, Glycerin, fatty acid esters 57-50-1D, Sucrose, fatty acid esters 57-55-6, Propylene glycol, biological studies 58-08-2, Caffeine, biological studies 61-76-7, Phenylephrine hydrochloride 90-84-6, Diethylpropion 94-09-7, Benzocaine 102-76-1, Triacetin 103-90-2, Acetaminophen 113-92-8 123-03-5, Cetylpyridinium chloride 124-90-3, Oxycodone hydrochloride 125-69-9, Dextromethorphan bromide 147-24-0, Diphenhydramine hydrochloride 345-78-8, Pseudoephedrine hydrochloride 357-08-4, Naloxone hydrochloride 437-38-7, Fentanyl 562-10-7 569-65-3, Meclizine 797-63-7, Levonorgestrel 1134-47-0, Baclofen 1197-21-3, Phentermine hydrochloride 1508-65-2, Oxybutynin hydrochloride 2216-51-5, L-Menthol 7232-21-5, Metoclopramide hydrochloride 7384-98-7, Propylene glycol dicaprylate 8050-81-5, Simethicone 9000-30-0, Guar gum 9000-40-2, Locust bean gum 9000-69-5, Pectin 9003-20-7, Polyvinyl acetate 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 9005-32-7, Alginic acid 9057-02-7, Pullulan 11138-66-2, Xanthan gum 12441-09-7D, Sorbitan, fatty acid esters 14611-52-0, Selegiline hydrochloride 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16679-58-6, Desmopressin 22071-15-4, Ketoprofen 22232-71-9, Mazindol 23828-92-4, Ambroxol hydrochloride 25322-68-3, Polyethylene oxide 27848-84-6, Nicergoline 28911-01-5, Triazolam 28981-97-7, Alprazolam 31565-12-5, Propylene glycol monocaprylate 34552-83-5, Loperamide hydrochloride 37220-82-9, Glycerol oleate 41100-52-1, Memantine hydrochloride 51481-61-9, Cimetidine 52485-79-7, Buprenorphine 56211-40-6, Torasemide 59729-32-7, Citalopram hydrobromide 64461-82-1, Tizanidine hydrochloride 66357-59-3, Ranitidine hydrochloride 71125-38-7, Meloxicam 72797-41-2, Tianeptine 73590-58-6, Omeprazole 76824-35-6, Famotidine 77883-43-3, Doxazosin mesylate 79794-75-5, Loratadine 82248-59-7, Atomoxetine hydrochloride 82626-48-0, Zolpidem 83480-29-9, Voglibose 83881-52-1, Cetirizine hydrochloride 84057-84-1, Lamotrigine 87333-19-5, Ramipril 90729-43-4, Ebastine 93479-97-1, Glimepiride 97240-79-4, Topiramate 99614-01-4, Ondansetron hydrochloride 99614-02-5, Ondansetron 100299-08-9, Pemirolast potassium 100643-71-8, Desloratadine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 106133-20-4, Tamsulosin 106266-06-2, Risperidone 109889-09-0, Granisetron 112885-41-3, Mosapride 119356-77-3, Dapoxetine 120011-70-3, Donepezil hydrochloride 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 132907-72-3, Ramosetron hydrochloride 139264-17-8, Zolmitriptan 139755-83-2, Sildenafil 140462-76-6, Olopatadine hydrochloride 144034-80-0, Rizatriptan 144689-63-4, Olmesartan medoxomil 151767-02-1, Montelukast sodium 153439-40-8, Fexofenadine hydrochloride 158966-92-8, Montelukast 170729-80-3, Aprepitant 171596-29-5, Tadalafil 171599-83-0, Sildenafil citrate 219861-08-2, Escitalopram oxalate

224785-91-5, Vardenafil hydrochloride 242478-38-2, Solifenacin succinate
246852-12-0, Amlodipine mesylate 268203-93-6, Udenafil 286930-03-8,
Fesoterodine fumarate 385367-47-5, Tarafenacin 823178-28-5
862189-96-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active
substance and its manufg. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active
substance and its manufg. method)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105873572 A	CN 2014-80071821	Register|Global Dossier
EP 3069716 A1	EP 2014-861454	Register|Federated Reg.
KR 1407922 B1	KR 2013-138040	Register|Global Dossier
US 20160279071 A1	US 2016-15036784	Register|Global Dossier
WO 2015072684 A1	WO 2014-KR10293	Register|Global Dossier

L5 ANSWER 41 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2014:2053394 CAPLUS Full-text
DOCUMENT NUMBER: 162:85982
TITLE: Lipid, protein, and/or cationic molecule coated pharmaceutically active particles and compositions comprising same
INVENTOR(S): Chawrai, Suresh; Prasad, Sudhanand; Bajaj, Kirti
PATENT ASSIGNEE(S): Vyome Biosciences Pvt. Ltd., India
ULTIMATE OWNER: VYOME THERAPEUTICS LIMITED
ULTIMATE OWNER STANDARD: Vyome
SOURCE: PCT Int. Appl., 221pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014195872	A1	20141211	WO 2014-IB61925	20140603
CA 2914583	A1	20141211	CA 2014-2914583	20140603
CA 2914583	C	20190618		

AU 2014276460	A1	20151224	AU 2014-276460	20140603
IL 242916	A	20160131	IL 2014-242916	20140603
KR 2016015335	A	20160212	KR 2015-7037272	20140603
KR 1814895	B1	20180104		
CN 105407718	A	20160316	CN 2014-80042031	20140603
CN 105407718	B	20190104		
EP 3003031	A1	20160413	EP 2014-739231	20140603
JP 2016523232	T	20160808	JP 2016-517716	20140603
BR 112015030501	A2	20170725	BR 2015-112015030501	20140603
NZ 714817	A	20170728	NZ 2014-714817	20140603
US 20160128944	A1	20160512	US 2015-14895738	20151203
MX 2015016675	A	20160715	MX 2015-16675	20151203
IN 2015CN07967	A	20160831	IN 2015-CN7967	20151224
AU 2017203374	A1	20170608	AU 2017-203374	20170519
AU 2018282407	A1	20190117	AU 2018-282407	20181221

PRIORITY APPLN. INFO.:

IN 2013-DE1684	A	20130604
AU 2014-276460	A3	20140603
WO 2014-IB61925	W	20140603
AU 2017-203374	A3	20170519

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2014195872	A1	Dead	20201201
CA 2914583	A1	Dead	20221013
CA 2914583	C	Dead	20221013
AU 2014276460	A1	Dead	20201121
KR 2016015335	A	Alive	20201121
KR 1814895	B1	Alive	20201121
CN 105407718	A	Dead	20221117
CN 105407718	B	Dead	20221117
EP 3003031	A1	Dead	20210715
JP 2016523232	T	Alive	20201121
BR 112015030501	A2	Alive	20210729
NZ 714817	A	Dead	20210820
US 20160128944	A1	Dead	20210408
MX 2015016675	A	Alive	20201120
AU 2017203374	A1	Alive	20201121
AU 2018282407	A1	Dead	20210708

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2014:2053394

AB The invention provides species of lipid, protein, and/or cationic mol. coated active agents and compns. comprising the coated particles. The compns. can be personal care compns. such as anti-dandruff shampoo or conditioner, skin care compns., creams, gels, toothpastes, mouth washes, and chewing gums.

IPCI A01N0025-12 [I]; A01N0025-34 [I]; A01N0037-06 [I]; A01N0043-12 [I]; A01N0043-40 [I]; A01N0057-12 [I]; A01N0059-16 [I]; A61K0008-11 [I]; A61K0008-49 [I]; A61Q0005-00 [I]; A61K0031-44 [I]; A61Q0019-00 [I]; A61K0009-00 [I]; A61K0031-496 [I]

IPCR A01N0025-34 [I]; A01N0025-12 [I]; A01N0037-06 [I]; A01N0043-12 [I]; A01N0043-40 [I]; A01N0057-12 [I]; A01N0059-16 [I]; A61K0008-11 [I]; A61K0008-49 [I]; A61K0009-00 [I]; A61K0031-44 [I]; A61K0031-496 [I]; A61Q0005-00 [I]; A61Q0019-00 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 62

IT Actins
Albumins
Alkaloids
Aminoglycosides
Androgens
Antibodies and Immunoglobulins
Apricot kernel oil
Avocado oil
Blood proteins
Carbapenems
Carbohydrates
Caseins
Citronella oil
Coal tar
Coconut oil
Collagen hydrolyzates
Collagens

Conchiolins
Corticosteroids
Curcuminoids
Echinocandins
Egg yolk lecithins
Elastins
Estrogens
Ethoxylated hydrogenated castor oil
Fibroin
Fibronectins
Flavanoids
Flavonoids
Fructooligosaccharides
Galactooligosaccharides
Gelatin hydrolyzates
Glycerolipids
Glycerophospholipids
Glycopeptides
Glycosaminoglycans
Hemoglobins
Hydrocarbon oils
Immunoglobulin fragments
Indoles
Integrins
Keratins
Ketolides
Lactalbumins
Lipids
Macrolides
Milk proteins
Neem oil
Oligosaccharides
Oxazolidinones
Palmarosa oil
Paraffin oils
Peppermint oil
Peptide analogs
Peptides
Phosphatidic acids
Phosphatidylcholines
Phosphatidylethanolamines
Phosphatidylinositol 4,5-bisphosphate
Phosphatidylinositol 4-phosphate
Phosphatidylinositols
Phosphatidylinositols
Phosphatidylserines
Phospholipids
Podophyllum (resin)
Polyamines
Polyamines (nonpolymeric)
Polyketides
Polyoxyalkylenes
Polysaccharides
Progestogens
Pyrethroids
Reticulin
Retinoids
Sericin hydrolyzates
Sericins
Soya lecithins
Soybean proteins
Sphingolipids
Sterols
Sulfonamides
Sunflower oil
Sweet orange peel oil
Tetracyclines
Tocopherols
Zeins
β-Lactams
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)

(lipid and protein and/or cationic mol. coated pharmaceutically active particles and compns. comprising same)

IT 84625-61-6, Itraconazole 84957-29-9, Cefpirome 85233-19-8, 1,2-Bis(o-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid 85441-61-8, Quinapril 85622-93-1, Temozolomide 85650-52-8, Mirtazapine 85721-33-1, Ciprofloxacin 86003-55-6, Nikkomycin 86386-73-4, Fluconazole 86541-75-5, Benazepril 86697-97-4, Sensomer CT-250 87061-04-9 87239-81-4, Cefpodoxime proxetil 87848-99-5, Acrivastine 88040-23-7, Cefepime 88150-42-9, Amlodipine 89365-50-4, Salmeterol 91161-71-6, Terbinafine 91374-21-9, Ropinirole 91832-40-5, Cefdinir 92348-62-4, Hydroxycaprylic acid 92665-29-7, Cefprozil 93413-69-5, Venlafaxine 95058-81-4, Gemcitabine 96036-03-2, Meropenem 97321-87-4 97519-39-6, Ceftibuten 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 99011-02-6, Imiquimod 99592-32-2, Sertaconazole 99614-02-5, Ondansetron 100643-71-8, Desloratadine 100986-85-4, Levofloxacin 101828-21-1, Butenafine 103060-53-3, Daptomycin 103577-45-3, Lansoprazole 103775-14-0, Moexiprilat 104227-87-4, Famciclovir 104632-26-0, Pramipexole 105462-24-6, Risedronic acid 105956-97-6, Clinafloxacin 106133-20-4, Tamsulosin 106266-06-2, Risperidone 106392-12-5, Poloxamer 407 106516-24-9, Sertindole 106650-56-0, Sibutramine 106685-40-9, Adapalene 107233-08-9, Cevimeline 107753-78-6, Zafirlukast 108319-06-8, Temafloxacin 110871-86-8, Sparfloxacin 111025-46-8, Pioglitazone 111974-69-7, Quetiapine 112362-50-2, Dalfopristin 112809-51-5, Letrozole 112811-59-3, Gatifloxacin 112965-21-6, Calcipotriene 113170-55-1 113665-84-2, Clopidogrel 113775-47-6, Dexmedetomidine 113806-05-6, Olopatadine 114798-26-4, Losartan 115103-54-3, Tiagabine 115256-11-6, Dofetilide 115956-12-2, Dolasetron 116539-59-4, Duloxetine 117467-28-4, Cefditoren pivoxil 117976-89-3, Rabeprazole 118292-40-3, Tazarotene 119141-88-7, Esomeprazole 119914-60-2, Grepafloxacin 120014-06-4, Donepezil 120138-50-3, Quinupristin 120279-96-1, Dorzolamide 120511-73-1, Anastrozole 121028-76-0 121708-81-4 123441-03-2, Rivastigmine 124937-51-5, Tolterodine 127045-41-4, Pazufloxacin 127254-12-0, Sitafloxacin 128196-01-0, Escitalopram 129618-40-2, Nevirapine 129639-79-8 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 132781-92-1 134678-17-4, Lamivudine 135729-61-2, Palonosetron 136470-78-5, Abacavir 136817-59-9, Delavirdine 137234-62-9, Voriconazole 138402-11-6, Irbesartan 139264-17-8, Zolmitriptan 139755-83-2, Sildenafil 141388-76-3, Besifloxacin 142340-99-6, Adefovir dipivoxil 143322-58-1, Eletriptan 143491-57-0, Emtricitabine 144034-80-0, Rizatriptan 144377-73-1, Linoleamidopropyl PG-dimonium chloride phosphate 144494-65-5, Tirofiban 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 145158-71-0, Tegaserod 146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 150378-17-9, Indinavir 151096-09-2, Moxifloxacin 151319-34-5, Zaleplon 151581-81-6, Pradimicin 152459-95-5, Imatinib 154323-57-6, Almotriptan 154592-20-8, Copper pyrithione 156259-68-6, Capmul MCM 159989-64-7, Nelfinavir 161465-32-3, Elaidolinolenyl alcohol 162011-90-7, Rofecoxib 162808-62-0, Caspofungin 165800-03-3, Linezolid 166663-25-8, Anidulafungin 169590-42-5, Celecoxib 170729-80-3, Aprepitant 171228-49-2, POsaconazole 171596-29-5, Tadalafil 175357-18-3 175463-14-6, Gemifloxacin 177933-73-2D, AMP (acrylate polymer), allyl methacrylate copolymer 179463-17-3, Cancidas 182760-06-1, Ravuconazole 184475-35-2, Gefitinib 187949-02-6, Albaconazole 188627-80-7, Eptifibatide 191114-48-4, Telithromycin 194804-75-6 195868-36-1, Phenyl trimethicone 198904-31-3, Atazanavir 201341-05-1, Tenofovir disoproxil 201531-68-2D, Pyridazinone, dimorpholino deriv. 220222-14-0, Lithium pyrithione 220222-18-4, Strontium pyrithione 224785-90-4, Vardenafil 226256-56-0, Cinacalcet 235114-32-6, Micafungin 241479-67-4, Isavuconazole 313998-09-3, Gold pyrithione 351420-48-9 351420-50-3 374629-79-5 433711-29-6, Carbopol Aqua SF 1 463965-85-7, Behentrimonium methosulfate 506412-91-5 577746-42-0 608514-56-3 830331-83-4 881038-57-9, Zinc selenide sulfide 915764-71-5 951216-62-9 1477911-63-9, Dimethicone PEG-7 Isostearate 1639929-04-6

RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lipid and protein and/or cationic mol. coated pharmaceutically active particles and compns. comprising same)

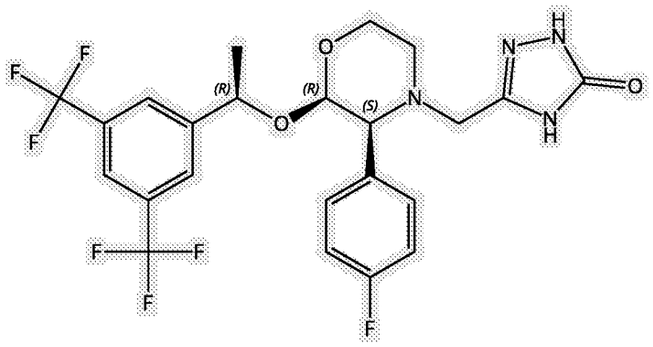
IT 170729-80-3, Aprepitant

RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)
(lipid and protein and/or cationic mol. coated pharmaceutically active particles and compns. comprising same)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2014276460 A1	AU 2014-276460	Register
AU 2017203374 A1	AU 2017-203374	Register
AU 2018282407 A1	AU 2018-282407	Register
BR 112015030501 A2	BR 2015-112015030501	Register
CA 2914583 A1	CA 2014-2914583	Register
CA 2914583 C	CA 2014-2914583	Register
CN 105407718 A	CN 2014-80042031	Register|Global Dossier
CN 105407718 B	CN 2014-80042031	Register|Global Dossier
EP 3003031 A1	EP 2014-739231	Register|Federated Reg.
IL 242916 A	IL 2014-242916	Register
IN 2015CN07967 A	IN 2015-CN7967	Register
JP 2016523232 T	JP 2016-517716	Register|Global Dossier
KR 1814895 B1	KR 2015-7037272	Register|Global Dossier
KR 2016015335 A	KR 2015-7037272	Register|Global Dossier
MX 2015016675 A	MX 2015-16675	Register
NZ 714817 A	NZ 2014-714817	Register
US 20160128944 A1	US 2015-14895738	Register|Global Dossier
WO 2014195872 A1	WO 2014-IB61925	Register|Global Dossier

L5 ANSWER 42 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN

ACCESSION NUMBER: 2014:1944702 CAPLUS Full-text

DOCUMENT NUMBER: 164:453599

TITLE: Statistical investigation of simulated intestinal fluid composition on the equilibrium solubility of biopharmaceutics classification system class II drugs

AUTHOR(S): Khadra, Ibrahim; Zhou, Zhou; Dunn, Claire; Wilson, Clive G.; Halbert, Gavin

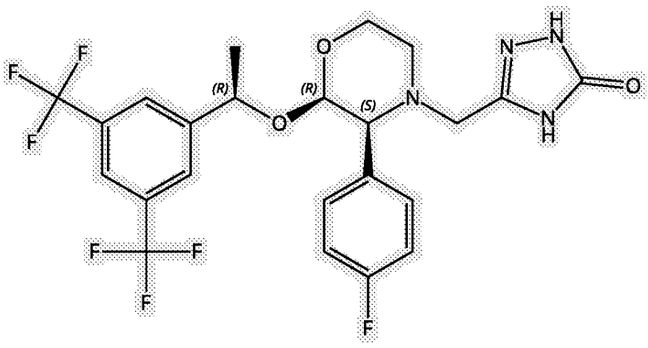
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK

SOURCE: European Journal of Pharmaceutical Sciences (2015), 67, 65-75
CODEN: EPSCED; ISSN: 0928-0987

DIGITAL OBJECT ID: 10.1016/j.ejps.2014.10.019

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB A drug's soly. and dissoln. behavior within the gastrointestinal tract is a key property for successful administration by the oral route and one of the key factors in the biopharmaceutics classification system. This property can be detd. by investigating drug soly. in human intestinal fluid (HIF) but this is difficult to obtain and highly variable, which has led to the development of multiple simulated intestinal fluid (SIF) recipes. Using a statistical design of expt. (DoE) technique this paper has investigated the effects and interactions on equil. drug soly. of seven typical SIF components (sodium taurocholate, lecithin, sodium phosphate, sodium chloride, pH, pancreatin and sodium oleate) within concn. ranges relevant to human intestinal fluid values. A range of poorly sol. drugs with acidic (naproxen, indomethacin, phenytoin, and piroxicam), basic (aprepitant, carvedilol, zafirlukast, tadalafil) or neutral (fenofibrate, griseofulvin, felodipine and probucol) properties have been investigated. The equil. soly. results detd. are comparable with literature studies of the drugs in either HIF or SIF indicating that the DoE is operating in the correct space. With the exception of pancreatin, all of the factors individually had a statistically significant influence on equil. soly. with variations in magnitude of effect between the acidic and basic or neutral compds. and drug specific interactions were evident. Interestingly for the neutral compds. pH was the factor with the second largest soly. effect. Around one third of all the possible factor combinations showed a significant influence on equil. soly. with variations in interaction significance and magnitude of effect between the acidic and basic or neutral compds. The least no. of significant media component interactions were noted for the acidic compds. with three and the greatest for the neutral compds. at seven, with again drug specific effects evident. This indicates that a drug's equil. soly. in SIF is influenced depending upon drug type by between eight to fourteen individual or combinations of media components with some of these drug specific. This illustrates the complex nature of these fluids and provides for individual drugs a visualisation of the possible soly. envelope within the gastrointestinal tract, which may be of importance for modeling in vivo behavior. In addn. the results indicate that the design of expt. approach can be employed to provide greater detail of drug soly. behavior, possible drug specific interactions and influence of variations in gastrointestinal media components due to disease. The approach is also feasible and amenable to adaptation for high throughput screening of drug candidates.
CC 63-5 (Pharmaceuticals)
IT 53-86-1, Indomethacin 57-41-0, Phenytoin 126-07-8, Griseofulvin 22204-53-1, Naproxen 23288-49-5, Probucol 36322-90-4, Piroxicam 49562-28-9, Fenofibrate 72509-76-3, Felodipine 72956-09-3, Carvedilol 107753-78-6, Zafirlukast 170729-80-3, Aprepitant 171596-29-5, Tadalafil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated intestinal fluid compn. on equil. soly. of biopharmaceutics classification system class II drugs)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated intestinal fluid compn. on equil. soly. of biopharmaceutics classification system class II drugs)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 55 THERE ARE 55 CAPLUS RECORDS THAT CITE THIS RECORD (55 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2014:1014062 CAPLUS Full-text
DOCUMENT NUMBER: 161:132468
TITLE: Orally disintegrating film comprising pharmacologically active substance and its manufacturing method
INVENTOR(S): Oh, Dong Hun; Lee, Jin Hu; Lee, So I.; Kang, Jun Hyeok; Lim, Chae Yun; Jung, Gyeong Tae; Yeon, Gyu Jeong; Park, Jin Gyu
PATENT ASSIGNEE(S): Seoul Pharmaceutical Co., Ltd., S. Korea
ULTIMATE OWNER: SEOUL PHARMA. CO., LTD.
ULTIMATE OWNER STANDARD: SEOUL PHARMA. CO., LTD.
SOURCE: Repub. Korea, 15pp.
CODEN: KRXXFC
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
KR 1407922	B1	20140617	KR 2013-138040		20131114
WO 2015072684	A1	20150521	WO 2014-KR10293		20141030
CN 105873572	A	20160817	CN 2014-80071821		20141030
EP 3069716	A1	20160921	EP 2014-861454		20141030
US 20160279071	A1	20160929	US 2016-15036784		20160513
PRIORITY APPLN. INFO.:			KR 2013-138040	A	20131114
			WO 2014-KR10293	W	20141030

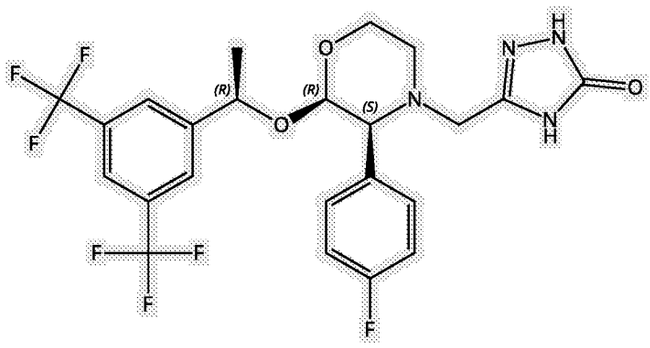
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
KR 1407922	B1	Dead	20201121
WO 2015072684	A1	Dead	20201202
CN 105873572	A	Dead	20201121
EP 3069716	A1	Dead	20201203
US 20160279071	A1	Dead	20201121

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2014:1014062
AB The title film has porosity of 10-35%, and contains more than one bubbling agent selected from nonionic surfactant, cationic surfactant, anionic surfactant and zwitterionic surfactant, more than one bubble stabilizer selected from pullulan, hydroxypropyl Me cellulose, polyvinyl acetate, polyethylene oxide, xanthan gum, guar gum, locust bean gum, starch, starch deriv., pectin, pectin hydrolyzate, alginic acid and alginic acid hydrolyzate, more than one plasticizer selected from glycerin, glycerol oleate, medium chain fatty acid, polyethylene glycol, propylene glycol, propylene glycol monocaprylate, propylene glycol dicaprylate, sugar, sugar

alc. and triacetin, and pharmacol. active substance.
IPCI A61K0009-70 [I]; A61P0003-10 [I]; A61P0003-04 [I]
IPCR A61K0009-70 [I]; A61P0003-04 [I]; A61P0003-10 [I]
CC 63-6 (Pharmaceuticals)
IT Alditols
Enzymes
Hormones, animal
Lecithins
Medium-chain fatty acids
Polyoxyalkylenes
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active substance and its manufg. method)
IT 50-02-2, Dexamethasone 50-58-8, Phendimetrazine tartrate 50-81-7, L-Ascorbic acid, biological studies 54-11-5, Nicotine 55-63-0, Nitroglycerin 56-81-5, Glycerin, biological studies 56-81-5D, Glycerin, fatty acid esters 57-50-1, Sugar, biological studies 57-50-1D, Sucrose, fatty acid esters 57-55-6, Propylene glycol, biological studies 58-08-2, Caffeine, biological studies 61-76-7, Phenylephrine hydrochloride 90-84-6, Diethylpropion 94-09-7, Benzocaine 102-76-1, Triacetin 103-90-2, Acetaminophen 113-92-8 123-03-5, Cetylpyridinium chloride 124-90-3, Oxycodone hydrochloride 125-69-9, Dextromethorphan bromide 147-24-0, Diphenhydramine hydrochloride 345-78-8, Pseudoephedrine hydrochloride 357-08-4, Naloxone hydrochloride 437-38-7, Fentanyl 562-10-7 569-65-3, Meclizine 797-63-7, Levonorgestrel 1134-47-0, Baclofen 1197-21-3, Phentermine hydrochloride 1508-65-2, Oxybutynin hydrochloride 2216-51-5, L-Menthol 7232-21-5, Metoclopramide hydrochloride 7384-98-7, Propylene glycol dicaprylate 8050-81-5, Simethicone 9000-30-0, Guar gum 9000-40-2, Locust bean gum 9000-69-5, Pectin 9003-20-7, Polyvinyl acetate 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 9005-32-7, Alginic acid 9057-02-7, Pullulan 11138-66-2, Xanthan gum 12441-09-7D, Sorbitan, fatty acid esters 14611-52-0, Selegiline hydrochloride 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16679-58-6, Desmopressin 22071-15-4, Ketoprofen 22232-71-9, Mazindol 23828-92-4, Ambroxol hydrochloride 25322-68-3, Polyethylene oxide 27848-84-6, Nicergoline 28911-01-5, Triazolam 28981-97-7, Alprazolam 31565-12-5, Propylene glycol monocaprylate 34552-83-5, Loperamide hydrochloride 37220-82-9, Glycerol oleate 41100-52-1, Memantine hydrochloride 51481-61-9, Cimetidine 52485-79-7, Buprenorphine 56211-40-6, Torasemide 59729-32-7, Citalopram hydrobromide 64461-82-1, Tizanidine hydrochloride 66357-59-3, Ranitidine hydrochloride 71125-38-7, Meloxicam 72797-41-2, Tianeptine 73590-58-6, Omeprazole 76824-35-6, Famotidine 77883-43-3, Doxazosin mesylate 79794-75-5, Loratadine 82248-59-7, Atomoxetine hydrochloride 83480-29-9, Voglibose 83881-52-1, Cetirizine hydrochloride 84057-84-1, Lamotrigine 87333-19-5, Ramipril 90729-43-4, Ebastine 93479-97-1, Glimepiride 97240-79-4, Topiramate 99614-01-4, Ondansetron hydrochloride 99614-02-5, Ondansetron 100299-08-9, Pemirolast potassium 100643-71-8, Desloratadine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 106133-20-4, Tamsulosin 106266-06-2, Risperidone 109889-09-0, Granisetron 112885-41-3, Mosapride 119356-77-3, Dapoxetine 120011-70-3, Donepezil hydrochloride 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 132907-72-3, Ramosetron hydrochloride 139264-17-8, Zolmitriptan 139755-83-2, Sildenafil 140462-76-6, Olopatadine hydrochloride 144034-80-0, Rizatriptan 144689-63-4, Olmesartan medoxomil 151767-02-1, Montelukast sodium 153439-40-8, Fexofenadine hydrochloride 158966-92-8, Montelukast 170729-80-3, Aprepitant 171596-29-5, Tadalafil 171599-83-0, Sildenafil citrate 219861-08-2, Escitalopram oxalate 224785-91-5, Vardenafil hydrochloride 242478-38-2, Solifenacin succinate 246852-12-0, Amlodipine mesylate 268203-93-6, Udenafil 286930-03-8, Fesoterodine fumarate 385367-47-5, Tarafenacin 823178-28-5 862189-96-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active substance and its manufg. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active

substance and its manufg. method)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105873572 A	CN 2014-80071821	Register|Global Dossier
EP 3069716 A1	EP 2014-861454	Register|Federated Reg.
KR 1407922 B1	KR 2013-138040	Register|Global Dossier
US 20160279071 A1	US 2016-15036784	Register|Global Dossier
WO 2015072684 A1	WO 2014-KR10293	Register|Global Dossier

L5 ANSWER 44 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2014:38255 CAPLUS Full-text
DOCUMENT NUMBER: 160:166366
TITLE: Preparation of stable injectable pharmaceutical compositions of neurokinin 1 receptor antagonist
INVENTOR(S): Karavas, Evangelos; Koutris, Efthimos; Bikiaris, Dimitrios; Chatidou, Sotiria; Diakidou, Amalia; Barmpalexis, Panagiotis; Konstanti, Louiza; Minioti, Katerina
PATENT ASSIGNEE(S): Pharmathen S.A., Greece
ULTIMATE OWNER: PARTNERS GROUP HOLDING AG
ULTIMATE OWNER STANDARD: Partners Group
SOURCE: PCT Int. Appl., 24pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014005606	A1	20140109	WO 2012-EP2854	20120706
EP 2866797	A1	20150506	EP 2012-756353	20120706
EP 2866797	B1	20200429		
RS 60599	B1	20200831	RS 2020-846	20120706
ES 2798103	T3	20201209	ES 2012-756353	20120706
US 20150165045	A1	20150618	US 2014-14412147	20141230
US 20200237920	A1	20200730	US 2020-16851779	20200417

PRIORITY APPLN. INFO.:

EP 2012-756353	A3	20120706
WO 2012-EP2854	W	20120706
US 2014-14412147	A1	20141230

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE

WO 2014005606	A1	Dead	20201202
EP 2866797	A1	Indeterminate	20201106
EP 2866797	B1	Indeterminate	20201107
RS 60599	B1	Alive	20201121
ES 2798103	T3	Alive	20201217
US 20150165045	A1	Dead	20220105
US 20200237920	A1	Dead	20231109

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2014:38255

AB The present invention relates to a controlled release sterile injectable formulation in the form of soln., suspension or sol-gel formulation for i.m. or s.c. administration comprising a therapeutically effective amt. of a neurokinin 1 receptor antagonist, in particular aprepitant or fosaprepitant or pharmaceutical acceptable salts, derivs. or metabolites thereof. It also relates to a process for developing such formulations. Thus, an aq. ready-to-use soln. comprised fosaprepitant dimeglumine 142.7, and HPMC-K100 6.7 g/L and water for injection qs to 1 L.

IPCI A61K0031-165 [I]; A61K0009-00 [I]

IPCR A61K0009-00 [I]; A61K0031-165 [I]

CC 63-6 (Pharmaceuticals)

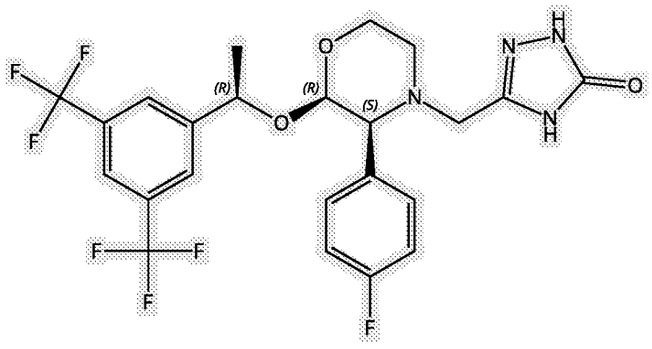
IT Castor oil
Cottonseed oil
Gelatins
Lecithins
Polymers
Polyoxyalkylenes
Sesame oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)

IT 170729-80-3, Aprepitant 172673-20-0 265121-04-8, Fosaprepitant dimeglumine
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

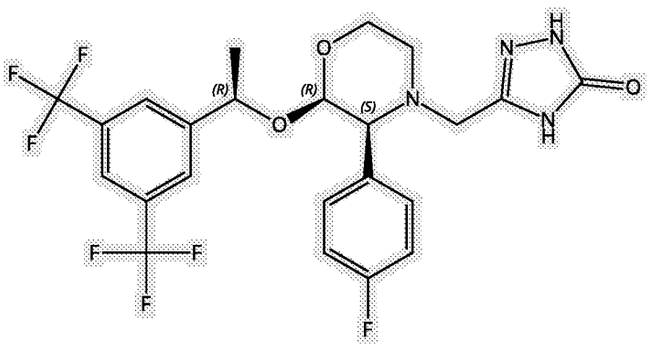
LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
EP 2866797 A1	EP 2012-756353	Register|Federated Reg.
EP 2866797 B1	EP 2012-756353	Register|Federated Reg.
ES 2798103 T3	ES 2012-756353	Register
RS 60599 B1	RS 2020-846	Register
US 20150165045 A1	US 2014-14412147	Register|Global Dossier
US 20200237920 A1	US 2020-16851779	Register|Global Dossier
WO 2014005606 A1	WO 2012-EP2854	Register|Global Dossier

L5 ANSWER 45 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2013:496643 CAPLUS Full-text
DOCUMENT NUMBER: 159:140262
TITLE: Preparation of aprepitant emulsion for intravenous injection
AUTHOR(S): Zhou, Wei; Chen, Fei; Chen, Ning; Mao, Ke
CORPORATE SOURCE: School of Pharmaceutical, Jiangsu Provincial Institute of Materia Medica, Nanjing University of Technology, Nanjing, Jiangsu Province, 211816, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2012), 43(12), 1003-1006
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The formulation of aprepitant emulsion for i.v. injection was optimized by single factor test and orthogonal design. The properties, such as appearance, particle size, ζ potential and stability of the product were investigated. The results showed that the type and amt. of emulsifier as well as the amt. of oleic acid had the greater effect on stability. The optimal formulation of aprepitant emulsion was as follows: aprepitant was 0.25%, soybean oil was 15%, egg yolk lecithin ESO was 2.5% and oleic acid was 0.125%. The appearance of the product was ivory. The av. particle size, PDI, centrifugal stability const. (Ke), ζ potential, pH value and drug content of the product before and after sterilization were (215.71±1.26) and (220.3±0.53) nm, 0.203±0.016 and 0.210±0.009, 0.21±0.01 and 0.34±0.01, (-37.5±0.2) and (-37.6±0.5) mV, 7.21±0.23 and 7.31±0.30, (101.03±0.89)% and (101.12±1.20)%, resp.

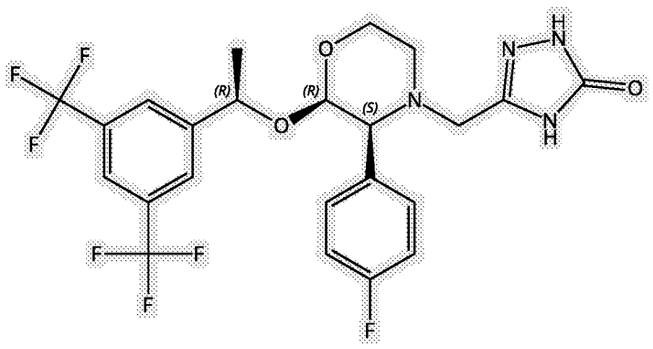
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
Soybean oil
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of aprepitant emulsion for i.v. injection)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of aprepitant emulsion for i.v. injection)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of aprepitant emulsion for i.v. injection)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

L5 ANSWER 46 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2010:1100829 CAPLUS Full-text
DOCUMENT NUMBER: 153:415489
TITLE: Simulating Fasted Human Intestinal Fluids: Understanding the Roles of Lecithin and Bile Acids
AUTHOR(S): Soederlind, Erik; Karlsson, Eva; Carlsson, Anders; Kong, Rui; Lenz, Anna; Lindborg, Sara; Sheng, Jennifer J.
CORPORATE SOURCE: Pharmaceutical Development, AstraZeneca, Moelndal, Swed.
SOURCE: Molecular Pharmaceutics (2010), 7(5), 1498-1507
CODEN: MPOHBP; ISSN: 1543-8384
DIGITAL OBJECT ID: 10.1021/mp100144v
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this work is to evaluate the roles of lecithin and bile salts in a new generation of fasted simulated small intestinal fluid (FaSSIF-II), thus enhancing the closer mimic of simulated fluids to the real human intestinal fluids (HIF) in drug discovery and drug product development. To assess the effects of lecithin in FaSSIF-II, soly. studies were conducted at 37 °C using four media including first generation simulated intestinal fluid (FaSSIF-I), FaSSIF-II, phosphate pH 6.5 buffer, and HIF. A total of 24 model compds. representing a wide range of biopharmaceutic properties were included. The drug soly. values measured in the FaSSIF-II were compared with those in FaSSIF-I, pH 6.5 buffer and HIF. To assess the effects of bile acids, soly. was measured for 4 compds. in the FaSSIF-I contg. five different bile acids of various concns. The lecithin concn. in the FaSSIF-II is lowered from 0.75 mM to 0.2 mM. The results suggested that the FaSSIF-II is a better medium to reflect HIF, compared with pH 6.5 phosphate buffer and FaSSIF-I. Soly. of neutral compds. including atovaquone, carbamazepine, cyclosporine, danazol, diethylstilbestrol, felodipine, griseofulvin and probucol in FaSSIF-II showed improvement in predicting the in vivo soly. The relative std. deviation (SD) of soly. measurement in FaSSIF-II is comparable with FaSSIF-I. For the acidic and basic tested compds., the FaSSIF-II performs similarly to the FaSSIF-I. Exptl. results showed that the level of bile salts typically is less than 5 mM under fasted state. Among the five studied bile acids, the conjugation (glycine or taurine) has no impact on the drug solubilization, while there may be a minimal effect of the degree of hydroxylation of the steroid ring system on solubilization. The lecithin concn. of 0.2 mM in FaSSIF-II has been demonstrated to closely represent HIF, for both neutral and ionizable compds. In the compn. of simulated intestinal fluids, the structure of bile acids has minimal effect, providing the flexibility of choosing one bile salt to represent complex in vivo bile acids.
CC 63-5 (Pharmaceuticals)
ST intestine fluid human lecithin bile acid drug soly
IT Artificial intestinal juice
Dissolution
Human
Hydroxylation
Intestinal juice
Solubility
Solubilization
(simulating fasted human intestinal fluids, roles of lecithin and bile acids)
IT Bile acids
Egg yolk lecithins
Phosphatidylcholines
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(simulating fasted human intestinal fluids, roles of lecithin and bile acids)
IT 81-24-3, Taurocholic acid 145-42-6, Sodium taurocholate 360-65-6, Glycodeoxycholic acid 475-31-0, Glycocholic acid 516-50-7, Taurodeoxycholic acid 640-79-9, Glycochenodeoxycholic acid
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(simulating fasted human intestinal fluids, roles of lecithin and bile acids)

IT 56-53-1, Diethylstilbestrol 57-66-9, Probenecid 58-32-2, Dipyridamole
68-26-8, Retinol 81-81-2, Warfarin 126-07-8, Griseofulvin 298-46-4,
Carbamazepine 530-78-9, Flufenamic acid 599-79-1, Sulfasalazine
1951-25-3, Amiodarone 15307-86-5, Diclofenac 17230-88-5, Danazol
23288-49-5, Probucol 29094-61-9, Glipizide 36322-90-4, Piroxicam
50679-08-8, Terfenadine 51803-78-2, Nimesulide 59865-13-3, Cyclosporin
A 65277-42-1, Ketoconazole 72509-76-3, Felodipine 72956-09-3,
Carvedilol 95233-18-4, Atovaquone 138402-11-6, Irbesartan
168273-06-1, Rimonabant 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(simulating fasted human intestinal fluids, roles of lecithin
and bile acids)
IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(simulating fasted human intestinal fluids, roles of lecithin
and bile acids)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS
RECORD (26 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 47 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2006:142759 CAPLUS Full-text
DOCUMENT NUMBER: 144:239925
TITLE: Solid carriers for improved delivery of active
ingredients containing surfactants and glycerides
INVENTOR(S): Patel, Mahesh
PATENT ASSIGNEE(S): USA
ULTIMATE OWNER: LIPOCINE INC.
ULTIMATE OWNER STANDARD: Lipocine
SOURCE: U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S.
Ser. No. 428,341.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060034937	A1	20060216	US 2005-196805	20050802
US 6248363	B1	20010619	US 1999-447690	19991123
CA 2706113	A1	20010531	CA 2000-2706113	20001122
US 20030064097	A1	20030403	US 2001-800593	20010306
US 6569463	B2	20030527		

US 20030215496	A1	20031120	US 2003-428341		20030501
US 6923988	B2	20050802			
WO 2007018943	A2	20070215	WO 2006-US27159		20060712
WO 2007018943	A3	20090507			
US 20090074859	A1	20090319	US 2008-326711		20081202
JP 2012116863	A	20120621	JP 2012-29635		20120214
US 20140357586	A1	20141204	US 2014-14460188		20140814
US 20150224130	A9	20150813			
US 20150273067	A1	20151001	US 2015-14713692		20150515
US 20180125978	A1	20180510	US 2017-15625764		20170616
US 20200061191	A1	20200227	US 2019-16289565		20190228
US 20210008212	A1	20210114	US 2020-16917731		20200630
PRIORITY APPLN. INFO.:			US 1999-447690	A3	19991123
			US 2001-800593	A1	20010306
			US 2003-428341	A2	20030501
			CA 2000-2391923	A3	20001122
			JP 2001-539423	A3	20001122
			US 2002-159601	A2	20020530
			US 2005-196805	A	20050802
			US 2008-326711	A1	20081202
			US 2014-14460188	A1	20140814
			US 2017-15625764	A1	20170616
			US 2019-16289565	A1	20190228

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20060034937	A1	Dead	20201107
US 6248363	B1	Dead	20201107
CA 2706113	A1	Dead	20201121
US 20030064097	A1	Dead	20201106
US 6569463	B2	Dead	20201106
US 20030215496	A1	Dead	20201106
US 6923988	B2	Dead	20201107
WO 2007018943	A2	Dead	20201201
WO 2007018943	A3	Dead	20201201
US 20090074859	A1	Dead	20201107
JP 2012116863	A	Alive	20201121
US 20140357586	A1	Dead	20201107
US 20150224130	A9	Dead	20201107
US 20150273067	A1	Dead	20201107
US 20180125978	A1	Dead	20201106
US 20200061191	A1	Dead	20201106
US 20210008212	A1	Dead	20210128

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2006:142759

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritional agents, cosmeceuticals and diagnostic agents. For example, particles contained glyburide, PEG stearate, glycerol monolaurate, and Nonpareil seed.

INCL 424497000

IPCI A61K0009-50 [I]; A61K0009-16 [I]

IPCR A61K0009-50 [I]; A61K0009-16 [I]

NCL 424/497.000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 18, 62

IT Lecithins
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

IT Diglycerides

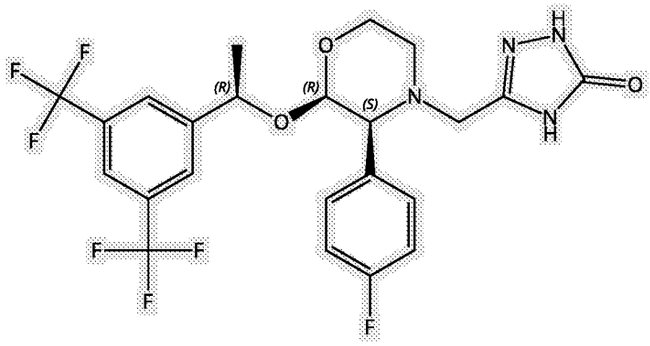
Ethoxylated hydrogenated castor oil
Glycerides
Lecithins
Oligopeptides
Peptides
Polyoxyalkylenes
Safflower oil
Sterols
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

IT 50-35-1, Thalidomide 50-49-7, Imipramine 52-01-7, Spironolactone
52-86-8, Haloperidol 53-03-2, Prednisone 53-39-4, Oxandrolone
57-83-0, Progesterone, biological studies 67-20-9, Nitrofurantoin
81-24-3 83-44-3, Deoxycholic acid 87-69-4D, Tartaric acid, esters
112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 124-07-2,
Octanoic acid, biological studies 145-42-6, Sodium taurocholate
151-41-7, Lauryl sulfate 302-79-4, Tretinoin 303-98-0, Coenzyme Q10
321-64-2, Tacrine 334-48-5, Decanoic acid 357-70-0, Galantamine
511-12-6, Dihydroergotamine 541-15-1D, Carnitine, analogs and derivs.
577-11-7, Sodium docusate 595-33-5, Megestrol acetate 1622-61-3,
Clonazepam 1972-08-3, Dronabinol 2644-64-6, DPPC 5633-20-5,
Oxybutynin 5786-21-0, Clozapine 5949-44-0, Testosterone undecanoate
9002-96-4 9003-39-8, PVP K30 9004-65-3, Hydroxypropyl methylcellulose
9004-96-0, Crodet O 100 9005-32-7D, Alginic acid, salts 9005-37-2,
Propylene glycol alginate 9005-38-3, Sodium alginate 9005-63-4,
Polyoxyethylene sorbitan 9005-64-5, PEG sorbitan monolaurate
9005-65-6, PEG sorbitan monooleate 9009-32-9, Polyglyceryl stearate
10041-19-7 10238-21-8, Glyburide 10540-29-1, Tamoxifen 11140-04-8,
Imwitor 988 14440-80-3, Stearyl lactylate 18656-38-7, DMPC
21256-18-8, Oxaprozin 25086-15-1, Eudragit L100 25322-68-3,
Polyethylene glycol 25322-68-3D, esters 25618-55-7, Polyglycerol
26545-74-4 27215-38-9, Monomuls 90-45 28721-07-5, Oxacarbazepine
29975-16-4, Estazolam 31566-31-1, Imwitor 191 34911-55-2, Bupropion
37220-82-9, Peceol 47931-85-1, Salmon calcitonin 49562-28-9,
Fenofibrate 51322-75-9, Tizanidine 51333-22-3, Budesonide
53123-88-9, Sirolimus 55142-85-3, Ticlopidine 63675-72-9, Nisoldipine
68475-42-3, Anagrelide 70458-96-7, Norfloxacin 71125-38-7, Meloxicam
72509-76-3, Felodipine 72956-09-3, Carvedilol 73590-58-6, Omeprazole
73963-72-1, Cilostazol 74504-64-6, Polyglyceryl laurate 75330-75-5,
Lovastatin 75695-93-1, Isradipine 77337-76-9, Acamprosate
79902-63-9, Simvastatin 81103-11-9, Clarithromycin 82410-32-0,
Ganciclovir 84057-84-1, Lamotrigine 84449-90-1, Raloxifene
84625-61-6, Itraconazole 87333-19-5, Ramipril 88150-42-9, Amlodipine
91374-21-9, Ropinirole 100427-26-7, Lercanidipine 100986-85-4,
Levofloxacin 103577-45-3, Lansoprazole 104987-11-3, Tacrolimus
106266-06-2, Risperidone 106308-44-5, Rufinamide 106392-12-5,
Oxyethylene-oxypropylene block copolymer 107724-20-9, Eplerenone
107753-78-6, Zafirlukast 111025-46-8, Pioglitazone 112811-59-3,
Gatifloxacin 115103-54-3, Tiagabine 124937-51-5, Tolterodine
127779-20-8, Saquinavir 127829-97-4, Solulan C-24 129318-43-0,
Alendronate sodium 129722-12-9, Aripiprazole 130929-57-6, Entacapone
132539-06-1, Olanzapine 133040-01-4, Eprosartan 134308-13-7, Tolcapone
134523-00-5, Atorvastatin 137862-53-4, Valsartan 139755-83-2,
Sildenafil 145158-71-0, Tegaserod 146478-45-7, Polyglycerol dioleate
146939-27-7, Ziprasidone 147536-97-8, Bosentan 154598-52-4, Efavirenz
156259-68-6, Capmul MCM 162011-90-7, Rofecoxib 169590-42-5, Celecoxib
170729-80-3, Aprepitant 174392-00-8, Polyglyceryl monooleate
197179-53-6, Nonpareil
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

IT 170729-80-3, Aprepitant
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX

NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 162 THERE ARE 162 CAPLUS RECORDS THAT CITE THIS RECORD (272 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CA 2706113 A1	CA 2000-2706113	Register
JP 2012116863 A	JP 2012-29635	Register|Global Dossier
US 6248363 B1	US 1999-447690	Register
US 20030064097 A1	US 2001-800593	Register
US 6569463 B2	US 2001-800593	Register
US 20030215496 A1	US 2003-428341	Register|Global Dossier
US 6923988 B2	US 2003-428341	Register|Global Dossier
US 20060034937 A1	US 2005-196805	Register|Global Dossier
US 20090074859 A1	US 2008-326711	Register|Global Dossier
US 20140357586 A1	US 2014-14460188	Register|Global Dossier
US 20150224130 A9	US 2014-14460188	Register|Global Dossier
US 20150273067 A1	US 2015-14713692	Register|Global Dossier
US 20180125978 A1	US 2017-15625764	Register|Global Dossier
US 20200061191 A1	US 2019-16289565	Register|Global Dossier
US 20210008212 A1	US 2020-16917731	Register|Global Dossier
WO 2007018943 A2	WO 2006-US27159	Register|Global Dossier
WO 2007018943 A3	WO 2006-US27159	Register|Global Dossier

L5 ANSWER 48 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2005:1311702 CAPLUS Full-text
DOCUMENT NUMBER: 144:57525
TITLE: Coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents
INVENTOR(S): Wilson, Michelle; Desai, Kishorkumar J.; Pauletti, Giovanni M.; Antoon, Mitchell K.; Clendening, Chris E.
PATENT ASSIGNEE(S): UMD, Inc., USA
ULTIMATE OWNER: U M D
ULTIMATE OWNER STANDARD: U M D
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 126,863
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050276836	A1	20051215	US 2005-180076	20050712
US 6197327	B1	20010306	US 1998-79897	19980515
US 6086909	A	20000711	US 1999-249963	19990212
US 6572874	B1	20030603	US 2000-626025	20000727
NZ 508130	A	20020301	NZ 2000-508130	20001113

AU 2001054192	A	20010913	AU 2001-54192		20010703
AU 765269	B2	20030911			
US 20030049302	A1	20030313	US 2002-226667		20020821
US 6982091	B2	20060103			
US 20040005345	A1	20040108	US 2003-349029		20030122
US 6905701	B2	20050614			
US 20040043071	A1	20040304	US 2003-600849		20030620
US 20050249774	A1	20051110	US 2005-126863		20050510
US 7744916	B2	20100629			
PRIORITY APPLN. INFO.:			US 1997-60049325	P	19970611
			US 1998-79897	A2	19980515
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			US 2002-226667	A2	20020821
			US 2003-349029	A2	20030122
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			US 2004-60587454	P	20040712
			US 2005-126863	A2	20050510
			AU 1998-76976	A3	19980610
			NZ 1998-502120	A1	19980610
			US 1999-249693	A2	19990212
			US 1999-60146218	P	19990728
			US 2001-60315877	P	20010829
			US 2002-60390748	P	20020621

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20050276836	A1	Dead	20201107
US 6197327	B1	Dead	20201107
US 6086909	A	Dead	20201106
US 6572874	B1	Dead	20201107
NZ 508130	A	Dead	20201121
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US 20030049302	A1	Dead	20201121
US 6982091	B2	Dead	20201121
US 20040005345	A1	Dead	20201107
US 6905701	B2	Dead	20201107
US 20040043071	A1	Dead	20201121
US 20050249774	A1	Dead	20220310
US 7744916	B2	Dead	20220310

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2005:1311702

AB Disclosed is a vaginal device for delivering therapeutical and/or health-promoting agents. The vaginal device partly or completely coated by, covered by or combined with a coating or covering comprising a film, foam, strip, cap, cup or particles. The coating of the device comprises a mucoadhesive compn. comprising a therapeutical and/or health-promoting agent. For example, sumatriptan vaginal suppository were prepd. from Suppocire AS2X, hydroxypropyl Me cellulose as a mucoadhesive agent, and Transcutol as a permeation enhancer.

INCL 424422000

IPCI A61F0013-00 [ICM,7]

IPCR A61F0013-00 [I]; A61K0009-00 [I]; A61K0009-02 [I]; A61K0009-12 [I]; A61K0009-19 [I]; A61K0009-70 [I]

NCL 424/422.000

CC 63-6 (Pharmaceuticals)

IT Alkaloids
Amino acids
Bile salts
Cellulosic fibers
Coenzymes
Cottonseed oil
Essential oils
Fats and Glyceridic oils
Interleukins
Lecithins
Minerals
Natural products, pharmaceutical
Peptides
Phenols
Polyketides

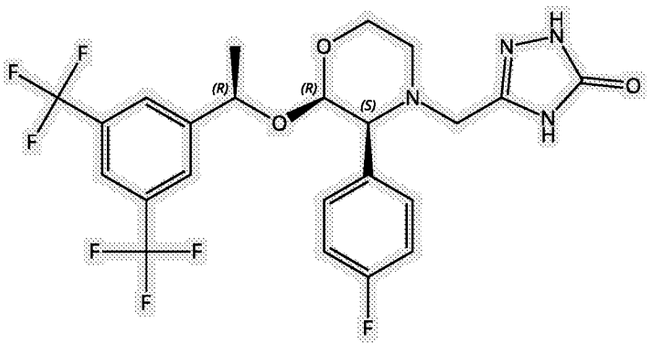
Polyoxyalkylenes
Proteins
Resins
Silicone rubber
Tannins
Terpenes
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents)

IT 68379-02-2, Clofilium 69655-05-6, Didanosine 70458-96-7, Norfloxacin 71048-87-8, Levonantradol 71125-38-7, Meloxicam 72479-26-6, Fenticonazole 72509-76-3, Felodipine 73573-87-2, Formoterol 74103-06-3, Ketorolac 74103-07-4, Ketorolac tromethamine 74191-85-8, Doxazosin 74545-79-2, Aloeresin A 75088-80-1, Manoalide 75330-75-5, Lovastatin 75695-93-1, Isradipine 76584-70-8, Divalproex sodium 79350-37-1, Cefixime 79778-41-9, Neridronate 80210-62-4, Cefpodoxime 80937-31-1, Flosulide 82410-32-0, Ganciclovir 83905-01-5, Azithromycin 83991-25-7, Ambasilide 84625-61-6, Itraconazole 85622-93-1, Temozolomide 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 88150-42-9, Amlodipine 89365-50-4, Salmeterol 89565-68-4, Tropisetron 89778-26-7, Toremifene 89987-06-4, Tiludronate 90357-06-5, Bicalutamide 90961-53-8, Tedisamil 91714-94-2, Bromfenac 92665-29-7, Cefprozil 95058-81-4, Gemcitabine 95298-47-8 95751-30-7, Charybdotoxin 97240-79-4, Topiramate 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 98225-48-0, Brevetoxin 99614-02-5, Ondansetron 101526-83-4, Sematilide 103628-46-2, Sumatriptan 104227-87-4, Famciclovir 105462-24-6 107868-30-4, Exemestane 110042-95-0, Acemannan 112455-84-2, Papuamine 112809-51-5, Letrozole 114084-78-5, Ibandronate 114977-28-5, Docetaxel 115256-11-6, Dofetilide 115956-12-2, Dolasetron 118072-93-8, Zoledronate 120511-73-1, Anastrozole 121368-58-9, Olpadronate 121679-13-8, Naratriptan 122647-31-8, Ibutilide 123948-87-8, Topotecan 127779-20-8, Saquinavir 129618-40-2, Nevirapine 132539-06-1, Olanzapine 134678-17-4, Lamivudine 135729-61-2, Palonosetron 136470-78-5, Abacavir 136817-59-9, Delavirdine 137234-62-9, Voriconazole 139110-80-8, Zanamivir 139226-28-1, Darbufelone 139264-17-8, Zolmitriptan 143322-58-1, Eletriptan 143491-57-0, Emtricitabine 144034-80-0, Rizatriptan 147127-20-6, Tenofovir 149908-53-2, Azimilide 150378-17-9, Indinavir 152459-95-5, Imatinib 153559-49-0, Bexarotene 154323-57-6, Almotriptan 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155213-67-5, Ritonavir 158751-64-5, ClAmikalant 159519-65-0, Enfuvirtide 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 169944-35-8, Bisulfan 170729-80-3, Aprepitant 181695-72-7, Valdecoxib 184475-35-2, Gefitinib 190017-00-6, Correolide 192725-17-0, Lopinavir 196618-13-0, Oseltamivir 198470-84-7, Parecoxib 198904-31-3, Atazanavir 202409-33-4, Etoricoxib 220991-20-8, Lumiracoxib 226700-79-4, Fosamprenavir 260792-29-8, 6β,7β-Diacetoxy-13-hydroxylabda-8,14-diene 264875-61-8, Cimiracemoside A 501938-01-8, 23-epi-26-Deoxyactein 856012-03-8 865111-98-4 865147-59-7, Altissinone 871260-93-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2001054192 A	AU 2001-54192	Register
AU 765269 B2	AU 2001-54192	Register
NZ 508130 A	NZ 2000-508130	Register
US 6197327 B1	US 1998-79897	Register
US 6086909 A	US 1999-249963	Register
US 6572874 B1	US 2000-626025	Register
US 20030049302 A1	US 2002-226667	Register
US 6982091 B2	US 2002-226667	Register
US 20040005345 A1	US 2003-349029	Register|Global Dossier
US 6905701 B2	US 2003-349029	Register|Global Dossier
US 20040043071 A1	US 2003-600849	Register|Global Dossier
US 20050249774 A1	US 2005-126863	Register|Global Dossier
US 7744916 B2	US 2005-126863	Register|Global Dossier
US 20050276836 A1	US 2005-180076	Register|Global Dossier

L5 ANSWER 49 OF 49 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2002:695760 CAPLUS Full-text
DOCUMENT NUMBER: 137:237717
TITLE: Inhalant compositions containing anticholinergics and NK1 receptor antagonists
INVENTOR(S): Meade, Christopher John Montague; Pairet, Michel; Pieper, Michael Paul
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069944	A2	20020912	WO 2002-EP1987	20020226
WO 2002069944	A3	20031002		
DE 10111058	A1	20020912	DE 2001-10111058	20010308
CA 2439915	A1	20020912	CA 2002-2439915	20020226
AU 2002251010	A1	20020919	AU 2002-251010	20020226
EP 1370293	A2	20031217	EP 2002-719915	20020226
JP 2004519484	T	20040702	JP 2002-569121	20020226
MX 2003008051	A	20031204	MX 2003-8051	20030905

PRIORITY APPLN. INFO.: DE 2001-10111058 A 20010308
WO 2002-EP1987 W 20020226

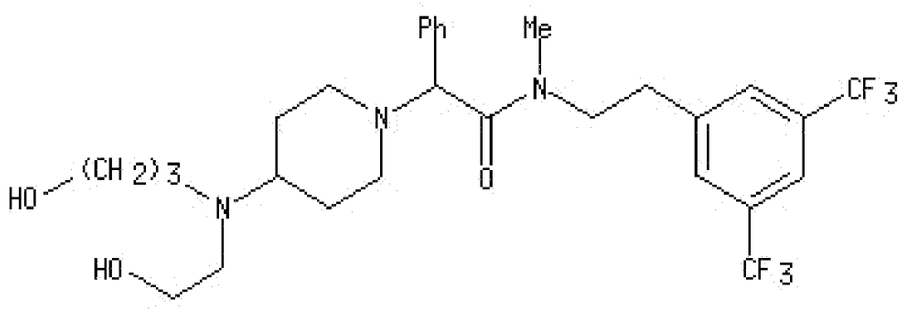
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
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WO 2002069944	A3	Dead	20201201
DE 10111058	A1	Dead	20201121
CA 2439915	A1	Dead	20201121
AU 2002251010	A1	Dead	20201121
EP 1370293	A2	Dead	20201202
JP 2004519484	T	Dead	20220303
MX 2003008051	A	Dead	20201121

OTHER SOURCE(S): MARPAT 137:237717; CASFORMULTNS 2002:695760

GI



AB The invention relates to drug compns. based on anticholinergics and on NK1 receptor antagonists, to methods for their prodn., and to their use as inhalants for the treatment of respiratory tract diseases. Synthesis of NK1 receptor antagonists from the group of bis-trifluoromethyl-phenyl-piperidine derivs. are described. The products are used in suspension aerosols. Thus a compn. contained (wt./wt.%): tiotropium bromide 0.015; NK1 receptor antagonist 0.066; soy lecithin 0.2; TG11: TG12 = 2:3 to 100.

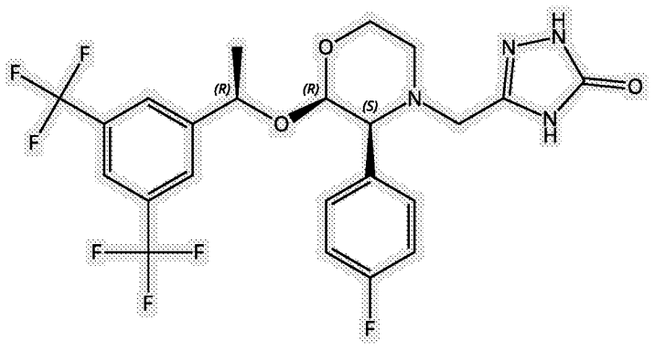
IPCI A61K0031-00 [ICM,7]

IPCR A61K0009-08 [I]; A61K0009-00 [I]; A61K0009-10 [I]; A61K0009-14 [I]; A61K0009-48 [I]; A61K0009-72 [I]; A61K0031-00 [I]; A61K0031-223 [I]; A61K0031-403 [I]; A61K0031-439 [I]; A61K0031-4468 [I]; A61K0031-46 [I]; A61K0031-4745 [I]; A61K0031-535 [I]; A61K0031-55 [I]; A61K0045-06 [I]; A61K0047-04 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-18 [I]; A61K0047-22 [I]; A61K0047-26 [I]; A61P0011-00 [I]; A61P0011-08 [I]; A61P0029-00 [I]; A61P0043-00 [I]

CC 63-6 (Pharmaceuticals)

IT 50-81-7, Ascorbic acid, biological studies 56-81-5, Glycerol, biological studies 57-55-6, Propylene glycol, biological studies 64-02-8 64-17-5, Ethanol, biological studies 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 65-85-0, Benzoic acid, biological studies 74-98-6, n-Propane, biological studies 75-28-5, Isobutane 77-92-9, Citric acid, biological studies 79-09-4, Propionic acid, biological studies 106-97-8, n-Butane, biological studies 110-15-6, Succinic acid, biological studies 110-16-7, Maleic acid, biological studies 110-17-8, Fumaric acid, biological studies 123-03-5, Cetylpyridinium chloride 431-89-0, TG227 526-83-0, Tartaric acid 811-97-2, TG134a 1406-18-4, Vitamin E 6915-15-7, Malic acid 7647-01-0, Hydrochloric acid, biological studies 7664-93-9, Sulfuric acid, biological studies 7697-37-2, Nitric acid, biological studies 10035-10-6, Hydrobromic acid, biological studies 11103-57-4, Vitamin A 25322-68-3, Polyethylene glycol 25322-68-3D, alcs. and fatty acid esters 25322-69-4, Polypropylene glycol 60205-81-4, Ipratropium 99571-64-9, Oxitropium 138449-07-7, FK-888 142001-63-6, Saredutant 145742-28-5, CP-122721 147116-64-1, CJ 11974 155418-05-6, SR 140333 168266-90-8, GR 205171 170566-84-4, Lanepitant 170739-80-3, MK-869 171272-39-2, MEN-10930 172673-20-0, L-758298 173941-19-0, YM 49244 173941-22-5, YM 35375 173941-74-7, YM 44778 174636-32-9, SB 223412 174661-97-3, DA-5018 178370-50-8, MDL 103896 183747-35-5, Nepadutant 188241-50-1, S-19752 193694-35-8, MDL-105172A 201152-86-5, SR-144190 206052-25-7, MEN-11149 209474-01-1, Neuronorm 214487-46-4, MEN-11467 217185-75-6, TAK-637 350610-25-2 350610-26-3, 6b-I 350610-27-4, DNK-33A 350610-29-6, ZM-274773 350610-34-3, DNK 333A 350610-51-4, CGP 60829 350610-61-6, NKP 608A 350610-64-9, NKP 608C 415917-13-4 457910-81-5 458568-84-8, TG 11 458569-01-2, TG 12
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhalant compns. contg. anticholinergics and NK1 receptor antagonists)
IT 170729-80-3, MK-869
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalant compns. contg. anticholinergics and NK1 receptor antagonists)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2002251010 A1	AU 2002-251010	Register
CA 2439915 A1	CA 2002-2439915	Register
DE 10111058 A1	DE 2001-10111058	Register
EP 1370293 A2	EP 2002-719915	Register|Federated Reg.
JP 2004519484 T	JP 2002-569121	Register
MX 2003008051 A	MX 2003-8051	Register
WO 2002069944 A2	WO 2002-EP1987	Register|Global Dossier
WO 2002069944 A3	WO 2002-EP1987	Register|Global Dossier

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	17	(A61K9/1075 AND A61K9/0019 AND A61K31/43 AND A61K31/496 AND A61K31/5377 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:29 PM
L2	19	(A61K9/1075 AND A61K9/0019 AND A61K31/496 AND A61K31/5377 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:30 PM
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L4	1402	(A61K9/1075 AND A61K9/0019 AND A61K47/10 AND	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY,	OR	ON	ON	2024/03/13 03:31 PM

		A61K47/44)	CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L5	31	((A61K9/1075 AND A61K9/0019 AND A61K47/10 AND A61K47/44) AND aprepitant)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:32 PM
L6	3999	(aprepitant AND phospholipid AND oil AND ethanol AND water AND inject$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/03/13 03:33 PM
L7	31	((("Heron") near3 ("Therapeutics") near3 ("Inc"))).AS,AANM.	(USPAT)	OR	ON	ON	2024/03/13 03:34 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
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		A61K47/44)					
N2	22	(A61K9/1075 AND A61K9/0019 AND A61K31/5377 AND A61K47/10 AND A61K47/44)	(US-PGPUB; USPAT)	OR	ON	ON	2024/03/13 03:31 PM
N3	1154	(aprepitant AND phospholipid AND oil AND ethanol AND water AND inject$)	(US-PGPUB; USPAT)	OR	ON	ON	2024/03/13 03:33 PM

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DICTIONARY FILE UPDATES:  10 MAR 2024  HIGHEST RN 3030174-11-6

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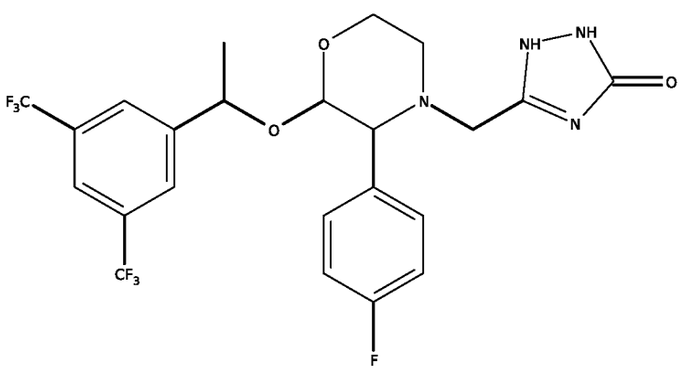
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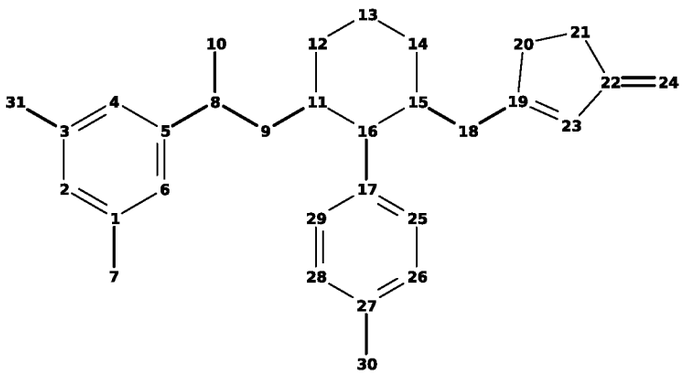
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Node Attributes
Ring Nodes : 1 2 3 4 5 6 11 12 13 14 15 16 17 19 22 23 25 26 27 28 29
Chain Nodes : 8 9 10 18 24 30
Bond Attributes
Ring Bonds : 1-2 2-3 3-4 4-5 5-6 6-1 11-12 12-13 13-14 14-15 15-16 16-11 17-25 19-20 20-21 21-22 22-23 23-19 25-26 26-27 27-28 28-29 29-17
Chain Bonds : 1-7 3-31 5-8 8-9 8-10 9-11 15-18 16-17 18-19 22-24 27-30
Exact Bonds : 1-7 3-31 5-8 8-10 16-17 18-19 27-30
Normalized Bonds : 1-2 2-3 3-4 4-5 5-6 6-1 17-25 25-26 26-27 27-28 28-29 29-17
Exact/Normalized Bonds : 8-9 9-11 11-12 12-13 13-14 14-15 15-16 15-18

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16-11  19-20  20-21  21-22  22-23  22-24  23-19
Markush Attributes
Match Level (ATOM) : 1  2  3  4  5  6  11  12  13  14  15  16  17  19  20  21
22  23  25  26  27  28  29
Match Level (CLASS) : 7  8  9  10  18  24  30  31
Element Count Level (LIMITED) : 1  2  3  4  5  6  7  8  9  10  11  12  13  14
15  16  17  18  19  20  21  22  23  24  25  26  27  28  29  30  31



L1      STRUCTURE UPLOADED

=> S L1 SSS FULL

FULL SEARCH INITIATED 15:59:31 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      802 TO ITERATE

100.0% PROCESSED        802 ITERATIONS                                68 ANSWERS
SEARCH TIME: 00.00.01

L2           68 SEA SSS FUL L1

=> FILE CAPLUS

COST IN U.S. DOLLARS                          SINCE FILE           TOTAL
                                                   ENTRY         SESSION
FULL ESTIMATED COST                              883.16          883.51

FILE 'CAPLUS' ENTERED AT 15:59:37 ON 11 MAR 2024
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FILE COVERS 1907 - 11 Mar 2024 VOL 186 ISS 1
FILE LAST UPDATED: 10 Mar 2024 (20240310/ED)

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Huge expansion of patent authority coverage in CA/Caplus
provides more complete patent families, expanded invention
coverage.  See NEWS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> S L2

L3         1679 L2

=> S L3 AND lecithin

          55293 LECITHIN
          62182 LECITHINS
          87410 LECITHIN
                (LECITHIN OR LECITHINS)
L4           48 L3 AND LECITHIN
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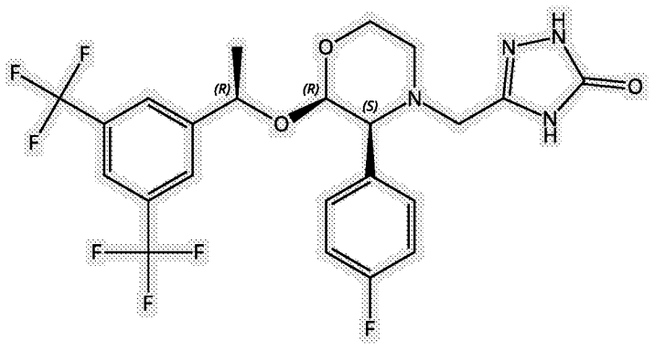
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=> S L4 AND emulsion

        426011 EMULSION
        262935 EMULSIONS
        526451 EMULSION
                 (EMULSION OR EMULSIONS)
L5          18 L4 AND EMULSION

=> D L5 1-18 IBIB ABS HITIND HITSTR


L5   ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER:        2024:141628  CAPLUS Full-text
TITLE:                   Aprepitant emulsion drug composition and preparation
                         method thereof
INVENTOR(S):             Chen, Xiangmei; Yu, Changhui; Wang, Xinlong; Lin,
                         Liyang; Shen, Li; Zhao, Dong
PATENT ASSIGNEE(S):      Sichuan Kelun Pharmaceutical Research Institute Co.,
                         Ltd., Peop. Rep. China
SOURCE:                  Faming Zhuanli Shenqing, 8pp.
                         CODEN: CNXXEV
DOCUMENT TYPE:           Patent
LANGUAGE:                Chinese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:
     PATENT NO.          KIND  DATE        APPLICATION NO.         DATE
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     CN 117414334         A    20240119    CN 2022-10811953        20220711
PRIORITY APPLN. INFO.:                     CN 2022-10811953        20220711
PATENT STATUS PATENT INFORMATION:
     PATENT NO.          KIND  STATUS          STATUS DATE
     ----------------    ----  -------------   -----------
     CN 117414334         A    Alive           20240125
AB   The present invention provides an aprepitant emulsion drug compn. and
     prepn. method thereof, which has the advantages of high quality and good
     stability.  The method comprises the following steps: stirring and
     dissolving aprepitant, phospholipid, ethanol and soybean oil to obtain an
     oil phase, adding an isotonic regulator, the phospholipid and a pH
     regulator into water for injection, stirring uniformly to obtain a water
     phase, online shearing and mixing the oil phase and the water phase to
     prep. a primary emulsion, homogenizing by high-pressure microjet,
     sterilizing, filtering and filling.
IPCI A61K0009-107; A61K0031-5377; A61K0047-24; A61K0047-44; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61K0047-44 [I];
     A61P0001-08 [I]
CC   63 (Pharmaceuticals)
ST   aprepitant emulsion drug prepn
IT   INDEXING IN PROGRESS
IT   Emulsions
     Filtration
     Mixing
     Sterilization and Disinfection
     Stirring
        (aprepitant emulsion drug compn. and prepn. method thereof)
IT   Egg yolk lecithins
     Soybean oil
     RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical
     process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (aprepitant emulsion drug compn. and prepn. method thereof)
IT   64-17-5, Ethanol
     RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical
     process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (aprepitant emulsion drug compn. and prepn. method thereof)
IT   57-50-1, D-Sucrose   143-19-1, Sodium oleate
     RL: PEP (Physical, engineering or chemical process); PROC (Process)
        (aprepitant emulsion drug compn. and prepn. method thereof)
IT   170729-80-3, Aprepitant
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (aprepitant emulsion drug compn. and prepn. method thereof)
```

IT 170729-80-3, Aprepitant
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(aprepitant emulsion drug compn. and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 117414334 A	CN 2022-10811953	Register|Global Dossier

L5 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:1355958 CAPLUS Full-text
DOCUMENT NUMBER: 179:75293
TITLE: Stable antiemetic emulsions
INVENTOR(S): Bhagwatwar, Harshal Prabhakar; Nerurkar, Manoj
PATENT ASSIGNEE(S): Steps BioSciences, Inc., USA
ULTIMATE OWNER: STEPS BIOSCIENCES
ULTIMATE OWNER STANDARD: STEPS BIOSCIENCES
SOURCE: U.S. Pat. Appl. Publ., 11pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

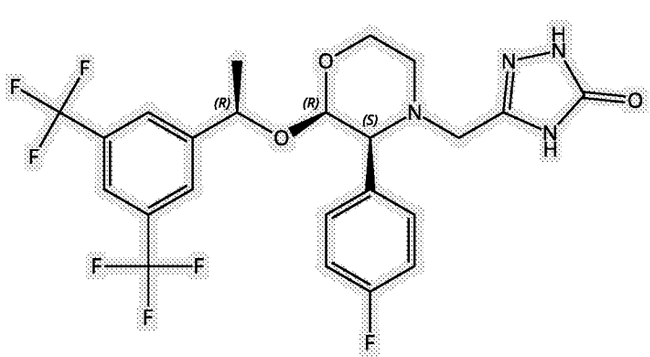
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20220160722	A1	20220526	US 2021-17531216		20211119
PRIORITY APPLN. INFO.:			IN 2020-41050531	A	20201120

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20220160722	A1	Alive	20220609

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2022:1355958
AB Emulsion formulations and systems for the i.v. or parenteral administration. of neurokinin-1 (NK-1) receptor antagonists for treatment of emesis are provided. Methods for prepg. the stable NK-1 receptor antagonist emulsions and pharmaceutical formulations are further provided. The emulsion formulations are prepd. and characterized as a formulation and process that will allow an NK-1 receptor antagonist compd. to be incorporated into an emulsion for i.v. injection and remain stable during the shelf life of the formulation. Specifically, emulsion formulations have an oil phase that includes oil, ethanol, egg lecithin , and the further addn. of sodium oleate that is mixed with an aq. phase and processed to form the emulsion formulation.
IPCI A61K0031-5377 [I]; A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-24 [I];

A61K0047-12 [I]; A61K0047-10 [I]; A61K0047-44 [I]
IPCR A61K0031-5377 [I]; A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-10 [I];
A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-44 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST antiemetic emulsion neurokinin receptor antagonist
IT Antiemetics
Buffers
Emulsifying agents
Neurokinin 1 receptor antagonists
Parenteral drug delivery systems
Pharmaceutical dispersions
Pharmaceutical emulsions
Pharmaceutical formulations
Pharmaceutical injections
Pharmaceutical intravenous injections
Pharmaceutical tonicity modifiers
Stability
Vomiting
Zeta potential
pH
(stable antiemetic emulsions)
IT Castor oil
Coconut oil
Corn oil
Cottonseed oil
Egg yolk lecithins
Lecithins
Olive oil
Safflower oil
Sesame oil
Soybean oil
Triglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
IT 57-50-1, Sucrose, biological studies 64-17-5, Ethanol, biological
studies 111-62-6, Ethyl oleate 143-19-1, Sodium oleate 303-43-5,
Cholesteryl oleate 544-35-4, Ethyl linoleate 604-33-1, Cholesteryl
linoleate 37220-82-9, Glyceryl oleate 37348-65-5, Glyceryl linoleate
136745-48-7, Octyl glycerate 152167-64-1, Decyl glycerate
170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
US 20220160722 A1	US 2021-17531216	Register|Global Dossier

L5 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:139737 CAPLUS Full-text
DOCUMENT NUMBER: 177:284905
TITLE: Pharmaceutical emulsion comprising an aprepitant, pharmaceutical injections, and methods of preparing emulsions
INVENTOR(S): Amano, Yohei; Katagiri, Kazumi
PATENT ASSIGNEE(S): Kewpie Corporation, Japan; FBC (Shanghai) Pharmaceutical Technology Co., Ltd.
ULTIMATE OWNER: FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; KEWPIE CORPORATION
ULTIMATE OWNER STANDARD: FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; Kewpie Corp
SOURCE: PCT Int. Appl., 28pp.; Chemical Indexing Equivalent to 174:540291 (JP)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2022014113	A1	20220120	WO 2021-JP15552	20210415
JP 6832468	B1	20210224	JP 2020-121438	20200715
JP 2022018370	A	20220127		
CA 3187858	A1	20220120	CA 2021-3187858	20210415
KR 2023040956	A	20230323	KR 2022-7045138	20210415
EP 4169515	A1	20230426	EP 2021-843280	20210415
US 20230310443	A1	20231005	US 2023-18015492	20230110

PRIORITY APPLN. INFO.: JP 2020-121438 A 20200715
WO 2021-JP15552 W 20210415

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2022014113	A1	Alive	20220203
JP 6832468	B1	Alive	20210304
JP 2022018370	A	Alive	20220224
CA 3187858	A1	Alive	20230216
KR 2023040956	A	Alive	20230420
EP 4169515	A1	Alive	20230427
US 20230310443	A1	Alive	20231012

AB The present invention pertains to an emulsion which contains an aprepitant, an emulsifier, an oil, a polyethylene glycol having an av. mol. wt. of 260-1100, and water, and to which ethanol is substantially not added. The content of the aprepitant is 0.50-0.90 w/v% based on the total amt., and the content of the emulsifier is 12.0-18 w/v%. The content of oil is 7.0-12.0 w/v %, and the content of polyethylene glycol is 0.5-10.0 w/v %. The av. particle diam. of the emulsion is 60-140 nm. According to the present invention, provided is an aprepitant-contg. emulsion having excellent stability without substantially adding ethanol.
IPCI A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]
IPCR A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
ST aprepitant pharmaceutical emulsion injection
IT Emulsifying agents
Pharmaceutical emulsions
Pharmaceutical injections
Tonicity modifiers
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)
IT Egg yolk lecithins
Phospholipids

Polyoxyalkylenes
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

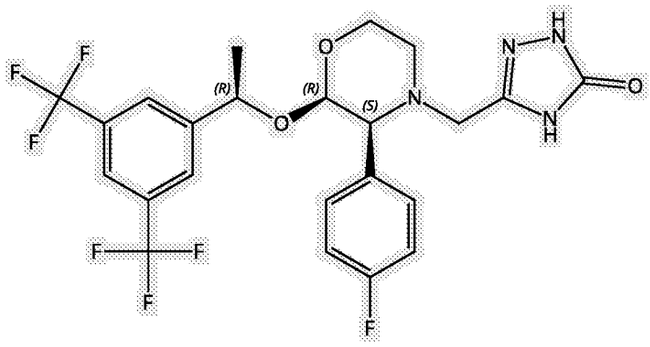
IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 57-50-1, biological studies 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 143-19-1 25322-68-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CA 3187858 A1	CA 2021-3187858	Register
EP 4169515 A1	EP 2021-843280	Register|Federated Reg.
JP 2022018370 A	JP 2020-121438	Register|Global Dossier
JP 6832468 B1	JP 2020-121438	Register|Global Dossier
KR 2023040956 A	KR 2022-7045138	Register|Global Dossier
US 20230310443 A1	US 2023-18015492	Register|Global Dossier
WO 2022014113 A1	WO 2021-JP15552	Register|Global Dossier

L5 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:2591917 CAPLUS Full-text
DOCUMENT NUMBER: 177:123225
TITLE: Preparation method of aprepitant emulsion injection for preventing nausea and emesis
INVENTOR(S): Guo, Shuer; Qin, Zhijun
PATENT ASSIGNEE(S): Guangzhou Manxiang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU MAXENMED MEDICINE
ULTIMATE OWNER STANDARD: GUANGZHOU MAXENMED MEDICINE
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

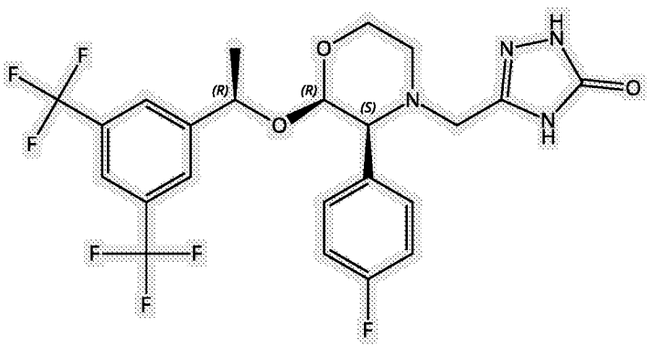
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 113712915	A	20211130	CN 2021-10018100	20210107

PRIORITY APPLN. INFO.: CN 2021-10018100 20210107
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 113712915	A	Alive	20211209

OTHER SOURCE(S): CASFORMULTNS 2021:2591917
AB The invention aprepitant emulsion injection is prepd. from (by wt%) aprepitant 0.2-1.2, pH regulator 0.25-0.75, permeation pressure regulator 3-8, injection water 56-75, emulsifier 12-15, cosolvent 2-5, and injection oil 5-15. The emulsifier is hydrogenated soybean lecithin or hydrogenated soybean phosphatidylcholine. The pH regulator is sodium hydroxide, sodium citrate, sodium dihydrogen phosphate or sodium oleate. The permeation pressure regulator is xylitol, sorbitol, mannitol or sucrose. The cosolvent is ethanol, glycerol, propylene glycol and polyethylene glycol. The injection oil is soybean oil, peanut oil, hydrogenated corn oil, triglyceride, medium-chain triglyceride, sesame oil and/or sunflower seed oil. By controlling content of emulsifier and shearing rotation speed, homogenization pressure and homogenization temp. in emulsion prepn. process, the invention preps. aprepitant emulsion injection with good oxidn. resistance and emulsification effect, and has operability, simple process and low device loss.
IPCI A61K0009-107; A61K0047-24; A61K0031-5377; A61P0001-08; A61P0035-00
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
ST aprepitant emulsion injection nausea emesis
IT Corn oil
Soya lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT Antiemetics
Biological permeation
Cosolvents
Emulsifying agents
Homo sapiens
Homogenization
Human
Nausea
Pharmaceutical emulsions
Pharmaceutical injections
Vomiting
pH
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT Hydrogenated soya phosphatidylcholines
Medium-chain glycerides
Oils
Peanut oil
Polyoxyalkylenes
Sesame oil
Soybean oil
Sunflower oil
Triglycerides
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT 50-70-4, Sorbitol, biological studies 56-81-5, Glycerol, biological studies 57-50-1, Sucrose, biological studies 57-55-6, Propylene glycol, biological studies 64-17-5, Ethanol, biological studies 68-04-2 69-65-8, D-Mannitol 87-99-0, Xylitol 143-19-1, Sodium oleate 1310-73-2, Sodium hydroxide, biological studies 7558-80-7, Sodium dihydrogen phosphate 25322-68-3, Polyethylene glycol
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 113712915 A	CN 2021-10018100	Register|Global Dossier

L5 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:1541826 CAPLUS Full-text
DOCUMENT NUMBER: 175:329880
TITLE: Aprepitant ready-to-use injection emulsion compositions
INVENTOR(S): Akasapu, Prem Sagar; Subramanian, Veerappan; Subramanian, Ilango
PATENT ASSIGNEE(S): Somerset Therapeutics LLC, USA
ULTIMATE OWNER: SOMERSET THERAPEUTICS LLC
ULTIMATE OWNER STANDARD: SOMERSET THERAPEUTICS LLC
SOURCE: U.S. Pat. Appl. Publ., 8pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20210212933	A1	20210715	US 2021-17147556	20210113
US 11517522	B2	20221206		

PRIORITY APPLN. INFO.: US 2020-62961039 P 20200114
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20210212933	A1	Alive	20210722
US 11517522	B2	Alive	20221215

OTHER SOURCE(S): CASFORMULTNS 2021:1541826
AB The present invention provides an emulsion compn. comprising aprepitant for treatment of emesis. Particularly, the invention is a ready-to-use emulsion compns. comprising aprepitant and medium chain triglycerides

for administration by i.v. infusion, wherein the emulsion compn. is also free of ethanol. Further, the invention also provides processes of prepg. such compns. and their use for the prevention and control of acute and delayed chemotherapy-induced nausea and vomiting, and/or for prevention of postoperative nausea and vomiting.

IPCI A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-14 [I]; A61M0005-24 [I]; A61K0031-5377 [I]; A61K0009-00 [I]; A61K0047-14 [I]; A61K0009-107 [I]; A61K0031-5377 [I]; A61M0005-24 [I]

IPCR A61K0009-00 [I]; A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-14 [I]; A61M0005-24 [I]

CC 63-6 (Pharmaceuticals)

ST aprepitant injection emulsion

IT Humidity
Nausea
Oil-in-water emulsions
Pharmaceutical emulsions
Pharmaceutical intravenous infusions
Vomiting
Zeta potential
pH
(aprepitant ready-to-use injection emulsion compns.)

IT Lecithins
Medium-chain glycerides
Polyoxyalkylenes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)

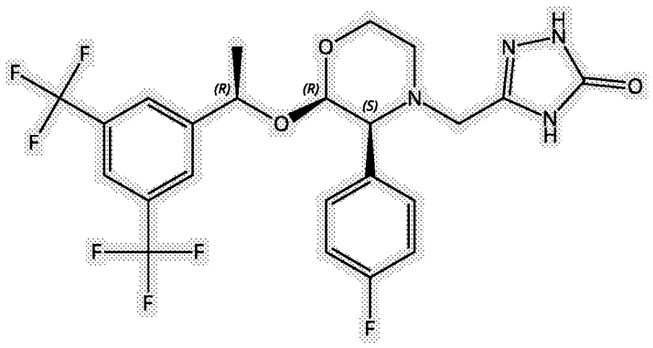
IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 56-81-5, Glycerol, biological studies 57-50-1, Sucrose, biological studies 57-55-6, Propylene glycol, biological studies 63-42-3, Lactose 64-17-5, Ethanol, biological studies 69-65-8, Mannitol 69-79-4, Maltose 87-99-0, Xylitol 99-20-7, Trehalose 512-69-6, Raffinose 7647-14-5, Sodium chloride, biological studies 9004-54-0, Dextran, biological studies 25322-68-3, Poly ethylene glycol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION
PUBLICATIONS APPLICATIONS REGISTER

US 11517522 B2	US 2021-17147556	Register|Global Dossier
US 20210212933 A1	US 2021-17147556	Register|Global Dossier

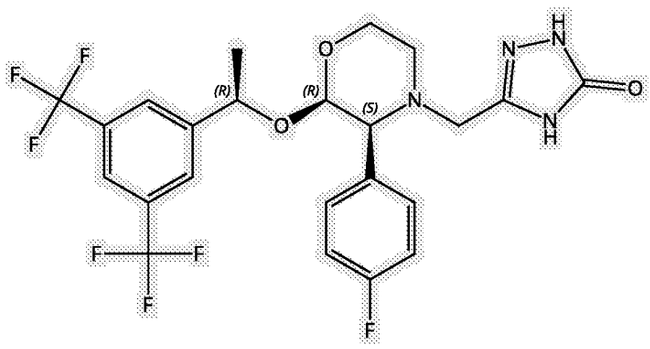
L5 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:685825 CAPLUS Full-text
DOCUMENT NUMBER: 178:140851
TITLE: Aprepitant submicroemulsion injection capable of being autoclaved, and its preparation method
INVENTOR(S): Qin, Linghao; Li, Yusheng; Zhu, Wanye; Wang, Wanting
PATENT ASSIGNEE(S): Guangdong Pharmaceutical University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 19pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 112535661	A	20210323	CN 2020-11524237	20201222
CN 112535661	B	20230407		

PRIORITY APPLN. INFO.: CN 2020-11524237 20201222
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 112535661	A	Alive	20210408
CN 112535661	B	Alive	20230427

OTHER SOURCE(S): CASFORMULTNS 2021:685825
AB A safe aprepitant submicroemulsion injection capable of being autoclaved having high efficiency, good stability and sterilization effect, and wide application in medicine field is provided. The aprepitant submicroemulsion injection comprises: polyethylene glycol 15hydroxystearate, phospholipids, aprepitant, oil for injection, emulsifier, co-emulsifier, solubilizer, stabilizer, isotonic agent, pH regulator and water for injection. The prepn. method comprises the following steps: (1) mixing aprepitant, injection oil and solubilizer, dissolving and dispersing with alc., and removing the alc. to obtain an oil phase mixt.; (2) stirring and mixing the emulsifier, co-emulsifier, stabilizer, isotonic agent and water for injection, and heat to dissolve to obtain the water phase mixt.; and (3) adding the oil phase mixt. to the water phase mixt., prepg. the emulsion , and autoclaving to obtain the aprepitant submicroemulsion injection. The aprepitant submicroemulsion injection is used in the prepn. of a medicine for treating nausea and vomiting.
IPCI A61K0009-107; A61K0031-5377; A61K0047-24; A61K0047-14; A61K0047-18; A61P0001-08; A61L0002-07
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-14 [I]; A61K0047-18 [I]; A61K0047-24 [I]; A61L0002-07 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Amino acids
Egg yolk lecithins
Oils
Phospholipids
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)
IT 56-41-7, L-Alanine, biological studies 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 63-91-2, L-Phenylalanine, biological studies 73-32-5, L-Isoleucine, biological studies 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 112535661 A	CN 2020-11524237	Register|Global Dossier
CN 112535661 B	CN 2020-11524237	Register|Global Dossier

L5 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:481715 CAPLUS Full-text
DOCUMENT NUMBER: 174:540291
TITLE: Pharmaceutical emulsion comprising an aprepitant, pharmaceutical injections, and methods of preparing emulsions
INVENTOR(S): Amano, Yohei; Katagiri, Kazumi
PATENT ASSIGNEE(S): Kewpie Corporation, Japan; FBC (Shanghai) Pharmaceutical Technology Co., Ltd.
ULTIMATE OWNER: KEWPIE CORPORATION; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY
ULTIMATE OWNER STANDARD: Kewpie Corp; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY
SOURCE: Jpn. Tokkyo Koho, 15pp.; Chemical Indexing Equivalent to 177:284905 (WO)
CODEN: JTXXFF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 6832468	B1	20210224	JP 2020-121438	20200715
JP 2022018370	A	20220127		
CA 3187858	A1	20220120	CA 2021-3187858	20210415
WO 2022014113	A1	20220120	WO 2021-JP15552	20210415
KR 2023040956	A	20230323	KR 2022-7045138	20210415
EP 4169515	A1	20230426	EP 2021-843280	20210415
CN 113952299	A	20220121	CN 2021-10772526	20210708
CN 117017915	A	20231110	CN 2023-11089804	20210708
US 20230310443	A1	20231005	US 2023-18015492	20230110

PRIORITY APPLN. INFO.:

JP 2020-121438	A	20200715
WO 2021-JP15552	W	20210415
CN 2021-10772526	A3	20210708

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
JP 6832468	B1	Alive	20210304
JP 2022018370	A	Alive	20220224
CA 3187858	A1	Alive	20230216
WO 2022014113	A1	Alive	20220203

KR 2023040956 A Alive 20230420
EP 4169515 A1 Alive 20230427
CN 113952299 A Alive 20220203
CN 117017915 A Alive 20231116
US 20230310443 A1 Alive 20231012

OTHER SOURCE(S): CASFORMULTNS 2021:481715

AB The emulsion comprises: an aprepitant, an emulsifier, an oil, polyethylene glycol and water, with substantially no addn. of ethanol. The emulsion comprises a pH regulator and having a pH of 8.0-9.0. The content of the aprepitant is 0.50 w/v% or more and 0.90 w/v% or less based on the total amt., and the content of the emulsifier is 12.0 w/v% or more and 12.0 w/v% or more based on the total amt. The emulsion is 0 w/v% or less, the emulsion in which the emulsifier is a phospholipid. According to the present invention, provided is an aprepitant-contg. emulsion having excellent stability without substantially adding ethanol.

IPCI A61K0031-5377 [I]; A61K0009-107 [I]; A61P0001-08 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0031-5377 [I]; A61P0001-08 [I]; A61K0047-24 [I]; A61K0047-44 [I]

IPCR A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]

CC 63-6 (Pharmaceuticals)

ST aprepitant pharmaceutical emulsion injection

IT Emulsifying agents
Pharmaceutical emulsions
Pharmaceutical injections
Tonicity modifiers
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT Egg yolk lecithins
Phospholipids
Polyoxyalkylenes
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

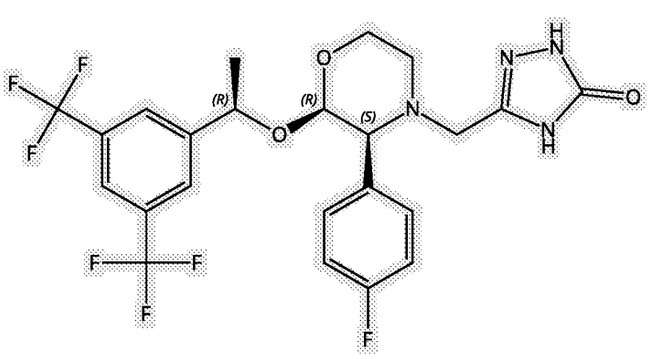
IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 57-50-1, biological studies 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 143-19-1 25322-68-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CA 3187858 A1	CA 2021-3187858	Register
CN 113952299 A	CN 2021-10772526	Register|Global Dossier
CN 117017915 A	CN 2023-11089804	Register|Global Dossier
EP 4169515 A1	EP 2021-843280	Register|Federated Reg.
JP 2022018370 A	JP 2020-121438	Register|Global Dossier
JP 6832468 B1	JP 2020-121438	Register|Global Dossier
KR 2023040956 A	KR 2022-7045138	Register|Global Dossier
US 20230310443 A1	US 2023-18015492	Register|Global Dossier
WO 2022014113 A1	WO 2021-JP15552	Register|Global Dossier

L5 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:485442 CAPLUS Full-text
DOCUMENT NUMBER: 177:51750
TITLE: Aprepitant Intravenous Emulsion Based on Ion Pairing/Phospholipid Complex for Improving Physical and Chemical Stability During Thermal Sterilization
AUTHOR(S): Zhang, Xinyu; Wei, Ying; Cao, Zhijun; Xu, Ying; Lu, Cong; Zhao, Meiqi; Gou, Jingxin; Yin, Tian; Zhang, Yu; He, Haibing; Wang, Yanjiao; Tang, Xing
CORPORATE SOURCE: Department of Pharmaceutics, Shenyang Pharmaceutical University, Shenyang, Peop. Rep. China
SOURCE: AAPS PharmSciTech (2020), 21(3), 75
CODEN: AAPHFZ; ISSN: 1530-9932
DIGITAL OBJECT ID: 10.1208/s12249-019-1605-7
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB An aprepitant (APT) cholesteryl hemisuccinate (CHEMS) ion pair complex emulsion (AIPE) with high lecithin content was prepd. to improve sterilization stability through the film dispersion homogenization method; therefore, it could be a promising delivery system of APT. Medium-chain triglycerides (MCT) was selected as the oil phase to improve the soly. and stability of APT in oil phase. DSC, XRD, FT-IR, and 1H-NMR spectroscopies confirmed that the APT-CHEMS ion pair (AIP) was formed between CHEMS and APT. The formation of AIP significantly increased the hydrophobicity of APT, allowing it to be completely embedded in the oil phase core to improve chem. stability and decrease hydrolysis of APT in the water phase. Also, CHEMS had a strong affinity with lecithin and could stabilize lipid membranes, forming a stronger and thicker interface membrane to increase the phys. stability of AIPE. As a result, AIPE could withstand autoclaving at 120°C for 8 min without any change of particle size or content. Furthermore, AIPE with a potential of - 53.4 mV remained stable through spatial repulsion during sterilization. The encapsulation efficiency of AIPE was over 90% and the particle size was 106.8 ± 65.62 nm(0.286). Pharmacokinetic study in rats was comparable with that of CINVANTI which yielded a relative bioavailability of 114.31% indicating that the AIPE had similar pharmacokinetic processes in vivo with the analog of CINVANTI. The AUC0-t of the AIPE was 4.31-fold that of the APT soln.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST aprepitant intravenous emulsion ion pairing phospholipid stability thermal sterilization
IT Chemical stability
Dissolution
Drug bioavailability
Encapsulation
Hydrolysis
Hydrophobicity
Ion pairs
Lipophilicity
Particle size distribution
Pharmaceutical emulsions
Pharmaceutical intravenous injections
Pharmacokinetics
Solubility

Surface structure
Thermal stability
Thermal sterilization
Zeta potential
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

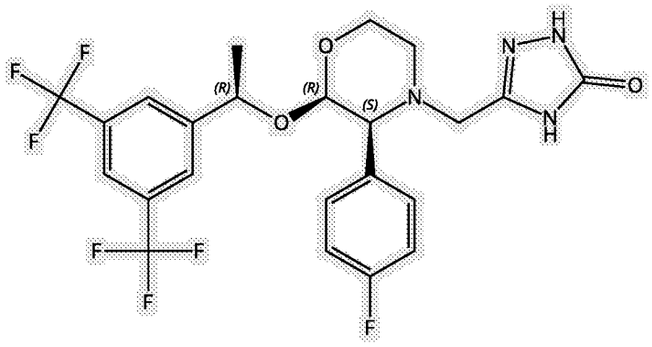
IT Egg yolk lecithins
Medium-chain glycerides
Soya lecithins
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

IT 1510-21-0
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

IT 170729-80-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

IT 170729-80-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:245679 CAPLUS Full-text
DOCUMENT NUMBER: 172:258881
TITLE: Emulsion containing high proportion emulsifier and preparation method thereof
INVENTOR(S): Niu, Yawei; Xu, Wendong; Tang, Shunzhi; Yuan, Cheng; Fu, Yuping; Guan, Weijian; Wang, Guocai; Mou, Xiaonan; Li, Jirong; Li, Yao

PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

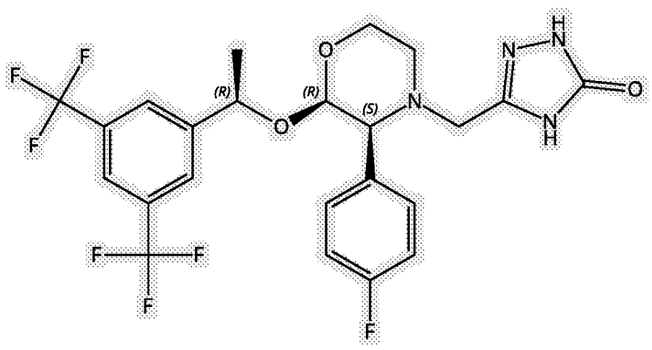
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 110772482	A	20200211	CN 2019-11215436	20191202

PRIORITY APPLN. INFO.: CN 2019-11215436 20191202
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 110772482	A	Dead	20230511

AB The invention discloses an emulsion contg. high proportion emulsifier and prepn. method thereof, which has the advantages of high drug loading and high bioavailability. The emulsion contg. high proportion emulsifier comprises the following raw materials in percentage by wt.: oil phase solvent 10-30%, emulsifier 10-30%, co-emulsifier 1-5%, volatile assistant 1-5%, stabilizer 0.05-0.6%, isoosmotic adjusting agent 1-5%, viscosity regulator 1-10%, active pharmaceutical ingredient 1-5%, and the balance of injection water.
IPCI A61K0009-107; A61K0047-26; A61K0047-44; A61K0047-14; A61K0047-10; A61K0031-5377
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-10 [I]; A61K0047-14 [I]; A61K0047-26 [I]; A61K0047-44 [I]
CC 63-7 (Pharmaceuticals)
ST emulsifier emulsion
IT Glycerides
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C8-10; emulsion contg. high proportion emulsifier and prepn. method thereof)
IT Emulsifying agents
Oilseed
Pharmaceutical emulsions
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT Carbohydrates
Castor oil
Egg yolk lecithins
Fish oil
Fructooligosaccharides
Olive oil
Phosphatidylcholines
Phosphatidylglycerols
Soya lecithins
Soybean oil
Triglycerides
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT Camellia
Coix
(seed oil; emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 9005-63-4D, fatty acid ester
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Polysorbate; emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 56-81-5, Glycerol, biological studies 57-48-7, D-Fructose, biological studies 57-50-1, D-Sucrose, biological studies 57-55-6, Propylene glycol, biological studies 64-17-5, Ethanol, biological studies 69-65-8, D-Mannitol 69-79-4, D-Maltose 87-79-6, L-Sorbose 112-80-1, Oleic acid, biological studies 143-19-1, Sodium oleate 538-23-8, Glycerin tricaprylate 538-24-9, Glycerol trilaurate 621-71-6, Glycerol

tridecanoate 106392-12-5, Poloxamer
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 170729-80-3, Aprepitant 552292-08-7, Rolapitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 110772482 A	CN 2019-11215436	Register|Global Dossier

L5 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:1475315 CAPLUS Full-text
DOCUMENT NUMBER: 171:221789
TITLE: Method of administering emulsion formulations of an NK-1 receptor antagonist
INVENTOR(S): Ottoboni, Thomas B.; Quart, Barry D.
PATENT ASSIGNEE(S): Heron Therapeutics, Inc., USA
ULTIMATE OWNER: HERON THERAPEUTICS, INC.
ULTIMATE OWNER STANDARD: HERON THERAPEUTICS, INC.
SOURCE: U.S. Pat. Appl. Publ., 23pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20190231688	A1	20190801	US 2019-16261459		20190129
WO 2019152430	A1	20190808	WO 2019-US15708		20190129
AU 2019214872	A1	20200806	AU 2019-214872		20190129
EP 3746051	A1	20201209	EP 2019-705044		20190129
JP 2021512091	T	20210513	JP 2020-541556		20190129
PRIORITY APPLN. INFO.:			US 2018-62624050	P	20180130
			WO 2019-US15708	W	20190129

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20190231688	A1	Alive	20230914
WO 2019152430	A1	Dead	20220929
AU 2019214872	A1	Dead	20230803
EP 3746051	A1	Dead	20211117
JP 2021512091	T	Alive	20210520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2019:1475315

AB Disclosed herein are methods of administering pharmaceutical formulations of a neurokinin-1 (NK-1) receptor antagonist to a subject in need of treatment of emesis.

IPCI A61K0009-107 [I]; A61K0031-5377 [I]; A61K0009-00 [I]; A61K0047-24 [I]; A61K0031-573 [I]; A61K0047-44 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-26 [I]; A61K0031-496 [I]

IPCR A61K0009-107 [I]; A61K0009-00 [I]; A61K0031-496 [I]; A61K0031-5377 [I]; A61K0031-573 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2

ST NK1 receptor antagonist dexamethasone emulsion administering method antiemetics

IT Surfactants
(co-; method of administering emulsion formulations of NK-1 receptor antagonist)

IT Antitumor agents
(emetogenic; method of administering emulsion formulations of NK-1 receptor antagonist)

IT Antiemetics
Emulsifying agents
Homo sapiens
Human
Nausea
Neurokinin 1 receptor antagonists
Pharmaceutical emulsions
Pharmaceutical intravenous injections
Pharmaceutical tonicity modifiers
Vomiting
pH-adjusting agents
(method of administering emulsion formulations of NK-1 receptor antagonist)

IT Alcohols
Egg yolk lecithins
Phospholipids
Soybean oil
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor antagonist)

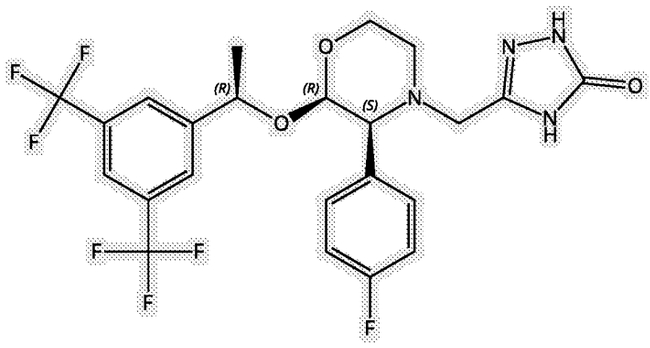
IT 64-17-5, Ethanol, biological studies 77-86-1, Tris buffer 143-19-1, Sodium oleate 7732-18-5, Water, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor antagonist)

IT 2392-39-4, Dexamethasone sodium phosphate 147116-64-1, Ezlopitant 147116-67-4, Maropitant 170729-80-3, Aprepitant 290296-68-3, Befetupitant 290297-26-6, Netupitant 334476-46-9, Vestipitant 414910-27-3, Casopitant 552292-08-7, Rolapitant 579475-18-6, Orvepitant 860642-69-9, Ser-lopitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor antagonist)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor antagonist)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2019214872 A1	AU 2019-214872	Register
EP 3746051 A1	EP 2019-705044	Register|Federated Reg.
JP 2021512091 T	JP 2020-541556	Register|Global Dossier
US 20190231688 A1	US 2019-16261459	Register|Global Dossier
WO 2019152430 A1	WO 2019-US15708	Register|Global Dossier

L5 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:425605 CAPLUS Full-text
DOCUMENT NUMBER: 170:406568
TITLE: Aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its preparation method and application
INVENTOR(S): Xu, Wendong; Tang, Shunzhi; Yuan, Cheng; Niu, Yawei; Fu, Yuping; Wang, Guocai; Guan, Weijian; Mou, Xiaonan; He, Jie; Li, Jirong; Yang, Yuqiong; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109432002	A	20190308	CN 2018-11587906	20181225

PRIORITY APPLN. INFO.: CN 2018-11587906 20181225
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109432002	A	Dead	20220825

OTHER SOURCE(S): CASFORMULTNS 2019:425605
AB An aprepitant emulsion useful for reducing nausea and vomiting in the pre and post-chemotherapy of the tumor, improving immunity and nutritional support of the tumor patient, and reducing acute and delayed nausea and vomiting in high-dose cisplatin combined with high-dose sensitized cancer chemotherapy is provided. The aprepitant emulsion comprises the following components in mass %: 0.05-2.5 of aprepitant, 10-30 of oil phase solvent, 0.8-18 of emulsifier, 0.03-0.6 of stabilizer, 1-5 of isotonicity regulator, and further comprising a pH regulator, balance being purified water, where the pH of the emulsion is 5.5-8. The prepn. method comprises the following steps: (1) weighing the oil phase solvent, emulsifier and antioxidant, heating in a water bath, dissolving all the emulsifiers, and adding aprepitant and dissolving well to obtain an oil phase; (2) weighing stabilizer, isotonicity regulator, pH regulator,

adding to purified water, and heating in water bath to obtain water phase; (3) slowly adding the oil phase to the water phase, shearing at high speed under stirring, adding the remaining purified water with high speed stirring to obtain colostrum; (4) subjecting obtained colostrum to microfluidization to obtain a final emulsion ; and (5) filling the colostrum with nitrogen, sealing and sterilizing in a rotary sterilizing pot to obtain an aprepitant emulsion .

IPCI A61K0009-107; A61K0031-5377; A23L0033-10; A23P0010-00; A61P0001-08; A61P0035-00

IPCR A61K0009-107 [I]; A23L0033-10 [I]; A23P0010-00 [I]; A61K0031-5377 [I]; A61P0001-08 [I]; A61P0035-00 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST aprepitant pharmaceutical emulsion antinausea chemotherapy

IT Antiemetics
Antioxidants
Chemotherapy
Emulsifying agents
Health products
Nausea
Pharmaceutical emulsions
Pharmaceutical tonicity modifiers
Stabilizing agents
Vomiting
pH
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT Egg yolk lecithins
Fatty acids
Phosphatidylcholines
Phosphatidylglycerols
Soya lecithins
Tocopherols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT Phosphatidylcholines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(egg yolk; aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT Coix lacryma-jobi ma-yuen
(seed, oil; aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT Ganoderma lucidum
(spore oil; aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

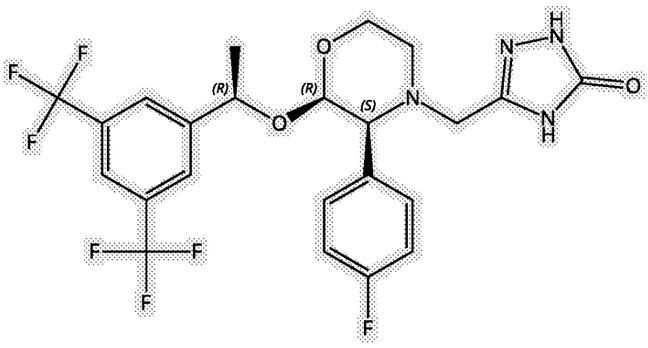
IT 1310-73-2, Sodium hydroxide, uses 7647-01-0, Hydrochloric acid, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT 50-99-7, D-Glucose, biological studies 56-81-5, Glycerin, biological studies 69-65-8, D-Mannitol 112-80-1, Oleic acid, biological studies 143-19-1, Sodium oleate 7631-90-5, Sodium bisulfite 7647-14-5, Sodium chloride, biological studies 7681-57-4, Sodium metabisulfite 7772-98-7, Sodium thiosulfate 9005-65-6, Polysorbate 80 106392-12-5, Poloxamer 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109432002 A	CN 2018-11587906	Register|Global Dossier

L5 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:340286 CAPLUS Full-text
DOCUMENT NUMBER: 170:348016
TITLE: Aprepitant intravenous emulsion for treating chemotherapy-induced nausea and vomiting, and its preparation method
INVENTOR(S): Yuan, Cheng; Xu, Wendong; Tang, Shunzhi; He, Jie; Niu, Yawei; Fu, Yuping; Wang, Guocai; Guan, Weijian; Mou, Xiaonan; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109364023	A	20190222	CN 2018-11588409	20181225

PRIORITY APPLN. INFO.: CN 2018-11588409 20181225
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109364023	A	Transitional	20240222

OTHER SOURCE(S): CASFORMULTNS 2019:340286
AB The present invention relates to an i.v. emulsion contg. the following components by mass percentage: 0.05-3% of aprepitant, 5-30% of oil phase solvent, 1.2-18% of emulsifier, 0.03-0.6% of stabilizer, 1-5% of isotonicity adjusting agent, and 0.02-0.5% of antioxidant. The i.v. emulsion further contains a pH adjusting agent and water for injection, where the pH of the i.v. emulsion is 5.5-8.0. The i.v. emulsion has greatly improved the clin. safety, and is utilized for treating acute and delayed nausea and vomiting caused by high-dose cisplatin combined with high-dose sensitizing cancer chemotherapy and reducing nausea and vomiting in the early and middle stages of tumor chemotherapy.
IPCI A61K0009-107; A61K0047-24; A61K0047-12; A61K0031-5377; A61P0035-00; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
ST chemotherapy nausea aprepitant intravenous emulsion
IT Chemotherapy

Homo sapiens
Human
Nausea
Pharmaceutical emulsions
Pharmaceutical intravenous injections
Vomiting
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

IT Castor oil
Egg yolk lecithins
Fish oil
Olive oil
Phosphatidylcholines
Phosphatidylglycerols
Soya phospholipids
Soybean oil
Teaseed oil
Tocopherols
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

IT Phosphatidylcholines
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(egg yolk; aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

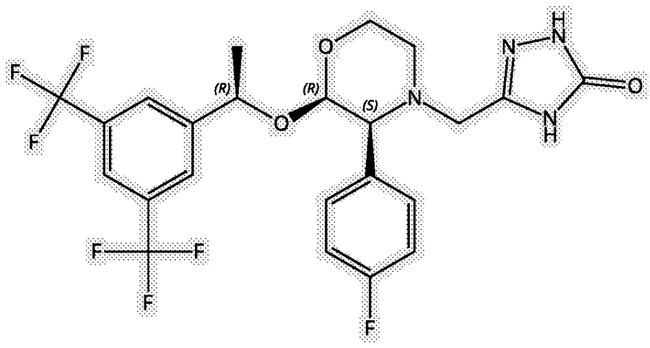
IT 50-99-7, D-Glucose, biological studies 56-81-5, Glycerin, biological studies 69-65-8, D-Mannitol 112-80-1, Oleic acid, biological studies 143-19-1, Sodium oleate 538-23-8, Tricaprylin 538-24-9, Glyceryl trilaurate 621-71-6, Glyceryl tricaprate 1310-73-2, Sodium hydroxide, biological studies 7631-90-5, Sodium hydrogen sulfite 7647-01-0, Hydrochloric acid, biological studies 7647-14-5, Sodium chloride, biological studies 7681-57-4, Sodium metabisulfite 7772-98-7, Sodium thiosulfate 9005-65-6, Polysorbate 80 11140-04-8, Glyceryl caprylate 106392-12-5, Poloxamer
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

IT 7727-37-9, Nitrogen, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109364023 A	CN 2018-11588409	Register|Global Dossier

L5 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:2521745 CAPLUS Full-text
DOCUMENT NUMBER: 170:140265
TITLE: High stability aprepitant nano-emulsion and preparation method thereof
INVENTOR(S): Fu, Jifeng; Wang, Wenjuan; Guo, Jia; Zhang, Liancheng
PATENT ASSIGNEE(S): Beijing Ruiyue Biomedical Technology Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: BEIJING RUIYUE BIOLOGY MEDICAL TECH
ULTIMATE OWNER STANDARD: BEIJING RUIYUE BIOLOGY MEDICAL TECH
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

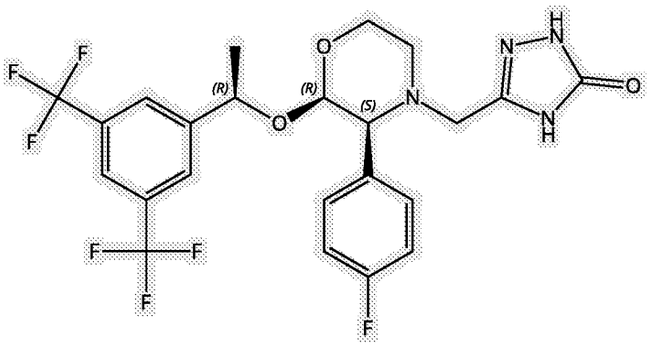
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109010272	A	20181218	CN 2018-11133738	20180927

PRIORITY APPLN. INFO.: CN 2018-11133738 20180927
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109010272	A	Dead	20230323

OTHER SOURCE(S): CASFORMULTNS 2018:2521745
AB The invention discloses a nano-emulsion of aprepitant as shown in structure I and prepn. method thereof. The nano-emulsion is prepd. with the following components in percentage by wt.: aprepitant 0.05-1.5%, soybean oil 2-20%, egg yolk lecithin 5-20%, ethanol 0.5-5%, sodium oleate 0.05-2%, sucrose 2-10%, and water for injection 40-80%. The sodium oleate is added into the oil phase to rapidly stabilize the oil droplets when contacts with the aq. phase, thereby increasing the stability of the nano-emulsion .
IPCI A61K0009-107; A61K0047-12; A61K0047-44; A61K0047-24; A61K0047-10; A61K0047-26; A61K0031-5377; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Pharmaceutical nanoemulsions
(High stability aprepitant nano-emulsion and prepn. method thereof)
IT Egg yolk lecithins
Soybean oil
RL: MOA (Modifier or additive use); NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(High stability aprepitant nano-emulsion and prepn. method thereof)
IT 57-50-1, D-Sucrose, biological studies 143-19-1, Sodium oleate
RL: MOA (Modifier or additive use); NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109010272 A	CN 2018-11133738	Register|Global Dossier

L5 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:2521716 CAPLUS Full-text
DOCUMENT NUMBER: 170:154781
TITLE: Fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting
INVENTOR(S): Liu, Jie; Liu, Yun; Zhou, Lili
PATENT ASSIGNEE(S): Fubicheng (Shanghai) Pharmaceutical Technology Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: FUBICHENG SHANGHAI MEDICINE TECH
ULTIMATE OWNER STANDARD: FUBICHENG SHANGHAI MEDICINE TECH
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109010269	A	20181218	CN 2018-10979074	20180827
CN 109010269	B	20210420		

PRIORITY APPLN. INFO.: CN 2018-10979074 20180827
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109010269	A	Alive	20201121
CN 109010269	B	Alive	20210430

OTHER SOURCE(S): CASFORMULTNS 2018:2521716

AB The title fat emulsion injection of aprepitant for treating chemotherapy-induced nausea and vomiting is prepd. from aprepitant, egg yolk lecithin , oil for injection (coconut oil, soybean oil, or olive oil), glycine, polyvinylpyrrolidone, water for injection, sodium oleate, and C1-5 short-chain alc. (ethanol or propanediol). The inventive prepn. has improved stability and reduced vascular irritation.

IPCI A61K0009-107; A61K0031-5377; A61K0047-18; A61K0047-32; A61K0031-439; A61K0009-08; A61P0001-08

IPCR A61K0009-107 [I]; A61K0009-08 [I]; A61K0031-439 [I]; A61K0031-5377 [I]; A61K0047-18 [I]; A61K0047-32 [I]; A61P0001-08 [I]

CC 63-6 (Pharmaceuticals)

ST aprepitant fat emulsion injection chemotherapy induced nausea vomiting antiemetic

IT Short-chain alcohols
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C1-5; fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)

IT Egg yolk lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Lipoid E 80; fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)

IT Antiemetics
Homo sapiens
Human
Nausea
Neurokinin 1 receptor antagonists
Pharmaceutical emulsions
Pharmaceutical injections
Vomiting
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)

IT Coconut oil
Olive oil
Safflower oil
Soybean oil
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)

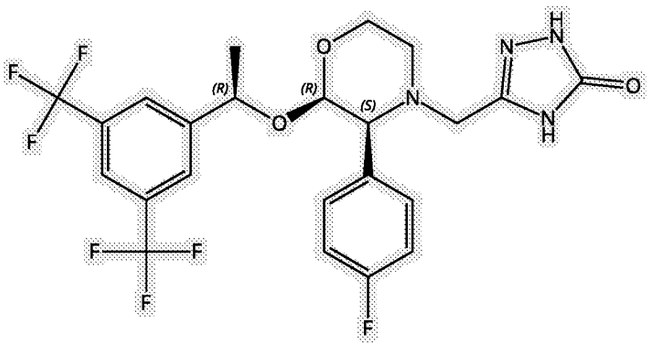
IT 56-40-6, Glycine, biological studies 64-17-5, Ethanol, biological studies 143-19-1, Sodium oleate 9003-39-8, Polyvinylpyrrolidone 26264-14-2, Propanediol
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

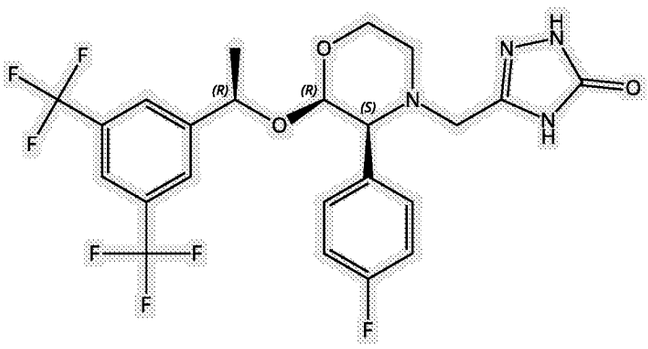
LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109010269 A	CN 2018-10979074	Register|Global Dossier
CN 109010269 B	CN 2018-10979074	Register|Global Dossier

L5 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:1723954 CAPLUS Full-text
DOCUMENT NUMBER: 172:411315
TITLE: Optimization of the Ussing chamber setup with excised rat intestinal segments for dissolution/permeation experiments of poorly soluble drugs
AUTHOR(S): Forner, Kristin; Roos, Carl; Dahlgren, David; Kesisoglou, Filippos; Konerding, Moritz A.; Mazur, Johanna; Lennernaes, Hans; Langguth, Peter
CORPORATE SOURCE: Department of Pharmaceutical Technology and Biopharmaceutics, Johannes Gutenberg University, Mainz, Germany
SOURCE: Drug Development and Industrial Pharmacy (2017), 43(2), 338-346
CODEN: DDIPD8; ISSN: 0363-9045
DIGITAL OBJECT ID: 10.1080/03639045.2016.1251449
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Prediction of the in vivo absorption of poorly sol. drugs may require simultaneous dissoln./permeation expts. In vivo predictive media have been modified for permeation expts. with Caco-2 cells, but not for excised rat intestinal segments. The present study aimed at improving the setup of dissoln./permeation expts. with excised rat intestinal segments by assessing suitable donor and receiver media. The regional compatibility of rat intestine in Ussing chambers with modified Fasted and Fed State Simulated Intestinal Fluids (Fa/FeSSIFmod) as donor media was evaluated via several parameters that reflect the viability of the excised intestinal segments. Receiver media that establish sink conditions were investigated for their foaming potential and toxicity. Dissoln./permeation expts. with the optimized conditions were then tested for two particle sizes of the BCS class II drug aprepitant. Fa/FeSSIFmod were toxic for excised rat ileal sheets but not duodenal sheets, the compatibility with jejunal segments depended on the bile salt concn. A non-foaming receiver medium contg. bovine serum albumin (BSA) and Antifoam B was nontoxic. With these conditions, the permeation of nanosized aprepitant was higher than of the unmilled drug formulations. The compatibility of Fa/FeSSIFmod depends on the excised intestinal region. The chosen conditions enable dissoln./permeation expts. with excised rat duodenal segments. The expts. correctly predicted the superior permeation of nanosized over unmilled aprepitant that is obsd. in vivo. The optimized setup uses FaSSIFmod as donor medium, excised rat duodenal sheets as permeation membrane and a receiver medium contg. BSA and Antifoam B.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 9
IT Lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)
IT 57-88-5, Cholesterol, biological studies 145-42-6, Sodium taurocholate 9002-96-4, Vit E TPGS) 54693-50-4, Antifoam B emulsion
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)
IT 81-81-2, Warfarin 15307-86-5, Diclofenac 29122-68-7, Atenolol 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:473657 CAPLUS Full-text
DOCUMENT NUMBER: 164:387016
TITLE: Emulsion formulations of aprepitant
INVENTOR(S): Ottoboni, Thomas B.; Han, Han
PATENT ASSIGNEE(S): Heron Therapeutics, Inc., USA
ULTIMATE OWNER: HERON THERAPEUTICS, INC.
ULTIMATE OWNER STANDARD: HERON THERAPEUTICS, INC.
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016044784	A1	20160324	WO 2015-US51050	20150918
US 20160082013	A1	20160324	US 2015-14859013	20150918
US 9808465	B2	20171107		

KR 2017056575	A	20170523	KR 2017-7008598		20150918
KR 2424837	B1	20220725			
CN 106852118	A	20170613	CN 2015-80050449		20150918
EP 3193830	A1	20170726	EP 2015-772163		20150918
EP 3193830	B1	20231101			
EP 3193830	C0	20231101			
JP 2017533183	T	20171109	JP 2017-514863		20150918
JP 6741655	B2	20200819			
US 20160206622	A1	20160721	US 2016-15083071		20160328
US 9561229	B2	20170207			
US 20170112847	A1	20170427	US 2017-15398928		20170105
US 10500208	B2	20191210			
US 20180000828	A1	20180104	US 2017-15705201		20170914
US 9974793	B2	20180522			
US 20180000829	A1	20180104	US 2017-15705208		20170914
US 9974794	B2	20180522			
JP 2019196398	A	20191114	JP 2019-137539		20190726
US 20200197404	A1	20200625	US 2019-16669262		20191030
US 10953018	B2	20210323			
US 20210186981	A1	20210624	US 2021-17194114		20210305
JP 2022092040	A	20220621	JP 2022-66236		20220413

PRIORITY APPLN. INFO.:

US 2014-62052948	P	20140919
JP 2017-514863	A3	20150918
US 2015-14859013	A1	20150918
WO 2015-US51050	W	20150918
US 2016-15083071	A1	20160328
US 2017-15398928	A1	20170105
JP 2019-137539	A3	20190726
US 2019-16669262	A1	20191030

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2016044784	A1	Dead	20201202
US 20160082013	A1	Alive	20201121
US 9808465	B2	Alive	20201120
KR 2017056575	A	Alive	20220602
KR 2424837	B1	Alive	20220811
CN 106852118	A	Transitional	20240307
EP 3193830	A1	Alive	20201201
EP 3193830	C0	Alive	20240104
JP 2017533183	T	Alive	20201121
JP 6741655	B2	Alive	20201121
US 20160206622	A1	Alive	20201120
US 9561229	B2	Alive	20201120
US 20170112847	A1	Alive	20201120
US 10500208	B2	Alive	20201120
US 20180000828	A1	Alive	20201121
US 9974793	B2	Alive	20201120
US 20180000829	A1	Alive	20201121
US 9974794	B2	Alive	20201120
JP 2019196398	A	Dead	20231026
US 20200197404	A1	Alive	20201121
US 10953018	B2	Alive	20210401
US 20210186981	A1	Alive	20231012
JP 2022092040	A	Dead	20231207

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2016:473657

AB Disclosed herein are novel pharmaceutical formulations of aprepitant suitable for parenteral administration including i.v. administration. Also included are formulations including both aprepitant and dexamethasone sodium phosphate. The pharmaceutical formulations are stable oil-in-water emulsions for non-oral treatment of emesis and are particularly useful for treatment of subjects undergoing cancer chemotherapy.

IPCI A61K0009-00 [I]; A61K0047-10 [I]; A61K0047-44 [I]; A61K0047-24 [I]; A61K0047-12 [I]; A61K0047-26 [I]

IPCR A61K0009-00 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]

CC 63-6 (Pharmaceuticals)

ST emulsion formulation aprepitant

IT Buffers
Emulsifying agents
Parenteral drug delivery systems

Particle size distribution
Pharmaceutical emulsions
Pharmaceutical intravenous injections
Pharmacokinetics
Stability
Zeta potential
pH
(emulsion formulations of aprepitant)

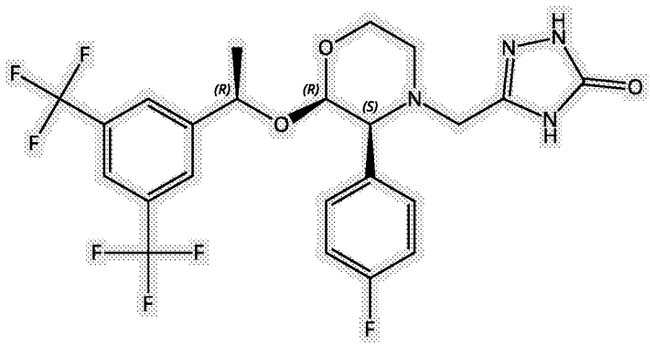
IT Alcohols
Egg yolk lecithins
Phospholipids
Soybean oil
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

IT 2392-39-4 170729-80-3
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

IT 64-17-5, Ethanol, biological studies 77-86-1 143-19-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

IT 170729-80-3
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 106852118 A	CN 2015-80050449	Register|Global Dossier
EP 3193830 A1	EP 2015-772163	Register|Federated Reg.
EP 3193830 B1	EP 2015-772163	Register|Federated Reg.
EP 3193830 C0	EP 2015-772163	Register|Federated Reg.
JP 2017533183 T	JP 2017-514863	Register|Global Dossier
JP 6741655 B2	JP 2017-514863	Register|Global Dossier
JP 2019196398 A	JP 2019-137539	Register|Global Dossier
JP 2022092040 A	JP 2022-66236	Register|Global Dossier
KR 2017056575 A	KR 2017-7008598	Register|Global Dossier
KR 2424837 B1	KR 2017-7008598	Register|Global Dossier
US 20160082013 A1	US 2015-14859013	Register|Global Dossier
US 9808465 B2	US 2015-14859013	Register|Global Dossier
US 20160206622 A1	US 2016-15083071	Register|Global Dossier

US 9561229 B2	US 2016-15083071	Register|Global Dossier
US 10500208 B2	US 2017-15398928	Register|Global Dossier
US 20170112847 A1	US 2017-15398928	Register|Global Dossier
US 20180000828 A1	US 2017-15705201	Register|Global Dossier
US 9974793 B2	US 2017-15705201	Register|Global Dossier
US 20180000829 A1	US 2017-15705208	Register|Global Dossier
US 9974794 B2	US 2017-15705208	Register|Global Dossier
US 10953018 B2	US 2019-16669262	Register|Global Dossier
US 20200197404 A1	US 2019-16669262	Register|Global Dossier
US 20210186981 A1	US 2021-17194114	Register|Global Dossier
WO 2016044784 A1	WO 2015-US51050	Register|Global Dossier

L5 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2015:1390403 CAPLUS Full-text
DOCUMENT NUMBER: 163:369597
TITLE: Compositions of pentosan polysulfate salts for oral administration and methods of use
INVENTOR(S): Parsons, C. Lowell; Goldberg, Michael; Meenan, Christopher P.
PATENT ASSIGNEE(S): Urigen Pharmaceuticals, Inc., USA
ULTIMATE OWNER: PLATINUM MONTAUR LIFE SCIENCES
ULTIMATE OWNER STANDARD: PLATINUM MONTAUR LIFE SCIENCES
SOURCE: PCT Int. Appl., 248pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2015127416	A1	20150827	WO 2015-US17205		20150224
CA 2949480	A1	20150827	CA 2015-2949480		20150224
AU 2015218642	A1	20161006	AU 2015-218642		20150224
EP 3110427	A1	20170104	EP 2015-751441		20150224
KR 2017003527	A	20170109	KR 2016-7026610		20150224
CN 106456662	A	20170222	CN 2015-80022057		20150224
JP 2017512757	T	20170525	JP 2016-554267		20150224
US 20170189443	A1	20170706	US 2016-15121312		20160824
PRIORITY APPLN. INFO.:			US 2014-61943824	P	20140224
			WO 2015-US17205	W	20150224

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2015127416	A1	Dead	20201201
CA 2949480	A1	Dead	20220428
AU 2015218642	A1	Dead	20210318
EP 3110427	A1	Dead	20210729
KR 2017003527	A	Alive	20201121
CN 106456662	A	Dead	20201121
JP 2017512757	T	Alive	20201120
US 20170189443	A1	Dead	20210324

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 163:369597; CASFORMULTNS 2015:1390403
AB The invention is directed to a pharmaceutical compn. comprising: (1) a therapeutically effective quantity of sodium pentosan polysulfate; (2) a quantity of a penetration enhancer sufficient to improve the bioavailability of the sodium pentosan polysulfate; and (3) optionally, a pharmaceutically acceptable carrier and to methods for the oral administration of sodium pentosan polysulfate with improved bioavailability for the treatment of interstitial cystitis and other urinary tract diseases and conditions. Such compns. and methods allow the administration of sodium pentosan polysulfate at lower dosages to reduce the frequency and severity of side effects.
IPCI A61K0031-715 [I]; C07H0005-10 [I]; A61K0047-14 [I]; A61P0019-02 [I]
IPCR A61K0031-715 [I]; A61K0047-14 [I]; A61P0019-02 [I]; C07H0005-10 [I]
CC 1-12 (Pharmacology)
IT Agglomeration preventers
Alzheimer disease
Analgesics
Ankylosing spondylitis
Anti-Alzheimer agents
Anti-HIV agents

Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antiatherosclerotics
Antifoaming agents
Antioxidants
Antipsoriatic agents
Antirheumatic agents
Antitumor agents
Asthma
Atherosclerosis
Bioavailability
Blood coagulation disorders
Bos taurus
Buccal drug delivery systems
Buffers
Canis familiaris
Capra hircus
Cat
Cattle
Chelating agents
Cholinergic antagonists
Coating materials
Coloring materials
Combination chemotherapy
Complexing agents
Cosmetic fragrance products
Creutzfeldt-Jakob disease
Cystitis
Dog
Drug bioavailability
Drug toxicity
Drying agents
Emulsifying agents
Equus caballus
Escherichia coli
Felis catus
Filter aids
Flavor
Goat
HIV infection
Homo sapiens
Horse
Human
Humectants
Inflammation
Intervertebral disc degeneration
Ionic surfactants
Juvenile rheumatoid arthritis
Lower urinary tract disease
Lupus erythematosus
Matrix metalloproteinase inhibitors
Micelles
Mule
Multiple sclerosis
Myocarditis
NMDA receptor antagonists
Nanoparticles
Narcotics
Nonionic detergents
Nonionic surfactants
Nonsteroidal anti-inflammatory agents
Oral drug delivery systems
Osteoarthritis
Osteonecrosis
Overactive bladder
Ovis aries
Pain
Peptidomimetics
Permeation enhancers
Pharmaceutical binders
Pharmaceutical carriers

Pharmaceutical diluents
Pharmaceutical disintegrants
Pharmaceutical emulsions
Pharmaceutical fillers
Pharmaceutical films
Pharmaceutical glidants
Pharmaceutical oils
Pharmaceutical viscosity enhancers
Plasticizers
Preservatives
Prion diseases
Prostate gland neoplasm
Prostatitis
Psoriasis
Psoriatic arthritis
Renal calculi
Rheumatoid arthritis
Selective estrogen receptor modulators
Sheep
Solubilizers
Solvents
Sorbents
Stiffening materials
Sublingual drug delivery systems
Sus scrofa domestica
Sweetening agents
Swine
Tachykinin antagonists
Tranquilizers
Urinary system infection
Wetting agents
(compns. of pentosan polysulfate salts for oral administration and methods of use)

IT Acrylic polymers
Acylcarnitines
Amino acids
Bile salts
Bone morphogenetic protein 7
Bone sialoproteins
Cartilage oligomeric matrix protein
Collagen type I
Collagen type II
Collagen type IX
Collagen type XI
Collagens
Crown compounds
Dendrimers
Diglycerides
Estrogens
Fatty acids
Insulin-like growth factor-binding protein 3
Lecithins
Matrix proteins
Medium-chain fatty acids
Monoclonal antibodies
Monoglycerides
Opioids
Osteocalcins
Osteonectin
Osteopontin
Peptides
Polyanhydrides
Polyoxyalkylenes
Proteins
Salicylates
Steroidal hormones
Sulfonanilides
Terpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and methods of use)

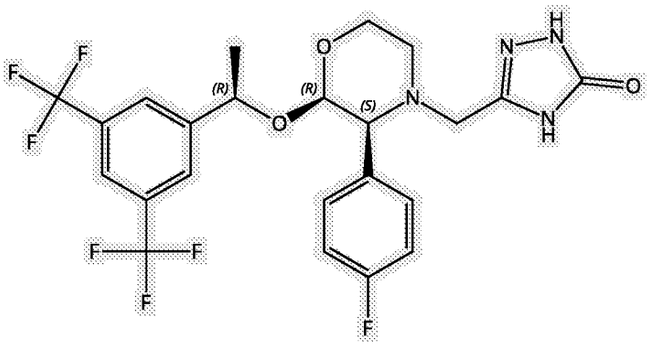
IT 15866-90-7, Metastat 15880-03-2 16011-96-4, 2-Iminopiperidine hydrochloride 16067-69-9, Strontium benzenesulfonate 16088-89-4, Strontium maleate 16139-18-7, Aminoguanidine hydrochloride 18847-18-2 19767-45-4, Mesna 19878-22-9 19982-08-2, Memantine 20093-91-8 20594-83-6, Nalbuphine 21084-57-1, 8-(Phthalimido)caprylic acid 21256-18-8, Oxaprozin 21463-31-0, 2-Amino-5,6-dihydro-6-methyl-4H-1,3-thiazine hydrochloride 22059-21-8, 1-Aminocyclopropane-1-carboxylic acid 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22410-94-2 22494-42-4, Diflunisal 22834-47-5 24314-23-6 24339-95-5 25087-26-7 25087-26-7D, derivs. 25322-68-3 25496-72-4 25518-54-1 25587-34-2 26009-03-0, Poly[oxy(1-oxo-1,2-ethanediyl)] 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26171-23-3, Tolmetin 26615-21-4, Zotepine 26864-56-2, Penfluridol 27203-92-5, Tramadol 27261-86-5 27540-07-4 27638-00-2 28945-89-3, 3-(3-Ethoxyphenyl)propanoic acid 28945-91-7, 3-(3-Butoxyphenyl)propanoic acid 29679-58-1, Fenoprofen 30762-02-8, 4-(Cyclopentyloxy)benzoic acid 31477-60-8, Ormeloxifene 33369-31-2, Zomepirac 34346-01-5 34816-55-2, Moxestrol 35197-20-7 36322-90-4, Piroxicam 36330-86-6 36440-58-1 36978-49-1 38194-50-2, Sulindac 39860-99-6, Pipotiazine 40182-75-0, Strontium citrate 40391-99-9 40472-00-2, Strontium succinate 41340-25-4, Etodolac 41839-80-9 42408-82-2, Butorphanol 42907-92-6 42907-93-7 43218-50-4 47739-98-0, Clocapramine 49594-75-4 50700-72-6, Vecuronium 51036-98-7 51333-22-3, Budesonide 51803-78-2, Nimesulide 52240-14-9 52349-26-5 52485-79-7, Buprenorphine 52888-70-7, 3-(3-Phenoxyphenyl)propanoic acid 53583-79-2, Sultopride 53597-27-6, Fendosal 53648-55-8, Dezocine 53716-49-7, Carprofen 53772-83-1, Zuclopenthixol 57648-21-2, Timiperone 57821-78-0 59122-46-2, Misoprostol 59227-89-3 59804-37-4, Tenoxicam 59865-13-3, Cyclosporine 60118-07-2, Endorphin 61126-74-7 61126-76-9 63471-88-5 64228-79-1, Atracurium 64779-07-3 64779-14-2 65576-45-6, Asenapine 66644-81-3, Veralipride 67763-96-6, Insulin like growth factor-1 68047-06-3, 4-Hydroxy-tamoxifen 68134-81-6, Gacyclidine 71125-38-7, Meloxicam 71675-85-9, Amisulpride 74103-06-3, Ketorolac 75221-40-8, [4-(Cyclohexylmethoxy)phenyl]acetic acid 75221-43-1 75272-39-8, Nemonapride 75706-12-6, Leflunomide 77086-21-6, Dizocilpine 77599-17-8, Panomifene 78994-23-7, Levormeloxifene 79055-68-8 79669-11-7, 3-(4-Isopropoxyphenyl)propanoic acid 79778-41-9, Neridronate 80125-14-0, Remoxipride 81093-37-0, Pravastatin 81109-85-5 82413-20-5, Droloxifene 83015-26-3, Atomoxetine 84449-90-1, Raloxifene 86111-26-4, Zindoxifene 89326-69-2, 5-(4-Ethylphenyl)pentanoic acid 89419-40-9, Mosapramine 89750-15-2, Glucagon like peptide-2 89778-26-7, Toremifene 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 98007-99-9 98774-23-3, Tesmilifene 100759-29-3 100944-08-9 101253-68-3 102676-47-1, Fadrozole 103735-76-8, erythro-MEA 103987-16-2 105462-24-6, Risedronate 106266-06-2, Risperidone 106516-24-9, Sertindole 107868-30-4, Exemestane 108179-99-3 110347-85-8, Selfotel 110931-77-6 111974-69-7, Quetiapine 112809-51-5, Letrozole 114084-78-5, Ibandronate 115767-74-3, TAT-59 116057-68-2 116057-75-1, Idoxifene 117910-70-0 117928-94-6, Rapastinel 118072-93-8, Zoledronic acid 119431-25-3, Eliprodil 120511-73-1, Anastrozole 121368-58-9, Olpadronate 122004-99-3 123663-49-0, T-614 124937-51-5, Tolterodine 124937-52-6, Detrol 128298-28-2, Remacemide 128607-22-7, Ospemifene 129318-43-0 129453-61-8, Fulvestrant 129612-87-9, Miproxifene 129722-12-9, Aripiprazole 129731-10-8, Vorozole 129948-69-2 130370-59-1, GI-129471 130370-60-4, Batimastat 131123-76-7, 5,7-Dichlorokynurenic acid 131692-21-2 132539-06-1, Olanzapine 132810-10-7, Blonanserin 133454-47-4, Iloperidone 133814-18-3, Doxacurium 134523-00-5, Atorvastatin 135459-87-9, Strontium ranelate 136013-76-8, 2-(Cyclopropylmethoxy)benzoic acid 136553-81-6, BQ-123 136982-36-0, CP-99994 137159-92-3, Aptiganel 137945-48-3, CT-3 138330-18-4, Incadronate 141620-66-8 142880-36-2, Ilomastat 144598-75-4, Paliperidone 145599-86-6, Cerivastatin 146490-38-2 146939-27-7, Ziprasidone 147536-97-8, Bosentan 148215-77-4, 2-(Cyclopentyloxy)benzoic acid 148700-85-0, L-733060 150403-89-7 150915-41-6, Perospirone 153322-05-5, Lanicemine 153438-49-4, RPR-100893 154039-60-8, Marimastat 155383-07-6, SDZ-PTS 893 156161-89-6, BQ-788 156806-79-0 157116-68-2 157116-71-7 158089-95-3, S-2474 158860-95-8, 3-(Cyclohexylmethoxy)benzoic acid 158860-99-2, 3-(Cyclopentyloxy)benzoic acid 159190-44-0 162011-90-7,

Rofecoxib 162752-13-8, 3-(4-Propylphenyl)propanoic acid 165536-41-4,
MDL-103323 168158-16-5, KB-R-7785 168266-90-8, Vofopitant
168980-06-1 168980-07-2 168980-08-3 168980-09-4 168980-10-7
168980-12-9 168980-13-0 169590-41-4, Deracoxib 169590-42-5,
Celecoxib 169799-04-6, MMI-270 169799-44-4, Keratin sulfate
170277-31-3, Infliximab 170566-84-4, Lanepitant 170713-75-4
170729-80-3, Aprepitant 172673-20-0, Fosaprepitant
173937-91-2, Atrasentan 175033-36-0, NCX4016 177036-94-1, Ambrisentan
177172-49-5 177653-18-8 177653-31-5 177653-36-0 177653-53-1
177653-62-2 177653-65-5 179545-77-8, Tanomastat 180064-38-4
180384-57-0, Tezosentan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and
methods of use)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and
methods of use)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

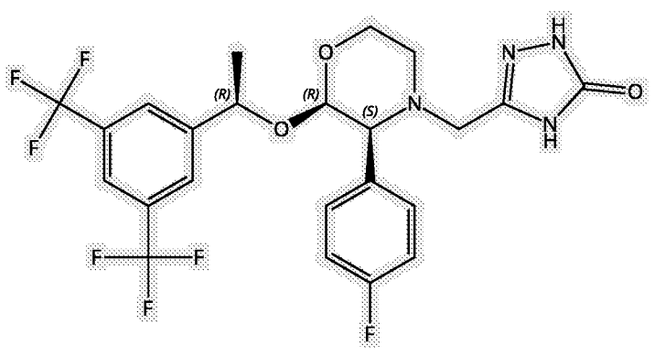
PUBLICATIONS	APPLICATIONS	REGISTER
AU 2015218642 A1	AU 2015-218642	Register
CA 2949480 A1	CA 2015-2949480	Register
CN 106456662 A	CN 2015-80022057	Register|Global Dossier
EP 3110427 A1	EP 2015-751441	Register|Federated Reg.
JP 2017512757 T	JP 2016-554267	Register|Global Dossier
KR 2017003527 A	KR 2016-7026610	Register|Global Dossier
US 20170189443 A1	US 2016-15121312	Register|Global Dossier
WO 2015127416 A1	WO 2015-US17205	Register|Global Dossier

L5 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2013:496643 CAPLUS Full-text
DOCUMENT NUMBER: 159:140262
TITLE: Preparation of aprepitant emulsion for intravenous injection
AUTHOR(S): Zhou, Wei; Chen, Fei; Chen, Ning; Mao, Ke
CORPORATE SOURCE: School of Pharmaceutical, Jiangsu Provincial Institute of Materia Medica, Nanjing University of Technology, Nanjing, Jiangsu Province, 211816, Peop. Rep. China

SOURCE: Zhongguo Yiyao Gongye Zazhi (2012), 43(12), 1003-1006
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The formulation of aprepitant emulsion for i.v. injection was optimized by single factor test and orthogonal design. The properties, such as appearance, particle size, ζ potential and stability of the product were investigated. The results showed that the type and amt. of emulsifier as well as the amt. of oleic acid had the greater effect on stability. The optimal formulation of aprepitant emulsion was as follows: aprepitant was 0.25%, soybean oil was 15%, egg yolk lecithin ESO was 2.5% and oleic acid was 0.125%. The appearance of the product was ivory. The av. particle size, PDI, centrifugal stability const. (Ke), ζ potential, pH value and drug content of the product before and after sterilization were (215.71±1.26) and (220.3±0.53) nm, 0.203±0.016 and 0.210±0.009, 0.21±0.01 and 0.34±0.01, (-37.5±0.2) and (-37.6±0.5) mV, 7.21±0.23 and 7.31±0.30, (101.03±0.89)% and (101.12±1.20)%, resp.

CC 63-6 (Pharmaceuticals)
ST aprepitant emulsion intravenous injection
IT Electric potential
Particle size
Pharmaceutical injections
Sterilization and Disinfection
(prepn. of aprepitant emulsion for i.v. injection)
IT Egg yolk lecithins
Soybean oil
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of aprepitant emulsion for i.v. injection)
IT 112-80-1, Oleic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of aprepitant emulsion for i.v. injection)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of aprepitant emulsion for i.v. injection)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of aprepitant emulsion for i.v. injection)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

=> D L4 1-48 IBIB ABS HITIND HITSTR

L4 ANSWER 1 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN

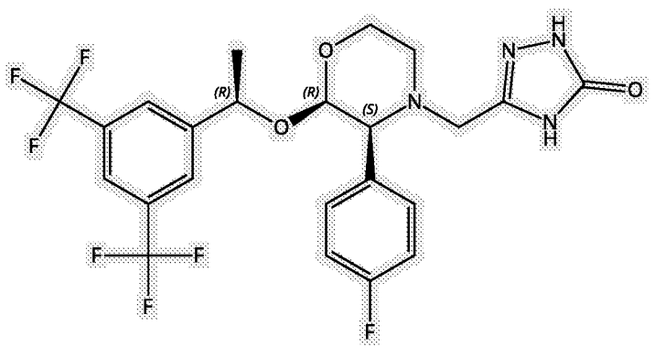
ACCESSION NUMBER: 2024:141628 CAPLUS Full-text
TITLE: Aprepitant emulsion drug composition and preparation method thereof
INVENTOR(S): Chen, Xiangmei; Yu, Changhui; Wang, Xinlong; Lin, Liyang; Shen, Li; Zhao, Dong
PATENT ASSIGNEE(S): Sichuan Kelun Pharmaceutical Research Institute Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 8pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 117414334	A	20240119	CN 2022-10811953	20220711

PRIORITY APPLN. INFO.: CN 2022-10811953 20220711
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 117414334	A	Alive	20240125

AB The present invention provides an aprepitant emulsion drug compn. and prepn. method thereof, which has the advantages of high quality and good stability. The method comprises the following steps: stirring and dissolving aprepitant, phospholipid, ethanol and soybean oil to obtain an oil phase, adding an isotonic regulator, the phospholipid and a pH regulator into water for injection, stirring uniformly to obtain a water phase, online shearing and mixing the oil phase and the water phase to prep. a primary emulsion, homogenizing by high-pressure microjet, sterilizing, filtering and filling.
IPCI A61K0009-107; A61K0031-5377; A61K0047-24; A61K0047-44; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]
CC 63 (Pharmaceuticals)
IT INDEXING IN PROGRESS
IT Egg yolk lecithins
Soybean oil
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(aprepitant emulsion drug compn. and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(aprepitant emulsion drug compn. and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(aprepitant emulsion drug compn. and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

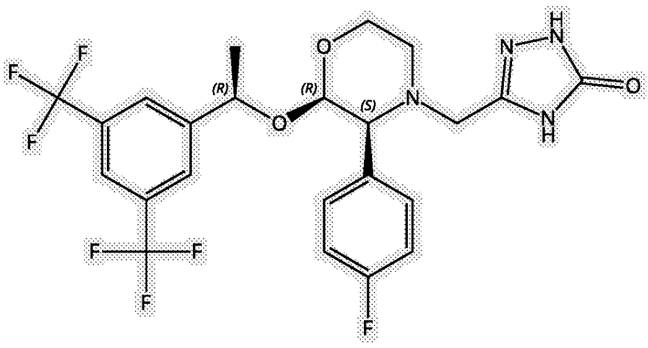
LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 117414334 A	CN 2022-10811953	Register|Global Dossier

L4 ANSWER 2 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2023:1752935 CAPLUS Full-text
DOCUMENT NUMBER: 184:181224
TITLE: Formulation and evaluation of lipid nanoparticulate drug delivery system of Aprepitant for the treatment of Cinv
AUTHOR(S): R., Joan Vijetha; Balamurugan, K.
CORPORATE SOURCE: College of Pharmacy, Sathyabama Institute of Science and Technology, Semmancheri, Chennai, 600119, India
SOURCE: Journal of Pharmaceutical Negative Results (2022), 13(Spec.Iss.10), 5114-5127
CODEN: JPNRBH; ISSN: 2229-7723
URL: https://www.pnrjournal.com/index.php/home/index
DIGITAL OBJECT ID: 10.47750/pnr.2022.13.s10.627
PUBLISHER: ResearchTrentz
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB The present study was to formulate and evaluate the Aprepitant USP is a substance P/neurokinin 1 (NK1) receptor antagonist as nanoparticulate lipid carriers (AP-NLC) drug delivery systems and comparing with the marketed product. The formulations of AP-NLC were prepd. by the homogenization followed by ultrasonication method using the solid lipid as Glyceryl behenate, the liq. lipid Caprylocaproyl polyoxyglycerides and polysorbate 80 as hydrophilic surfactant. Based on the trial expts., the compn. of optimized formulation was AP-NLC blend consist of 125 mg of Aprepitant, 210 mg Glyceryl behenate, 90 mg Caprylocaproyl polyoxyglycerides, 36 mg polysorbate 80 and 20 mg soya lecithin. By liquisolid technique mesoporous silica gel taken was 160.4 mg was mixed with above AP-NLC blend to form from the optimized AP-NLC12 capsules. The AP NLC12 was found to be with mean particle size of mean av. of 200.6 nm with max. intensity of 541.0 nm particles, The dissoln. data demonstrates that the drug release was increased by 5-12% increase in drug release in initial time points upto 3 h as compared to the marketed product and the release is sustained up to 30 h as compared to the 10 h for the marketed product. The drug release kinetics of AP NLC 12 was by Korsmeyer-Peppas model confirms the drug release from a polymeric system and release mechanisms was diffusion followed by erosion.This research is an attempt was made to design Aprepitant USP nanoparticulate lipid carrier drug delivery systems for sustained drug release in treatment chemotherapy induced nausea and vomiting (CINV).

CC 63-6 (Pharmaceuticals)
IT Soya lecithins
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and evaluation of lipid nanoparticulate drug delivery system of aprepitant for treatment of chemotherapy induced nausea and vomiting)
IT 9005-65-6 18641-57-1 170729-80-3
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and evaluation of lipid nanoparticulate drug delivery system of aprepitant for treatment of chemotherapy induced nausea and vomiting)
IT 170729-80-3
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and evaluation of lipid nanoparticulate drug delivery system of aprepitant for treatment of chemotherapy induced nausea and vomiting)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2023:1213332 CAPLUS Full-text
DOCUMENT NUMBER: 183:142125
TITLE: Personalized starvation therapy for cancer by administering an inhibitor of the mevalonate pathway with a diet low in cholesterol or lipids
INVENTOR(S): Maddocks, Oliver D. K.; Mishra, Swati
PATENT ASSIGNEE(S): Faeth Therapeutics, Inc., USA
ULTIMATE OWNER: FAETH THERAPEUTICS
ULTIMATE OWNER STANDARD: FAETH THERAPEUTICS
SOURCE: PCT Int. Appl., 210pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2023108146	A1	20230615	WO 2022-US81307		20221209
PRIORITY APPLN. INFO.:			US 2021-63288062	P	20211210

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2023108146	A1	Alive	20230629

AB Disclosed herein are methods of administering an inhibitor of the mevalonate pathway with a diet low in cholesterol or lipids. The methods of the present invention can be used to treat conditions such as cancer.
IPCI A61K0031-33 [I]; A61K0031-045 [I]; A61K0031-395 [I]; A61K0031-01 [N]
IPCR A61K0031-33 [I]; A61K0031-01 [N]; A61K0031-045 [I]; A61K0031-395 [I]
CC 1-6 (Pharmacology)
Section cross-reference(s): 18, 63
IT Castor oil
Lanolin
Lecithins
Tannins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(personalized starvation therapy for cancer by administering an inhibitor of mevalonate pathway with a diet low in cholesterol or lipids and combination with other agents)
IT 9031-14-5, Lecithin-cholesterol acyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; personalized starvation therapy for cancer by administering an inhibitor of mevalonate pathway with a diet low in cholesterol or lipids and combination with other agents)
IT 118292-40-3, Tazarotene 119169-78-7, Epristeride 119302-91-9, Rocuronium (Bromide) 119413-54-6, Topotecan (Hydrochloride) 119478-55-6, Danofloxacin (mesylate) 119478-56-7, Meropenem (trihydrate)

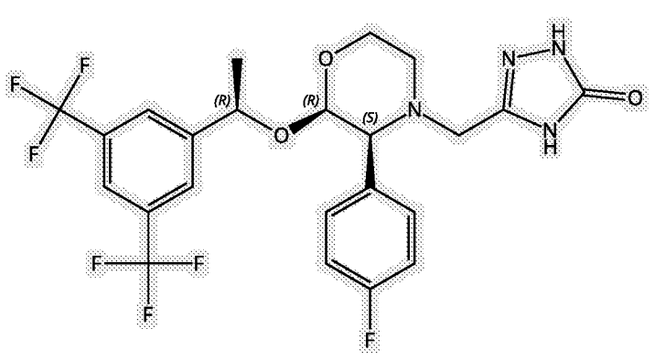
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Donepezil (Hydrochloride) 120014-06-4, Donepezil 120068-37-3, Fipronil
120202-66-6, Clopidogrel (hydrogen sulfate) 120410-24-4, Biapenem
120511-73-1, Anastrozole 120638-55-3 120685-11-2, Midostaurin
120876-23-5 121032-29-9, Nelarabine 121123-17-9, Cefprozil
(monohydrate) 121268-17-5 121808-62-6, Pidotimod 122111-03-9,
Gemcitabine (hydrochloride) 122320-73-4, Rosiglitazone 122341-38-2,
Temoporfin 122547-49-3, Faropenem sodium 122647-32-9, Ibutilide
(fumarate) 122841-12-7, Cefoselis (sulfate) 122852-69-1, Alosetron
(Hydrochloride) 122892-31-3, Itopride (hydrochloride) 123040-16-4,
Azasetron hydrochloride 123171-59-5, Cefepime (Dihydrochloride
Monohydrate) 123318-82-1, Clofarabine 123441-03-2, Rivastigmine
123447-62-1, Prulifloxacin 123524-52-7, Azelnidipine 123663-49-0,
Iguratimod 124750-99-8, Losartan (potassium) 124832-27-5, Valacyclovir
(hydrochloride) 124858-35-1, Nadifloxacin 124937-51-5, Tolterodine
124937-52-6, Tolterodine (tartrate) 125572-93-2, Rotigotine
(Hydrochloride) 125602-71-3, Bepotastine 126544-47-6, Ciclesonide
126784-99-4, Ulipristal acetate 127373-66-4, Sivelestat 127779-20-8,
Saquinavir 127984-74-1, Lanreotide (acetate) 128607-22-7, Ospemifene
128794-94-5, Mycophenolate Mofetil 129101-54-8, Rivastigmine (tartrate)
129453-61-8, Fulvestrant 129497-78-5, Verteporfin 129618-40-2,
Nevirapine 129722-12-9, Aripiprazole 129938-20-1, Dapoxetine
(hydrochloride) 130018-87-0, Levocetirizine (dihydrochloride)
130209-82-4, Latanoprost 130693-82-2, Dorzolamide (hydrochloride)
130726-68-0, Neticonazole 130773-02-3, Neticonazole (hydrochloride)
130929-57-6, Entacapone 131410-48-5, Gadodiamide 131707-23-8,
Umifenovir (hydrochloride) 132112-35-7, Ropivacaine (hydrochloride
monohydrate) 132203-70-4, Cilnidipine 132539-06-1, Olanzapine
132810-10-7, Blonanserin 132866-11-6, Lercanidipine (hydrochloride)
132907-72-3, Ramosetron (Hydrochloride) 133033-93-9, (±)-Darifenacin
133099-07-7, Darifenacin (hydrobromide) 133454-47-4, Iloperidone
133865-89-1 134308-13-7, Tolcapone 134418-28-3, Dehydroandrographolide
134523-00-5, Atorvastatin 134523-03-8, Atorvastatin calcium
134678-17-4, Lamivudine 135062-02-1, Repaglinide 135159-51-2,
Sarpogrelate (hydrochloride) 135326-22-6, Gadoxetate (Disodium)
135729-62-3, Palonosetron (Hydrochloride) 136087-85-9, Fidarestat
136310-93-5, Tiotropium (Bromide) 136434-34-9, Duloxetine
(hydrochloride) 136470-78-5, Abacavir 136572-09-3, Irinotecan
(hydrochloride trihydrate) 137071-32-0, Pimecrolimus 137234-62-9,
Voriconazole 137281-23-3, Pemetrexed 137862-53-4, Valsartan
137975-06-5, Mozavaptan 138112-76-2, Agomelatine 138402-11-6,
Irbesartan 138470-70-9, Mozavaptan (hydrochloride) 138530-94-6,
(R)-Lansoprazole 138614-30-9, Icatibant (acetate) 138786-67-1,
Pantoprazole (sodium) 138890-62-7, Brinzolamide 138926-19-9,
Ibandronate (Sodium Monohydrate) 138982-67-9, Ziprasidone (hydrochloride
monohydrate) 139110-80-8, Zanamivir 139481-59-7, Candesartan
139755-83-2, Sildenafil 139755-85-4, Lodenafil 140462-76-6,
Olopatadine (hydrochloride) 140678-14-4, Mangafodipir (trisodium)
140898-91-5, Hexaminolevulinate (hydrochloride) 141396-28-3, Argatroban
(monohydrate) 141433-60-5, Berberine (chloride hydrate) 141505-33-1,
Levosimendan 141625-93-6, Dronedarone (Hydrochloride) 141626-36-0,
Dronedarone 141702-36-5, Faropenem daloxate 142128-59-4,
(+)-Ketoconazole 142340-99-6, Adefovir dipivoxil 143388-64-1,
Naratriptan (hydrochloride) 143491-57-0, Emtricitabine 144060-53-7,
Febuxostat 144143-96-4, Eprosartan (mesylate) 144481-98-1, Landiolol
(hydrochloride) 144598-75-4, Paliperidone 144675-97-8, Pixantrone
(dimaleate) 144689-24-7, Olmesartan 144689-63-4, Olmesartan medoxomil
144701-48-4, Telmisartan 145040-37-5, Candesartan Cilexetil
145108-58-3, Dexmedetomidine (hydrochloride) 145202-66-0, Rizatriptan
(benzoate) 145435-72-9, Gamithromycin 145525-41-3, Mitiglinide
(Calcium) 145672-81-7, Cetrorelix (Acetate) 145781-92-6, Goserelin
(acetate) 145821-59-6, Tiagabine (hydrochloride) 146464-95-1,
Pralatrexate 146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin
147084-10-4, Alcaftadine 147098-20-2, Rosuvastatin calcium
147127-20-6, Tenofovir 147221-93-0, Delavirdine (mesylate)
147403-03-0, Azilsartan 147511-69-1, Pitavastatin 147526-32-7,
Pitavastatin calcium 147536-97-8, Bosentan 148408-66-6, Docetaxel
(Trihydrate) 148849-67-6, Ivabradine (hydrochloride) 149003-01-0,
Dexrazoxane (hydrochloride) 149647-78-9, Vorinostat 149709-62-6,
Sacubitril 149845-06-7, Saquinavir (Mesylate) 150322-43-3, Prasugrel
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Perospirone 151767-02-1, Montelukast (sodium) 152459-95-5, Imatinib
152520-56-4, Nebivolol (hydrochloride) 152658-17-8, Nalfurafine
(hydrochloride) 153439-40-8, Fexofenadine (hydrochloride) 153504-70-2,
Cevimeline (hydrochloride hemihydrate) 153559-49-0, Bexarotene
154229-18-2, Abiraterone acetate 154229-19-3, Abiraterone 154361-50-9,
Capecitabine 154598-52-4, Efavirenz 155141-29-0, Rosiglitazone
(maleate) 155148-31-5, Plerixafor (octahydrochloride) 155206-00-1,
Bimatoprost 155213-67-5, Ritonavir 155270-99-8, Istradefylline
155558-32-0, Hydroxyfasudil (hydrochloride) 155569-91-8, Emamectin
(Benzoate) 156137-99-4, Rapacuronium bromide 157212-55-0, Bosentan
(hydrate) 157283-68-6, Travoprost 157810-81-6, Indinavir (sulfate)
158681-13-1, Rimonabant (Hydrochloride) 158930-17-7, Frovatriptan
succinate hydrate 159351-69-6, Everolimus 159989-64-7, Nelfinavir
159989-65-8, Nelfinavir (Mesylate) 160970-54-7, Silodosin 161715-24-8,
Tebipenem pivoxil 161735-79-1, Rasagiline (mesylate) 161804-20-2
161814-49-9, Amprenavir 161973-10-0, Esomeprazole magnesium
162011-90-7, Rofecoxib 162359-55-9, Fingolimod 162359-56-0, Fingolimod
(hydrochloride) 162401-32-3, Roflumilast 162635-04-3, Temsirolimus
163222-33-1, Ezetimibe 163252-36-6, Clevudine 163253-37-0
163451-81-8, Teriflunomide 163521-08-2, Vilazodone (Hydrochloride)
163521-12-8, Vilazodone 163521-19-5 163680-77-1, Pazufloxacin
(mesylate) 163706-36-3, Cangrelor (tetrasodium) 164650-44-6,
Efinaconazole 164656-23-9, Dutasteride 165800-03-3, Linezolid
165800-06-6, Zoledronic acid (monohydrate) 166663-25-8, Anidulafungin
166734-83-4 167221-71-8, Clevidipine 167933-07-5, Flibanserin
168626-94-6, Conivaptan (hydrochloride) 169590-41-4, Deracoxib
169590-42-5, Celecoxib 170098-38-1, Alvimopan (dihydrate) 170105-16-5,
Imidafenacin 170729-80-3, Aprepitant 171228-49-2,
Posaconazole 171596-29-5, Tadalafil 171599-83-0, Sildenafil (citrate)
172152-36-2, Ilaprazole 172152-50-0, Ilaprazole (sodium) 173334-57-1,
Aliskiren 173334-58-2, Aliskiren (hemifumarate) 173352-39-1
174484-41-4, Tipranavir 174671-46-6, Tavaborole 175865-59-5,
Valganciclovir (hydrochloride) 177036-94-1, Ambrisentan 177834-92-3,
Eletriptan (hydrobromide) 178307-42-1, Revaprazan (hydrochloride)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(personalized starvation therapy for cancer by administering an
inhibitor of mevalonate pathway with a diet low in cholesterol or
lipids and combination with other agents)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(personalized starvation therapy for cancer by administering an
inhibitor of mevalonate pathway with a diet low in cholesterol or
lipids and combination with other agents)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
WO 2023108146 A1	WO 2022-US81307	Register|Global Dossier

L4 ANSWER 4 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:2496852 CAPLUS Full-text
DOCUMENT NUMBER: 180:210930
TITLE: Compositions having improved bioavailability of therapeutics
INVENTOR(S): Brew, John; Gooding, Daniel; Bannister, Robin M.
PATENT ASSIGNEE(S): TRx Biosciences Limited, UK
ULTIMATE OWNER: TRX BIOSCIENCES
ULTIMATE OWNER STANDARD: TRX BIOSCIENCES
SOURCE: U.S. Pat. Appl. Publ., 202pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20220305125	A1	20220929	US 2022-17656702	20220328
CA 3212583	A1	20221006	CA 2022-3212583	20220328
WO 2022207580	A2	20221006	WO 2022-EP58180	20220328
WO 2022207580	A3	20221229		
AU 2022248850	A1	20231109	AU 2022-248850	20220328
EP 4312978	A2	20240207	EP 2022-718916	20220328
KR 2024021751	A	20240219	KR 2023-7037012	20220328
WO 2023174948	A2	20230921	WO 2023-EP56506	20230314
WO 2023174948	A3	20231026		
US 20240075147	A1	20240307	US 2023-18487486	20231016
IN 202347072261	A	20231215	IN 2023-47072261	20231023

PRIORITY APPLN. INFO.:

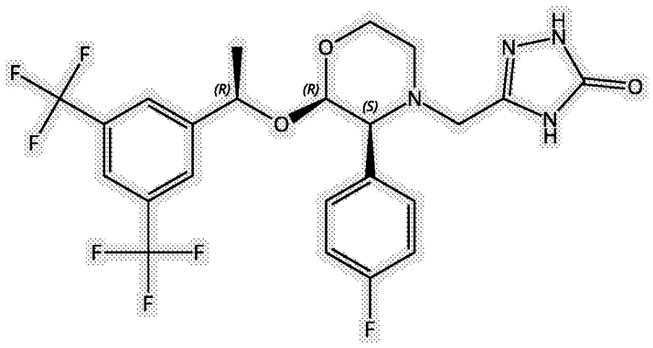
US 2021-63166995	P	20210327
US 2022-63269330	P	20220314
US 2022-17656702	A1	20220328
WO 2022-EP58180	W	20220328

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20220305125	A1	Alive	20221006
CA 3212583	A1	Alive	20231005
WO 2022207580	A2	Alive	20221013
WO 2022207580	A3	Alive	20230112
AU 2022248850	A1	Alive	20231116
EP 4312978	A2	Alive	20240208
WO 2023174948	A2	Alive	20230928

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2022:2496852
AB The present specification discloses pharmaceutical compn. disclosed herein comprises one or more therapeutic compds., one or more glycerolipids, and one or more digestion enhancers. The disclosed glycerolipids comprise one or more hard fats and one or more liq. fats. The disclosed digestion enhancers comprise one or more bile acids, one or more phospholipids, one or more free C14-24 fatty acids, one or more free C14-24 fatty acid surfactants, or any combination thereof. The present specification also discloses methods and procedures to formulate the disclosed one or more therapeutic compds. into the disclosed pharmaceutical compns.
IPCI A61K0047-14 [I]; A61K0047-28 [I]; A61K0031-12 [I]; A61K0031-216 [I]; A61K0031-05 [I]; A61K0031-58 [I]; A61K0031-7135 [I]; A61K0031-192 [I]; A61K0031-553 [I]; A61K0031-4418 [I]; A61K0031-4453 [I]; A61K0031-196 [I]; A61K0031-44 [I]; A61K0031-4184 [I]; A61K0031-436 [I]; A61K0031-5377 [I]; A61K0031-502 [I]; A61K0031-496 [I]; A61K0031-4025 [I]; A61K0038-12 [I]
IPCR A61K0047-14 [I]; A61K0031-05 [I]; A61K0031-12 [I]; A61K0031-192 [I]; A61K0031-196 [I]; A61K0031-216 [I]; A61K0031-4025 [I]; A61K0031-4184 [I]; A61K0031-436 [I]; A61K0031-44 [I]; A61K0031-4418 [I]; A61K0031-4453 [I]; A61K0031-496 [I]; A61K0031-502 [I]; A61K0031-5377 [I]; A61K0031-553 [I]; A61K0031-58 [I]; A61K0031-7135 [I]; A61K0038-12 [I]; A61K0047-28 [I]
CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1
IT Bile acids
Fats and Glyceridic oils
Fatty acids
Glycerolipids
Lecithins
Monoglycerides
Phospholipids
Polyoxyalkylenes
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. having improved bioavailability of therapeutics)
IT 458-37-7, Curcumin 4394-00-7, Niflumic acid 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22204-53-1, Naproxen 31121-93-4 31431-39-7, Mebendazole 34031-32-8, Auranofin 53179-13-8, Pirfenidone 68302-57-8, Amlexanox 88170-10-9, Diclofenac calcium 120685-11-2, Midostaurin 130308-48-4, Icatibant 144701-48-4, Telmisartan 154229-19-3, Abiraterone 170729-80-3, Aprepitant 362665-56-3, Pitolisant 491833-29-5, Eliglustat 656247-17-5, Nintedanib 763113-22-0, Olaparib
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. having improved bioavailability of therapeutics)
IT 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. having improved bioavailability of therapeutics)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2022248850 A1	AU 2022-248850	Register
CA 3212583 A1	CA 2022-3212583	Register
EP 4312978 A2	EP 2022-718916	Register|Federated Reg.
IN 202347072261 A	IN 2023-47072261	Register
KR 2024021751 A	KR 2023-7037012	Register|Global Dossier
US 20220305125 A1	US 2022-17656702	Register|Global Dossier
US 20240075147 A1	US 2023-18487486	Register|Global Dossier
WO 2022207580 A2	WO 2022-EP58180	Register|Global Dossier
WO 2022207580 A3	WO 2022-EP58180	Register|Global Dossier
WO 2023174948 A2	WO 2023-EP56506	Register|Global Dossier
WO 2023174948 A3	WO 2023-EP56506	Register|Global Dossier

L4 ANSWER 5 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN

ACCESSION NUMBER: 2022:2221248 CAPLUS Full-text
DOCUMENT NUMBER: 181:431761
TITLE: Small scale in vitro method to determine a potential bioequivalent equilibrium solubility range for fed human intestinal fluid
AUTHOR(S): Ines Silva, Maria; Khadra, Ibrahim; Pyper, Kate; Halbert, Gavin W.
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, Glasgow, G4 0RE, UK
SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (2022), 177, 126-134
CODEN: EJPBEL; ISSN: 0939-6411
DIGITAL OBJECT ID: 10.1016/j.ejpb.2022.06.005
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Intestinal drug soly. is a key parameter controlling oral absorption but varies both intra and inter individuals and between the fasted and fed states, with food intake known to alter the bioavailability of many compds. Intestinal soly. can be measured in vitro either using sampled fed human intestinal fluid (FeHIF) or simulated fed intestinal fluid (SIF) but neither approach is optimal. FeHIF is difficult to obtain and variable, while for fed SIF multiple recipes are available with no consensus on the ideal version. A recent study characterised FeHIF aspirates using a multidimensional approach and calcd. nine simulated media recipes that covered over ninety percent of FeHIF compositional variability. In this study the equil. soly. of thirteen drugs have been measured using the nine simulated media recipes and compared to multiple previous design of expt. (DoE) studies, which have examd. the impact of fed SIF media components on soly. The measured nine media soly. data set is only statistically equiv. to the large scale 92 media DoE in 4 out of 13 drug comparisons, but has improved equivalence against small scale DoEs (9 or 10 media) with 6 out of 9 or 10 out of 12 (9 and 10 media resp.) equiv. Selective removal of non-biorelevant compns. from the 92 media DoE improves statistical equivalence to 9 out of 13 comparisons. The results indicate that soly. equivalence is linked to media component concns. and compns., the nine media system is measuring a similar soly. space to previous systems, with a narrower soly. range than the 92 point DoE but equiv. to smaller DoE systems. Phenytoin and tadalafil display a narrow soly. range, a behavior consistent with previous studies in fed and fasted states and only revealed through the multiple media approach. Custom DoE anal. of the nine media results to det. the most statistically significant component influencing soly. does not detect significant components. Indicating that the approach has a low statistical resoln. and is not appropriate if detn. of media component significance is required. This study demonstrates that it is possible to assess the fed intestinal equil. soly. envelope using the nine media recipes obtained from a multi-dimensional anal. of fed HIF. The derivation of the nine media compns. coupled with the results in this study indicate that the soly. results are more likely to reflect the fed intestinal soly. envelope than previous DoE studies and highlight that the system is worthy of further investigation.

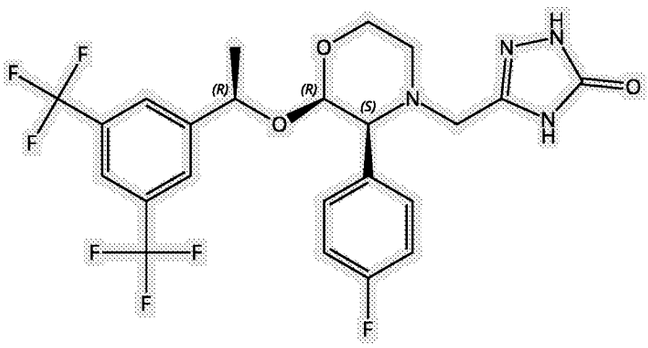
CC 63-6 (Pharmaceuticals)

IT Lecithins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale in vitro method to det. potential bioequivalent equil. soly. range for fed human intestinal fluid)

IT 53-86-1 57-41-0 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies 110-16-7, 2-Butenedioic acid (2Z)-, biological studies 111-03-5 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 145-42-6 14265-44-2, Phosphate, biological studies 15687-27-1 23288-49-5 25614-03-3 49562-28-9 72509-76-3 72956-09-3 84625-61-6 107753-78-6 137862-53-4 170729-80-3 171596-29-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale in vitro method to det. potential bioequivalent equil. soly. range for fed human intestinal fluid)

IT 170729-80-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale in vitro method to det. potential bioequivalent equil. soly. range for fed human intestinal fluid)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:1355958 CAPLUS Full-text
DOCUMENT NUMBER: 179:75293
TITLE: Stable antiemetic emulsions
INVENTOR(S): Bhagwatwar, Harshal Prabhakar; Nerurkar, Manoj
PATENT ASSIGNEE(S): Steps BioSciences, Inc., USA
ULTIMATE OWNER: STEPS BIOSCIENCES
ULTIMATE OWNER STANDARD: STEPS BIOSCIENCES
SOURCE: U.S. Pat. Appl. Publ., 11pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

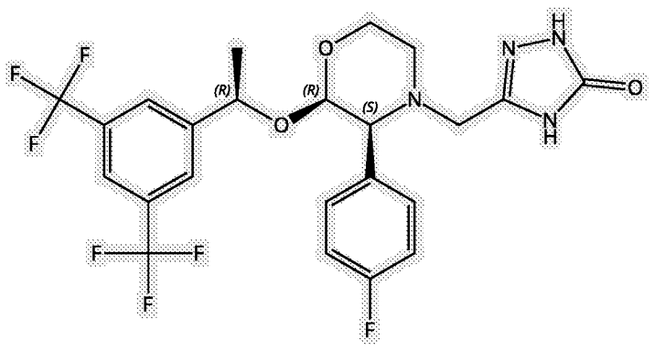
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20220160722	A1	20220526	US 2021-17531216	20211119
PRIORITY APPLN. INFO.:			IN 2020-41050531 A	20201120

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20220160722	A1	Alive	20220609

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2022:1355958
AB Emulsion formulations and systems for the i.v. or parenteral administration. of neurokinin-1 (NK-1) receptor antagonists for treatment of emesis are provided. Methods for prepg. the stable NK-1 receptor antagonist emulsions and pharmaceutical formulations are further provided. The emulsion formulations are prepd. and characterized as a formulation and process that will allow an NK-1 receptor antagonist compd. to be incorporated into an emulsion for i.v. injection and remain stable during the shelf life of the formulation. Specifically, emulsion formulations have an oil phase that includes oil, ethanol, egg lecithin , and the further addn. of sodium oleate that is mixed with an aq. phase and processed to form the emulsion formulation.
IPCI A61K0031-5377 [I]; A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-24 [I]; A61K0047-12 [I]; A61K0047-10 [I]; A61K0047-44 [I]
IPCR A61K0031-5377 [I]; A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-44 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT Castor oil
Coconut oil
Corn oil
Cottonseed oil
Egg yolk lecithins
Lecithins
Olive oil
Safflower oil
Sesame oil
Soybean oil
Triglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
IT 57-50-1, Sucrose, biological studies 64-17-5, Ethanol, biological studies 111-62-6, Ethyl oleate 143-19-1, Sodium oleate 303-43-5, Cholesteryl oleate 544-35-4, Ethyl linoleate 604-33-1, Cholesteryl linoleate 37220-82-9, Glyceryl oleate 37348-65-5, Glyceryl linoleate 136745-48-7, Octyl glycerate 152167-64-1, Decyl glycerate 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable antiemetic emulsions)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
US 20220160722 A1	US 2021-17531216	Register|Global Dossier

L4 ANSWER 7 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2022:139737 CAPLUS Full-text
DOCUMENT NUMBER: 177:284905
TITLE: Pharmaceutical emulsion comprising an aprepitant, pharmaceutical injections, and methods of preparing emulsions
INVENTOR(S): Amano, Yohei; Katagiri, Kazumi
PATENT ASSIGNEE(S): Kewpie Corporation, Japan; FBC (Shanghai) Pharmaceutical Technology Co., Ltd.
ULTIMATE OWNER: FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; KEWPIE CORPORATION
ULTIMATE OWNER STANDARD: FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; Kewpie Corp
SOURCE: PCT Int. Appl., 28pp.; Chemical Indexing Equivalent to

174:540291 (JP)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2022014113	A1	20220120	WO 2021-JP15552	20210415
JP 6832468	B1	20210224	JP 2020-121438	20200715
JP 2022018370	A	20220127		
CA 3187858	A1	20220120	CA 2021-3187858	20210415
KR 2023040956	A	20230323	KR 2022-7045138	20210415
EP 4169515	A1	20230426	EP 2021-843280	20210415
US 20230310443	A1	20231005	US 2023-18015492	20230110

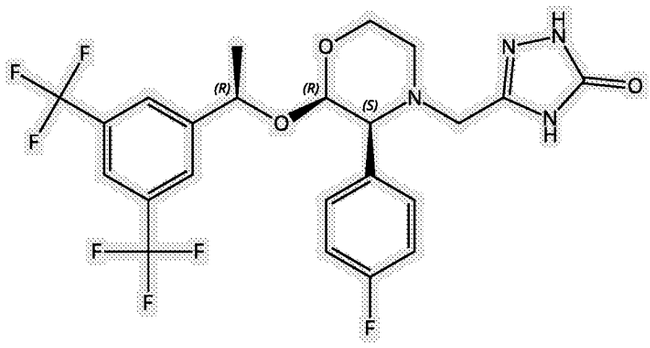
PRIORITY APPLN. INFO.: JP 2020-121438 A 20200715
WO 2021-JP15552 W 20210415

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2022014113	A1	Alive	20220203
JP 6832468	B1	Alive	20210304
JP 2022018370	A	Alive	20220224
CA 3187858	A1	Alive	20230216
KR 2023040956	A	Alive	20230420
EP 4169515	A1	Alive	20230427
US 20230310443	A1	Alive	20231012

AB The present invention pertains to an emulsion which contains an aprepitant, an emulsifier, an oil, a polyethylene glycol having an av. mol. wt. of 260-1100, and water, and to which ethanol is substantially not added. The content of the aprepitant is 0.50-0.90 w/v% based on the total amt., and the content of the emulsifier is 12.0-18 w/v%. The content of oil is 7.0-12.0 w/v %, and the content of polyethylene glycol is 0.5-10.0 w/v %. The av. particle diam. of the emulsion is 60-140 nm. According to the present invention, provided is an aprepitant-contg. emulsion having excellent stability without substantially adding ethanol.

IPCI A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]
IPCR A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
Phospholipids
Polyoxyalkylenes
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)
IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)
IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CA 3187858 A1	CA 2021-3187858	Register
EP 4169515 A1	EP 2021-843280	Register|Federated Reg.
JP 2022018370 A	JP 2020-121438	Register|Global Dossier
JP 6832468 B1	JP 2020-121438	Register|Global Dossier
KR 2023040956 A	KR 2022-7045138	Register|Global Dossier
US 20230310443 A1	US 2023-18015492	Register|Global Dossier
WO 2022014113 A1	WO 2021-JP15552	Register|Global Dossier

L4 ANSWER 8 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:2591917 CAPLUS Full-text
DOCUMENT NUMBER: 177:123225
TITLE: Preparation method of aprepitant emulsion injection for preventing nausea and emesis
INVENTOR(S): Guo, Shuer; Qin, Zhijun
PATENT ASSIGNEE(S): Guangzhou Manxiang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU MAXENMED MEDICINE
ULTIMATE OWNER STANDARD: GUANGZHOU MAXENMED MEDICINE
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

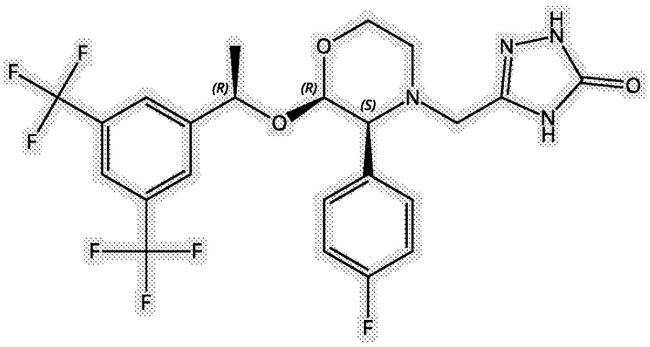
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 113712915	A	20211130	CN 2021-10018100	20210107

PRIORITY APPLN. INFO.: CN 2021-10018100 20210107
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 113712915	A	Alive	20211209

OTHER SOURCE(S): CASFORMULTNS 2021:2591917
AB The invention aprepitant emulsion injection is prepd. from (by wt%) aprepitant 0.2-1.2, pH regulator 0.25-0.75, permeation pressure regulator 3-8, injection water 56-75, emulsifier 12-15, cosolvent 2-5, and injection oil 5-15. The emulsifier is hydrogenated soybean lecithin or hydrogenated soybean phosphatidylcholine. The pH regulator is sodium hydroxide, sodium citrate, sodium dihydrogen phosphate or sodium oleate. The permeation pressure regulator is xylitol, sorbitol, mannitol or sucrose. The cosolvent is ethanol, glycerol, propylene glycol and polyethylene glycol. The injection oil is soybean oil, peanut oil, hydrogenated corn oil, triglyceride, medium-chain triglyceride, sesame oil and/or sunflower seed oil. By controlling content of emulsifier and shearing rotation speed, homogenization pressure and homogenization temp. in emulsion prepn. process, the invention preps. aprepitant emulsion injection with good oxidn. resistance and emulsification effect, and has

operability, simple process and low device loss.
IPCI A61K0009-107; A61K0047-24; A61K0031-5377; A61P0001-08; A61P0035-00
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
IT Corn oil
Soya lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. method of aprepitant emulsion injection for preventing nausea and emesis)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 113712915 A	CN 2021-10018100	Register|Global Dossier

L4 ANSWER 9 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:1541826 CAPLUS Full-text
DOCUMENT NUMBER: 175:329880
TITLE: Aprepitant ready-to-use injection emulsion compositions
INVENTOR(S): Akasapu, Prem Sagar; Subramanian, Veerappan; Subramanian, Ilango
PATENT ASSIGNEE(S): Somerset Therapeutics LLC, USA
ULTIMATE OWNER: SOMERSET THERAPEUTICS LLC
ULTIMATE OWNER STANDARD: SOMERSET THERAPEUTICS LLC
SOURCE: U.S. Pat. Appl. Publ., 8pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20210212933	A1	20210715	US 2021-17147556		20210113
US 11517522	B2	20221206			
PRIORITY APPLN. INFO.:			US 2020-62961039	P	20200114

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20210212933	A1	Alive	20210722
US 11517522	B2	Alive	20221215

OTHER SOURCE(S): CASFORMULTNS 2021:1541826

AB The present invention provides an emulsion compn. comprising aprepitant for treatment of emesis. Particularly, the invention is a ready-to-use emulsion compns. comprising aprepitant and medium chain triglycerides for administration by i.v. infusion, wherein the emulsion compn. is also free of ethanol. Further, the invention also provides processes of prepg. such compns. and their use for the prevention and control of acute and delayed chemotherapy-induced nausea and vomiting, and/or for prevention of postoperative nausea and vomiting.

IPCI A61K0009-00 [I]; A61K0009-107 [I]; A61K0047-14 [I]; A61M0005-24 [I]; A61K0031-5377 [I]; A61K0009-00 [I]; A61K0047-14 [I]; A61K0009-107 [I]; A61K0031-5377 [I]; A61M0005-24 [I]

IPCR A61K0009-00 [I]; A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-14 [I]; A61M0005-24 [I]

CC 63-6 (Pharmaceuticals)

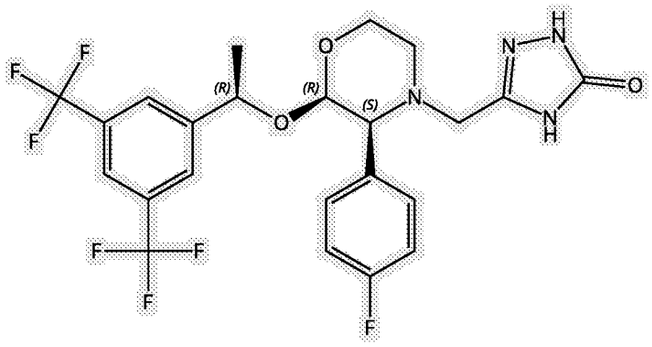
IT Lecithins
Medium-chain glycerides
Polyoxyalkylenes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant ready-to-use injection emulsion compns.)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
US 11517522 B2	US 2021-17147556	Register|Global Dossier
US 20210212933 A1	US 2021-17147556	Register|Global Dossier

L4 ANSWER 10 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN

ACCESSION NUMBER: 2021:685825 CAPLUS Full-text

DOCUMENT NUMBER: 178:140851

TITLE: Aprepitant submicroemulsion injection capable of being autoclaved, and its preparation method

INVENTOR(S): Qin, Linghao; Li, Yusheng; Zhu, Wanye; Wang, Wanting

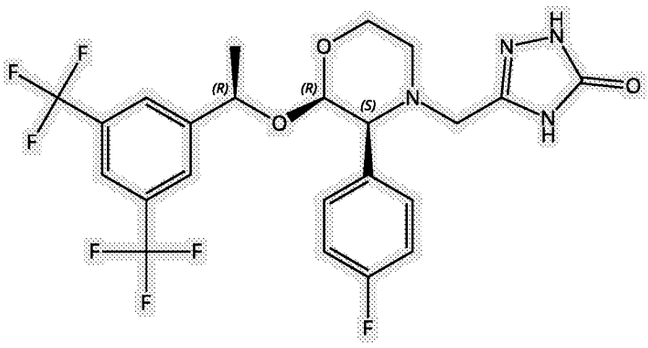
PATENT ASSIGNEE(S): Guangdong Pharmaceutical University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 19pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 112535661	A	20210323	CN 2020-11524237	20201222
CN 112535661	B	20230407		

PRIORITY APPLN. INFO.: CN 2020-11524237 20201222
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 112535661	A	Alive	20210408
CN 112535661	B	Alive	20230427

OTHER SOURCE(S): CASFORMULTNS 2021:685825
AB A safe aprepitant submicroemulsion injection capable of being autoclaved having high efficiency, good stability and sterilization effect, and wide application in medicine field is provided. The aprepitant submicroemulsion injection comprises: polyethylene glycol 15hydroxystearate, phospholipids, aprepitant, oil for injection, emulsifier, co-emulsifier, solubilizer, stabilizer, isotonic agent, pH regulator and water for injection. The prepn. method comprises the following steps: (1) mixing aprepitant, injection oil and solubilizer, dissolving and dispersing with alc., and removing the alc. to obtain an oil phase mixt.; (2) stirring and mixing the emulsifier, co-emulsifier, stabilizer, isotonic agent and water for injection, and heat to dissolve to obtain the water phase mixt.; and (3) adding the oil phase mixt. to the water phase mixt., prepg. the emulsion, and autoclaving to obtain the aprepitant submicroemulsion injection. The aprepitant submicroemulsion injection is used in the prepn. of a medicine for treating nausea and vomiting.
IPCI A61K0009-107; A61K0031-5377; A61K0047-24; A61K0047-14; A61K0047-18; A61P0001-08; A61L0002-07
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-14 [I]; A61K0047-18 [I]; A61K0047-24 [I]; A61L0002-07 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Amino acids
Egg yolk lecithins
Oils
Phospholipids
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)
IT 56-41-7, L-Alanine, biological studies 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 63-91-2, L-Phenylalanine, biological studies 73-32-5, L-Isoleucine, biological studies 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant submicroemulsion injection capable of being autoclaved, and its prepn. method)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 112535661 A	CN 2020-11524237	Register|Global Dossier
CN 112535661 B	CN 2020-11524237	Register|Global Dossier

L4 ANSWER 11 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2021:481715 CAPLUS Full-text
DOCUMENT NUMBER: 174:540291
TITLE: Pharmaceutical emulsion comprising an aprepitant, pharmaceutical injections, and methods of preparing emulsions
INVENTOR(S): Amano, Yohei; Katagiri, Kazumi
PATENT ASSIGNEE(S): Kewpie Corporation, Japan; FBC (Shanghai) Pharmaceutical Technology Co., Ltd.
ULTIMATE OWNER: KEWPIE CORPORATION; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY
ULTIMATE OWNER STANDARD: Kewpie Corp; FBC SHANGHAI PHARMACEUTICAL TECH; FUBICHENG SHANGHAI MEDICAL TECH; FBC SHANGHAI PHARMACEUTICAL TECHNOLOGY
SOURCE: Jpn. Tokkyo Koho, 15pp.; Chemical Indexing Equivalent to 177:284905 (WO)
CODEN: JTXXFF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 6832468	B1	20210224	JP 2020-121438	20200715
JP 2022018370	A	20220127		
CA 3187858	A1	20220120	CA 2021-3187858	20210415
WO 2022014113	A1	20220120	WO 2021-JP15552	20210415
KR 2023040956	A	20230323	KR 2022-7045138	20210415
EP 4169515	A1	20230426	EP 2021-843280	20210415
CN 113952299	A	20220121	CN 2021-10772526	20210708
CN 117017915	A	20231110	CN 2023-11089804	20210708
US 20230310443	A1	20231005	US 2023-18015492	20230110

PRIORITY APPLN. INFO.:

JP 2020-121438	A	20200715
WO 2021-JP15552	W	20210415
CN 2021-10772526	A3	20210708

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
JP 6832468	B1	Alive	20210304
JP 2022018370	A	Alive	20220224
CA 3187858	A1	Alive	20230216
WO 2022014113	A1	Alive	20220203
KR 2023040956	A	Alive	20230420

EP 4169515	A1	Alive	20230427
CN 113952299	A	Alive	20220203
CN 117017915	A	Alive	20231116
US 20230310443	A1	Alive	20231012

OTHER SOURCE(S): CASFORMULTNS 2021:481715

AB The emulsion comprises: an aprepitant, an emulsifier, an oil, polyethylene glycol and water, with substantially no addn. of ethanol. The emulsion comprises a pH regulator and having a pH of 8.0-9.0. The content of the aprepitant is 0.50 w/v% or more and 0.90 w/v% or less based on the total amt., and the content of the emulsifier is 12.0 w/v% or more and 12.0 w/v% or more based on the total amt. The emulsion is 0 w/v% or less, the emulsion in which the emulsifier is a phospholipid. According to the present invention, provided is an aprepitant-contg. emulsion having excellent stability without substantially adding ethanol.

IPCI A61K0031-5377 [I]; A61K0009-107 [I]; A61P0001-08 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0031-5377 [I]; A61P0001-08 [I]; A61K0047-24 [I]; A61K0047-44 [I]

IPCR A61K0031-5377 [I]; A61K0009-107 [I]; A61K0047-10 [I]; A61K0047-24 [I]; A61K0047-44 [I]; A61P0001-08 [I]

CC 63-6 (Pharmaceuticals)

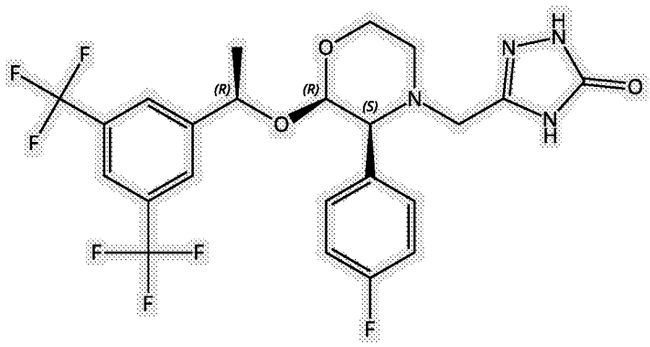
IT Egg yolk lecithins
Phospholipids
Polyoxyalkylenes
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

IT 170729-80-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion comprising aprepitant, pharmaceutical injections, and methods of prepg. emulsions)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

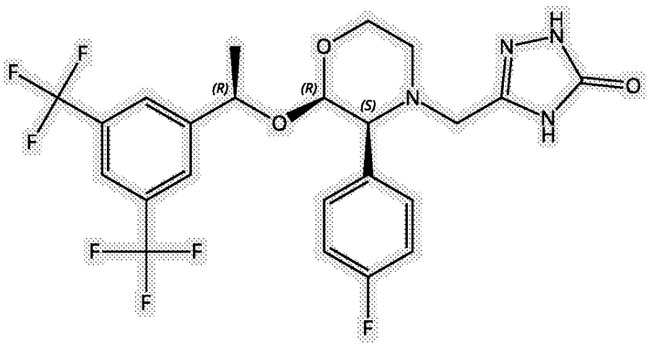
PUBLICATIONS	APPLICATIONS	REGISTER
CA 3187858 A1	CA 2021-3187858	Register
CN 113952299 A	CN 2021-10772526	Register|Global Dossier
CN 117017915 A	CN 2023-11089804	Register|Global Dossier

EP 4169515 A1	EP 2021-843280	Register|Federated Reg.
JP 2022018370 A	JP 2020-121438	Register|Global Dossier
JP 6832468 B1	JP 2020-121438	Register|Global Dossier
KR 2023040956 A	KR 2022-7045138	Register|Global Dossier
US 20230310443 A1	US 2023-18015492	Register|Global Dossier
WO 2022014113 A1	WO 2021-JP15552	Register|Global Dossier

L4 ANSWER 12 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:2334591 CAPLUS Full-text
DOCUMENT NUMBER: 174:387650
TITLE: Enhanced transdermal permeation of BCS class IV aprepitant using binary ethosome: Optimization, characterization and ex vivo permeation
AUTHOR(S): Abouhussein, Dalia M. N.
CORPORATE SOURCE: Department of Pharmaceutics, Egyptian Drug Authority Formerly Known As National Organization for Drug Control and Research (NODCAR), Egypt
SOURCE: Journal of Drug Delivery Science and Technology (2021), 61, 102185
CODEN: JDDSAL; ISSN: 1773-2247
DIGITAL OBJECT ID: 10.1016/j.jddst.2020.102185
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Aprepitant (APR) belongs to the Biopharmaceutics Classification System (BCS) class IV that is characterized by both low soly. and permeability. This study aims to develop a new transdermal APR nanovesicle for chemotherapy-induced nausea and vomiting. APR binary ethosomes (BEs) were developed using 32 factorial design where two independent variables namely; wt. of lecithin and propylene glycol were studied. The formulations were fully characterized through entrapment efficiency (EE), vesicle size (VS) and zeta potential (ZP). The optimized formulation was designated through the desirability value obtained by Design Expert program, visualized using transmission electron microscope (TEM) and studied for stability. Then the optimized formulation was incorporated in 0.8% carbopol 934 gel which was characterized and tested for in vitro and ex vivo release. F9 contg. 100 mg lecithin and 2.5 g propylene glycol was selected to be the optimum formulation. It showed desirability value of 0.958 as it displayed 89.6% EE, VS of 77 nm, -51.1 as ZP in addn. to adequate stability. The APR BE gel showed satisfactory phys., mech., rheol. and occlusive properties. The optimum formulation showed 4.9 folds higher permeation than APR suspension. BE gel exhibited a promising dosage form for the transdermal delivery of APR.

CC 63-5 (Pharmaceuticals)
IT Lecithins
Phospholipids
RL: MOA (Modifier or additive use); USES (Uses)
(optimum formulation of aprepitant binary ethosomes gel showed satisfactory phys., mech., rheol. and occlusive properties for transdermal delivery)
IT 170729-80-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimum formulation of aprepitant binary ethosomes gel showed satisfactory phys., mech., rheol. and occlusive properties for transdermal delivery)
IT 170729-80-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimum formulation of aprepitant binary ethosomes gel showed satisfactory phys., mech., rheol. and occlusive properties for transdermal delivery)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:485442 CAPLUS Full-text
DOCUMENT NUMBER: 177:51750
TITLE: Aprepitant Intravenous Emulsion Based on Ion Pairing/Phospholipid Complex for Improving Physical and Chemical Stability During Thermal Sterilization
AUTHOR(S): Zhang, Xinyu; Wei, Ying; Cao, Zhijun; Xu, Ying; Lu, Cong; Zhao, Meiqi; Gou, Jingxin; Yin, Tian; Zhang, Yu; He, Haibing; Wang, Yanjiao; Tang, Xing
CORPORATE SOURCE: Department of Pharmaceutics, Shenyang Pharmaceutical University, Shenyang, Peop. Rep. China
SOURCE: AAPS PharmSciTech (2020), 21(3), 75
CODEN: AAPHFZ; ISSN: 1530-9932
DIGITAL OBJECT ID: 10.1208/s12249-019-1605-7
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB An aprepitant (APT) cholesteryl hemisuccinate (CHEMS) ion pair complex emulsion (AIPE) with high lecithin content was prepd. to improve sterilization stability through the film dispersion homogenization method; therefore, it could be a promising delivery system of APT. Medium-chain triglycerides (MCT) was selected as the oil phase to improve the soly. and stability of APT in oil phase. DSC, XRD, FT-IR, and 1H-NMR spectroscopies confirmed that the APT-CHEMS ion pair (AIP) was formed between CHEMS and APT. The formation of AIP significantly increased the hydrophobicity of APT, allowing it to be completely embedded in the oil phase core to improve chem. stability and decrease hydrolysis of APT in the water phase. Also, CHEMS had a strong affinity with lecithin and could stabilize lipid membranes, forming a stronger and thicker interface membrane to increase the phys. stability of AIPE. As a result, AIPE could withstand autoclaving at 120°C for 8 min without any change of particle size or content. Furthermore, AIPE with a potential of - 53.4 mV remained stable through spatial repulsion during sterilization. The encapsulation efficiency of AIPE was over 90% and the particle size was 106.8 ± 65.62 nm(0.286). Pharmacokinetic study in rats was comparable with that of CINVANTI which yielded a relative bioavailability of 114.31% indicating that the AIPE had similar pharmacokinetic processes in vivo with the analog of CINVANTI. The AUC0-t of the AIPE was 4.31-fold that of the APT soln.
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Egg yolk lecithins
Medium-chain glycerides
Soya lecithins
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

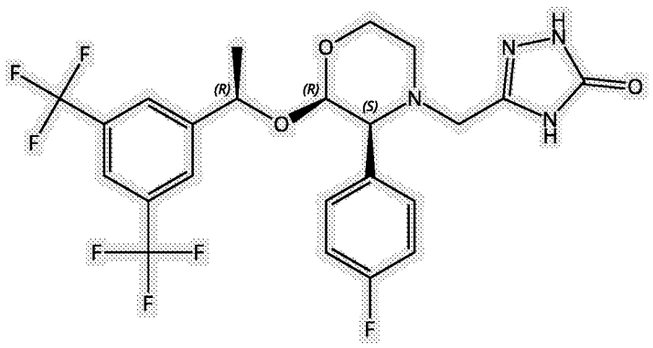
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

IT 170729-80-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

IT 170729-80-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion based on ion pairing/phospholipid complex for improving phys. and chem. stability during thermal sterilization)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN

ACCESSION NUMBER: 2020:456048 CAPLUS Full-text

DOCUMENT NUMBER: 177:51649

TITLE: Small scale design of experiment investigation of equilibrium solubility in simulated fasted and fed intestinal fluid

AUTHOR(S): McPherson, Stephanie; Perrier, Jeremy; Dunn, Claire; Khadra, Ibrahim; Davidson, Scott; Ainousah, Bayan; Wilson, Clive G.; Halbert, Gavin

CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK

SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (2020), 150, 14-23
CODEN: EJPBEL; ISSN: 0939-6411

DIGITAL OBJECT ID: 10.1016/j.ejpb.2020.01.016

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB It is widely recognized that drug soly. within the gastrointestinal tract (GIT) differs from values detd. in a simple aq. buffer and to circumvent this problem measurement in biorelevant fluids is detd. Biorelevant fluids are complex mixts. of components (sodium taurocholate, lecithin, sodium phosphate, sodium chloride, pancreatin and sodium oleate) at various concns. and pH levels to provide systems simulating fasted (FaSSIF) or fed (FeSSIF) intestinal media. Design of Expt. (DoE) studies have been applied to investigate FaSSIF and FeSSIF and indicate that a drugs equil. soly. varies over orders of magnitude, is influenced by the drug type and individual or combinations of media components, with some of

these interactions being drug specific. Although providing great detail on the drug media interactions these studies are resource intensive requiring up to ninety individual expts. for FeSSIF. In this paper a low sample no. or reduced DoE system has been investigated by restricting components with minimal soly. impact to a single value and only investigating variations in the concns. of sodium taurocholate, lecithin, sodium oleate, pH and addnl. in the case of fed media, monoglyceride. This reduces the expts. required to ten (FaSSIF) and nine (FeSSIF). Twelve poorly sol. drugs (Ibuprofen, Valsartan, Zafirlukast, Indomethacin, Fenofibrate, Felodipine, Probucol, Tadalafil, Carvedilol, Aprepitant, Bromocriptine and Itraconazole) were investigated and the results compared to published DoE studies and literature soly. values in human intestinal fluid (HIF), FaSSIF or FeSSIF. The soly. range detd. by the reduced DoE is statistically equiv. to the larger scale published DoE results in over eighty five percent of the cases. The reduced DoE range also covers HIF, FaSSIF or FeSSIF literature soly. values. In addn. the reduced DoE provides lowest measured soly. values that agree with the published DoE values in ninety percent of the cases. However, the reduced DoE only identified single and in some cases none of the major components influencing soly. in contrast to the larger published DoE studies which identified multiple individual components and component interactions. The identification of significant components within the reduced DoE was also dependent upon the drug and system under investigation. The study demonstrates that the lower exptl. no. reduces statistical power of the DoE to resolve the impact of media components on soly. However, in a situation where only the soly. range is required the reduced DoE can provide the desired information, which will be of benefit during in vitro development studies. Further refinements are possible to extend the reduced DoE protocol to improve biorelevance and application into areas such as PBPK modeling.

CC 63-5 (Pharmaceuticals)

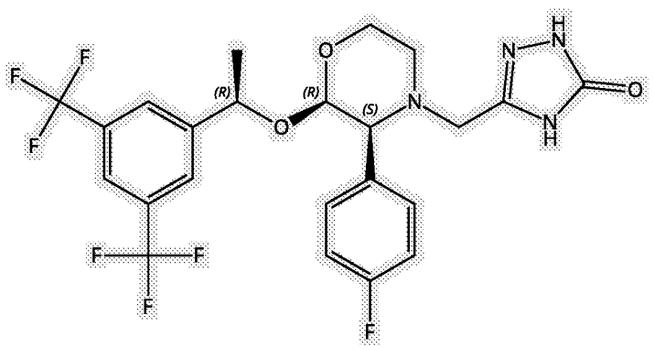
IT Lecithins
Monoglycerides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(small scale design of expt. investigation of equil. soly. in simulated fasted and fed intestinal fluid)

IT 53-86-1 143-19-1 145-42-6 15687-27-1 23288-49-5 25614-03-3 49562-28-9 72509-76-3 72956-09-3 84625-61-6 107753-78-6 137862-53-4 170729-80-3 171596-29-5
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale design of expt. investigation of equil. soly. in simulated fasted and fed intestinal fluid)

IT 170729-80-3
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small scale design of expt. investigation of equil. soly. in simulated fasted and fed intestinal fluid)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:418384 CAPLUS Full-text
DOCUMENT NUMBER: 172:285814
TITLE: Preparation of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents
INVENTOR(S): Martin, Brice; Mignet, Nathalie; Corvis, Yohann
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique (CNRS), Fr.; Universite Paris Descartes; Institut National de la Sante et de la Recherche Medicale (INSERM); Ecole Nat Superieure de Chimie Paris
SOURCE: PCT Int. Appl., 66pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2020043735	A1	20200305	WO 2019-EP72873	20190827
EP 3616688	A1	20200304	EP 2018-306138	20180827
EP 3843705	A1	20210707	EP 2019-756406	20190827
EP 3843705	B1	20231129		
EP 3843705	C0	20231129		
US 20210315831	A1	20211014	US 2021-17269802	20210219

PRIORITY APPLN. INFO.: EP 2018-306138 A 20180827
WO 2019-EP72873 W 20190827

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2020043735	A1	Dead	20230427
EP 3616688	A1	Dead	20210909
EP 3843705	A1	Indeterminate	20231130
EP 3843705	B1	Indeterminate	20231130
EP 3843705	C0	Alive	20240215
US 20210315831	A1	Alive	20211121

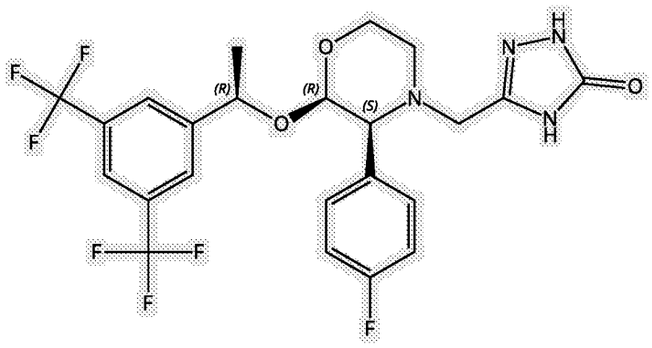
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention relates to a method for manufg. a nanostructured powder comprising nanocryst. agglomerates contg. active pharmaceutical ingredient (API) in its cryst. form, said method comprising (i) Prepg. a first soln. comprising API and an API solvent; (ii) Mixing the first soln. with a second soln. comprising an API antisolvent and optionally a stabilizing agent P1 to obtain a third mixt.; (iii) Evapg. the third mixt. until both the API solvent and the API antisolvent are evapd., advantageously under vacuum; characterized in that when the stabilizing agent P1 is present, the third mixt. has a stabilizing agent P1 to API wt. ratio equal or less than 5, preferably less than 2. The invention also concerns a nanostructured powder and a nanosuspension.
IPCI A61K0009-14 [I]; A61K0009-51 [I]; A61K0031-365 [I]; A61K0031-7048 [I]; A61P0035-00 [I]
IPCR A61K0009-14 [I]; A61K0009-51 [I]; A61K0031-365 [I]; A61K0031-7048 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Albumins
Asialofetuins
Egg yolk lecithins
Lecithins
Soya phosphatidylcholines
Transferrins
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents)
IT 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 50-24-8, Prednisolone 52-01-7, Spironolactone 53-86-1, Indometacin 61-68-7, Mefenamic acid 126-07-8, Griseofulvin 127-40-2, Lutein 137-66-6, Ascorbyl palmitate

153-18-4, Rutin 458-37-7, Curcumin 501-36-0, Resveratrol 520-33-2, Hesperetin 528-48-3, Fisetin 1198-77-2, Monosodium urate 1397-89-3, Amphotericin B 2030-63-9, Clofazimine 2608-24-4, Piposulfan 3681-99-0, Puerarin 7689-03-4, Camptothecin 10238-21-8, Glibenclamide 15307-86-5, Diclofenac acid 15687-27-1, Ibuprofen 17230-88-5, Danazol 19685-09-7, Hydroxycamptothecin 21967-41-9, Baicalin 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22888-70-6, Silybin 22916-47-8, Miconazole 23214-92-8, Doxorubicin 28957-04-2, Oridonin 29990-52-1, Methyltryptophan 31431-39-7, Mebendazole 33069-62-4, Paclitaxel 49562-28-9, Fenofibrate 54965-21-8, Albendazole 59865-13-3, Cyclosporine 63675-72-9, Nisoldipine 66085-59-4, Nimodipine 71125-38-7, Meloxicam 73590-58-6, Omeprazole 73963-72-1, Cilostazole 79902-63-9, Simvastatin 80841-47-0, Asulacrine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 88426-33-9, Buparvaquone 98093-93-7, Riccardin D 114977-28-5, Docetaxel 116122-36-2, Breviscapine 129722-12-9, Aripiprazole 141374-81-4, Tarazepide 145040-37-5, Candesartan cilexetil 146939-27-7, Ziprasidone 147362-57-0, Loviride 153559-49-0, Bexarotene 154598-52-4, Efavirenz 169590-42-5, Celecoxib 170729-80-3, Aprepitant 183133-96-2, Cabazitaxel 206361-99-1, Darunavir 330784-47-9, Avanafil 1257228-26-4, Amoitone B
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of nanosuspension comprising nanocrystals of active pharmaceutical ingredients with little or no stabilizing agents)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
EP 3616688 A1	EP 2018-306138	Register|Federated Reg.
EP 3843705 A1	EP 2019-756406	Register|Federated Reg.
EP 3843705 B1	EP 2019-756406	Register|Federated Reg.
EP 3843705 C0	EP 2019-756406	Register|Federated Reg.
US 20210315831 A1	US 2021-17269802	Register|Global Dossier
WO 2020043735 A1	WO 2019-EP72873	Register|Global Dossier

L4 ANSWER 16 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2020:245679 CAPLUS Full-text
DOCUMENT NUMBER: 172:258881
TITLE: Emulsion containing high proportion emulsifier and preparation method thereof

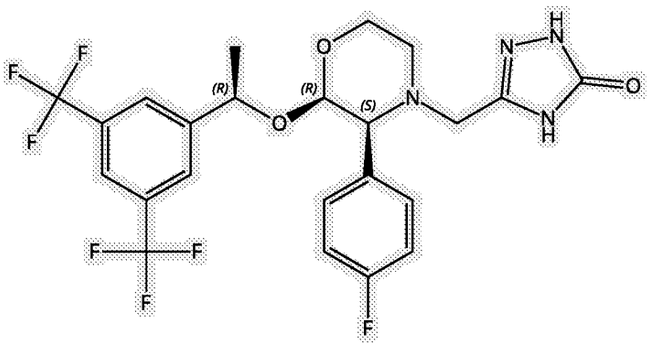
INVENTOR(S): Niu, Yawei; Xu, Wendong; Tang, Shunzhi; Yuan, Cheng; Fu, Yuping; Guan, Weijian; Wang, Guocai; Mou, Xiaonan; Li, Jirong; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 110772482	A	20200211	CN 2019-11215436	20191202

PRIORITY APPLN. INFO.: CN 2019-11215436 20191202
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 110772482	A	Dead	20230511

AB The invention discloses an emulsion contg. high proportion emulsifier and prepn. method thereof, which has the advantages of high drug loading and high bioavailability. The emulsion contg. high proportion emulsifier comprises the following raw materials in percentage by wt.: oil phase solvent 10-30%, emulsifier 10-30%, co-emulsifier 1-5%, volatile assistant 1-5%, stabilizer 0.05-0.6%, isoosmotic adjusting agent 1-5%, viscosity regulator 1-10%, active pharmaceutical ingredient 1-5%, and the balance of injection water.
IPCI A61K0009-107; A61K0047-26; A61K0047-44; A61K0047-14; A61K0047-10; A61K0031-5377
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-10 [I]; A61K0047-14 [I]; A61K0047-26 [I]; A61K0047-44 [I]
CC 63-7 (Pharmaceuticals)
IT Carbohydrates
Castor oil
Egg yolk lecithins
Fish oil
Fructooligosaccharides
Olive oil
Phosphatidylcholines
Phosphatidylglycerols
Soya lecithins
Soybean oil
Triglycerides
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 170729-80-3, Aprepitant 552292-08-7, Rolapitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion contg. high proportion emulsifier and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 110772482 A	CN 2019-11215436	Register|Global Dossier

L4 ANSWER 17 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:1744396 CAPLUS Full-text
DOCUMENT NUMBER: 171:388517
TITLE: Aqueous formulations for insoluble drugs
INVENTOR(S): Chen, Andrew Xian; Islam, Mohammad Saiful; Chu, Jan-Jon; Xu, Jianmin
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2019173526	A1	20190912	WO 2019-US21029	20190306
CA 3088017	A1	20190912	CA 2019-3088017	20190306
AU 2019231699	A1	20200716	AU 2019-231699	20190306
AU 2019231699	B2	20230309		
CN 111867562	A	20201030	CN 2019-80017435	20190306
CN 111867562	B	20230707		
EP 3761961	A1	20210113	EP 2019-764228	20190306
JP 2021515048	T	20210617	JP 2020-570411	20190306
US 20200368159	A1	20201126	US 2020-16993017	20200813
US 11541006	B2	20230103		

PRIORITY APPLN. INFO.: US 2018-62639710 P 20180307
WO 2019-US21029 W 20190306

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2019173526	A1	Dead	20221110
CA 3088017	A1	Alive	20201121
AU 2019231699	A1	Alive	20201121
AU 2019231699	B2	Alive	20230316
CN 111867562	A	Alive	20201120
CN 111867562	B	Alive	20230720
EP 3761961	A1	Alive	20210118
JP 2021515048	T	Alive	20210624
US 20200368159	A1	Alive	20221020
US 11541006	B2	Alive	20230119

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2019:1744396
AB This invention relates to clear one-phase liq. formulation vehicles

comprising lecithin , MCT, bile salt and water. In an aspect, this invention provides a clear and one-phase aq. liq. compn. comprising: a lecithin , MCT, bile salt, and water, in a four-component LMBW compn., their prepn. and applications in drug formulations.

IPCI A61K0009-08 [I]; A61K0009-00 [I]; A61K0047-14 [I]; A61K0047-54 [I]

IPCR A61K0009-08 [I]; A61K0009-00 [I]; A61K0047-14 [I]; A61K0047-54 [I]

CC 63-6 (Pharmaceuticals)

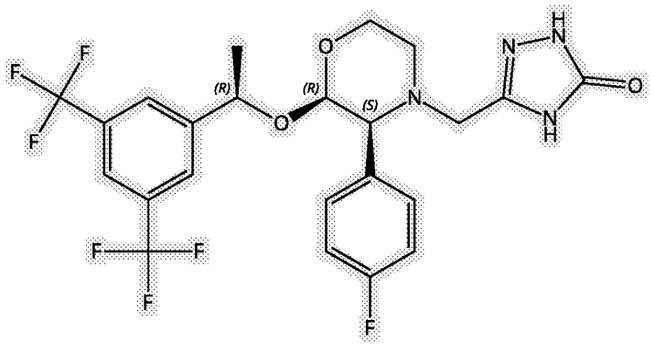
IT Bile salts
Egg yolk lecithins
Lecithins
Medium-chain glycerides
Polyoxyalkylenes
Sesame oil
Soya phosphatidylcholines
Soybean oil
Tocopherols
RL: MOA (Modifier or additive use); USES (Uses)
(aq. formulations for insol. drugs)

IT 52-21-1, Prednisolone Acetate 57-83-0, Progesterone, biological studies 59-92-7, Levodopa, biological studies 60-18-4, L-Tyrosine, biological studies 84-80-0, Phytonadione 501-36-0, Resveratrol 1951-25-3, Amiodarone 2078-54-8, Propofol 7553-56-2, Iodine, biological studies 7689-03-4, Camptothecin 12633-72-6, Amphotericin 15687-27-1, Ibuprofen 33069-62-4, Paclitaxel 59865-13-3, Cyclosporine 81103-11-9, Clarithromycin 84625-61-6, Itraconazole 100286-90-6, Irinotecan hydrochloride 169590-42-5, Celecoxib 170729-80-3, Aprepitant 171228-49-2, Posaconazole
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aq. formulations for insol. drugs)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aq. formulations for insol. drugs)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2019231699 A1	AU 2019-231699	Register
AU 2019231699 B2	AU 2019-231699	Register
CA 3088017 A1	CA 2019-3088017	Register
CN 111867562 A	CN 2019-80017435	Register|Global Dossier
CN 111867562 B	CN 2019-80017435	Register|Global Dossier
EP 3761961 A1	EP 2019-764228	Register|Federated Reg.
JP 2021515048 T	JP 2020-570411	Register|Global Dossier
US 11541006 B2	US 2020-16993017	Register|Global Dossier

US 20200368159 A1 US 2020-16993017 Register|Global Dossier
WO 2019173526 A1 WO 2019-US21029 Register|Global Dossier

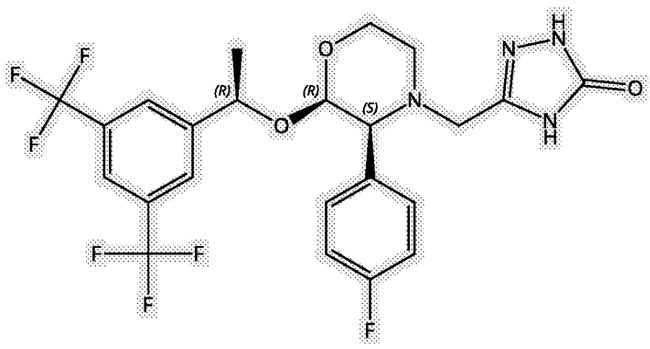
L4 ANSWER 18 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:1475315 CAPLUS Full-text
DOCUMENT NUMBER: 171:221789
TITLE: Method of administering emulsion formulations of an NK-1 receptor antagonist
INVENTOR(S): Ottoboni, Thomas B.; Quart, Barry D.
PATENT ASSIGNEE(S): Heron Therapeutics, Inc., USA
ULTIMATE OWNER: HERON THERAPEUTICS, INC.
ULTIMATE OWNER STANDARD: HERON THERAPEUTICS, INC.
SOURCE: U.S. Pat. Appl. Publ., 23pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20190231688	A1	20190801	US 2019-16261459		20190129
WO 2019152430	A1	20190808	WO 2019-US15708		20190129
AU 2019214872	A1	20200806	AU 2019-214872		20190129
EP 3746051	A1	20201209	EP 2019-705044		20190129
JP 2021512091	T	20210513	JP 2020-541556		20190129
PRIORITY APPLN. INFO.:			US 2018-62624050	P	20180130
			WO 2019-US15708	W	20190129

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20190231688	A1	Alive	20230914
WO 2019152430	A1	Dead	20220929
AU 2019214872	A1	Dead	20230803
EP 3746051	A1	Dead	20211117
JP 2021512091	T	Alive	20210520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2019:1475315
AB Disclosed herein are methods of administering pharmaceutical formulations of a neurokinin-1 (NK-1) receptor antagonist to a subject in need of treatment of emesis.
IPCI A61K0009-107 [I]; A61K0031-5377 [I]; A61K0009-00 [I]; A61K0047-24 [I]; A61K0031-573 [I]; A61K0047-44 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-26 [I]; A61K0031-496 [I]
IPCR A61K0009-107 [I]; A61K0009-00 [I]; A61K0031-496 [I]; A61K0031-5377 [I]; A61K0031-573 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
IT Alcohols
Egg yolk lecithins
Phospholipids
Soybean oil
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor antagonist)
IT 2392-39-4, Dexamethasone sodium phosphate 147116-64-1, Ezlopitant 147116-67-4, Maropitant 170729-80-3, Aprepitant 290296-68-3, Befetupitant 290297-26-6, Netupitant 334476-46-9, Vestipitant 414910-27-3, Casopitant 552292-08-7, Rolapitant 579475-18-6, Orvepitant 860642-69-9, Ser-lopitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor antagonist)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of administering emulsion formulations of NK-1 receptor antagonist)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2019214872 A1	AU 2019-214872	Register
EP 3746051 A1	EP 2019-705044	Register|Federated Reg.
JP 2021512091 T	JP 2020-541556	Register|Global Dossier
US 20190231688 A1	US 2019-16261459	Register|Global Dossier
WO 2019152430 A1	WO 2019-US15708	Register|Global Dossier

L4 ANSWER 19 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:425605 CAPLUS Full-text
DOCUMENT NUMBER: 170:406568
TITLE: Aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its preparation method and application
INVENTOR(S): Xu, Wendong; Tang, Shunzhi; Yuan, Cheng; Niu, Yawei; Fu, Yuping; Wang, Guocai; Guan, Weijian; Mou, Xiaonan; He, Jie; Li, Jirong; Yang, Yuqiong; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109432002	A	20190308	CN 2018-11587906	20181225

PRIORITY APPLN. INFO.: CN 2018-11587906 20181225
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109432002	A	Dead	20220825

OTHER SOURCE(S): CASFORMULTNS 2019:425605
AB An aprepitant emulsion useful for reducing nausea and vomiting in the pre and post-chemotherapy of the tumor, improving immunity and nutritional support of the tumor patient, and reducing acute and delayed nausea and vomiting in high-dose cisplatin combined with high-dose sensitized cancer chemotherapy is provided. The aprepitant emulsion comprises the following components in mass %: 0.05-2.5 of aprepitant, 10-30 of oil phase solvent, 0.8-18 of emulsifier, 0.03-0.6 of stabilizer, 1-5 of isotonicity regulator, and further comprising a pH regulator, balance being purified water, where the pH of the emulsion is 5.5-8. The prepn. method comprises the following steps: (1) weighing the oil phase solvent, emulsifier and antioxidant, heating in a water bath, dissolving all the emulsifiers, and adding aprepitant and dissolving well to obtain an oil phase; (2) weighing

stabilizer, isotonicity regulator, pH regulator, adding to purified water, and heating in water bath to obtain water phase; (3) slowly adding the oil phase to the water phase, shearing at high speed under stirring, adding the remaining purified water with high speed stirring to obtain colostrum; (4) subjecting obtained colostrum to microfluidization to obtain a final emulsion; and (5) filling the colostrum with nitrogen, sealing and sterilizing in a rotary sterilizing pot to obtain an aprepitant emulsion.

IPCI A61K0009-107; A61K0031-5377; A23L0033-10; A23P0010-00; A61P0001-08; A61P0035-00

IPCR A61K0009-107 [I]; A23L0033-10 [I]; A23P0010-00 [I]; A61K0031-5377 [I]; A61P0001-08 [I]; A61P0035-00 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

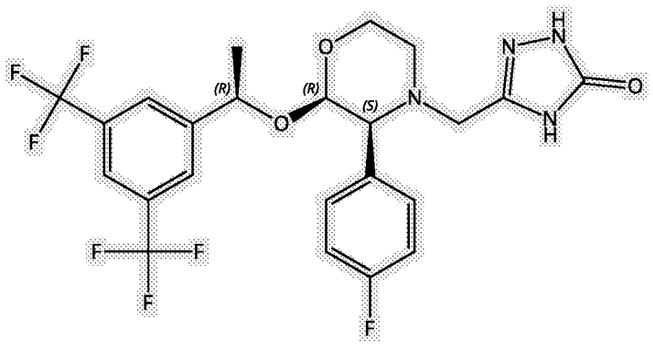
IT Egg yolk lecithins
Fatty acids
Phosphatidylcholines
Phosphatidylglycerols
Soya lecithins
Tocopherols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT 50-99-7, D-Glucose, biological studies 56-81-5, Glycerin, biological studies 69-65-8, D-Mannitol 112-80-1, Oleic acid, biological studies 143-19-1, Sodium oleate 7631-90-5, Sodium bisulfite 7647-14-5, Sodium chloride, biological studies 7681-57-4, Sodium metabisulfite 7772-98-7, Sodium thiosulfate 9005-65-6, Polysorbate 80 106392-12-5, Poloxamer 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant emulsion for treating nausea and vomiting after chemotherapy in tumor patient, and its prepn. method and application)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109432002 A	CN 2018-11587906	Register|Global Dossier

L4 ANSWER 20 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2019:340286 CAPLUS Full-text
DOCUMENT NUMBER: 170:348016
TITLE: Aprepitant intravenous emulsion for treating chemotherapy-induced nausea and vomiting, and its

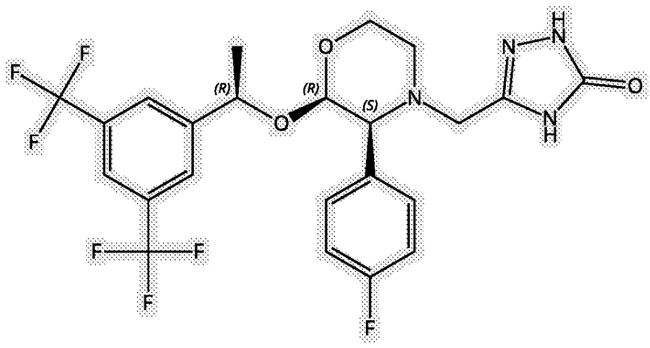
preparation method
INVENTOR(S): Yuan, Cheng; Xu, Wendong; Tang, Shunzhi; He, Jie; Niu, Yawei; Fu, Yuping; Wang, Guocai; Guan, Weijian; Mou, Xiaonan; Li, Yao
PATENT ASSIGNEE(S): Guangzhou Baiyunshan Hanfang Pharmaceutical Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: GUANGZHOU BAIYUNSHAN PHARMACEUTICAL HOLDINGS CO., LTD.
ULTIMATE OWNER STANDARD: Guangzhou Baiyunshan Pharma
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109364023	A	20190222	CN 2018-11588409	20181225

PRIORITY APPLN. INFO.: CN 2018-11588409 20181225
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109364023	A	Transitional	20240222

OTHER SOURCE(S): CASFORMULTNS 2019:340286
AB The present invention relates to an i.v. emulsion contg. the following components by mass percentage: 0.05-3% of aprepitant, 5-30% of oil phase solvent, 1.2-18% of emulsifier, 0.03-0.6% of stabilizer, 1-5% of isotonicity adjusting agent, and 0.02-0.5% of antioxidant. The i.v. emulsion further contains a pH adjusting agent and water for injection, where the pH of the i.v. emulsion is 5.5-8.0. The i.v. emulsion has greatly improved the clin. safety, and is utilized for treating acute and delayed nausea and vomiting caused by high-dose cisplatin combined with high-dose sensitizing cancer chemotherapy and reducing nausea and vomiting in the early and middle stages of tumor chemotherapy.
IPCI A61K0009-107; A61K0047-24; A61K0047-12; A61K0031-5377; A61P0035-00; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0035-00 [I]
CC 63-6 (Pharmaceuticals)
IT Castor oil
Egg yolk lecithins
Fish oil
Olive oil
Phosphatidylcholines
Phosphatidylglycerols
Soya phospholipids
Soybean oil
Teaseed oil
Tocopherols
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant i.v. emulsion for treating chemotherapy-induced nausea and vomiting, and its prepn. method)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109364023 A	CN 2018-11588409	Register|Global Dossier

L4 ANSWER 21 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:2521745 CAPLUS Full-text
DOCUMENT NUMBER: 170:140265
TITLE: High stability aprepitant nano-emulsion and preparation method thereof
INVENTOR(S): Fu, Jifeng; Wang, Wenjuan; Guo, Jia; Zhang, Liancheng
PATENT ASSIGNEE(S): Beijing Ruiyue Biomedical Technology Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: BEIJING RUIYUE BIOLOGY MEDICAL TECH
ULTIMATE OWNER STANDARD: BEIJING RUIYUE BIOLOGY MEDICAL TECH
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

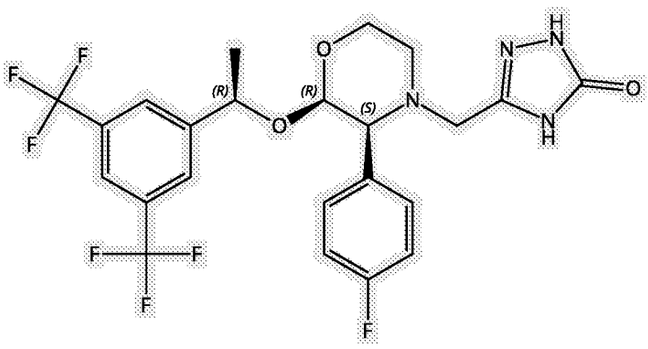
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109010272	A	20181218	CN 2018-11133738	20180927

PRIORITY APPLN. INFO.: CN 2018-11133738 20180927
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109010272	A	Dead	20230323

OTHER SOURCE(S): CASFORMULTNS 2018:2521745
AB The invention discloses a nano-emulsion of aprepitant as shown in structure I and prepn. method thereof. The nano-emulsion is prepd. with the following components in percentage by wt.: aprepitant 0.05-1.5%, soybean oil 2-20%, egg yolk lecithin 5-20%, ethanol 0.5-5%, sodium oleate 0.05-2%, sucrose 2-10%, and water for injection 40-80%. The sodium oleate is added into the oil phase to rapidly stabilize the oil droplets when contacts with the aq. phase, thereby increasing the stability of the nano-emulsion.
IPCI A61K0009-107; A61K0047-12; A61K0047-44; A61K0047-24; A61K0047-10; A61K0047-26; A61K0031-5377; A61P0001-08
IPCR A61K0009-107 [I]; A61K0031-5377 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
Soybean oil
RL: MOA (Modifier or additive use); NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)
IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(High stability aprepitant nano-emulsion and prepn. method thereof)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109010272 A	CN 2018-11133738	Register|Global Dossier

L4 ANSWER 22 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:2521716 CAPLUS Full-text
DOCUMENT NUMBER: 170:154781
TITLE: Fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting
INVENTOR(S): Liu, Jie; Liu, Yun; Zhou, Lili
PATENT ASSIGNEE(S): Fubicheng (Shanghai) Pharmaceutical Technology Co., Ltd., Peop. Rep. China
ULTIMATE OWNER: FUBICHENG SHANGHAI MEDICINE TECH
ULTIMATE OWNER STANDARD: FUBICHENG SHANGHAI MEDICINE TECH
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

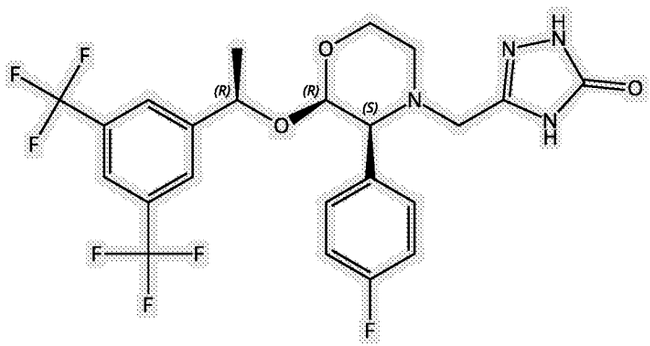
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 109010269	A	20181218	CN 2018-10979074	20180827
CN 109010269	B	20210420		
PRIORITY APPLN. INFO.:			CN 2018-10979074	20180827

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 109010269	A	Alive	20201121
CN 109010269	B	Alive	20210430

OTHER SOURCE(S): CASFORMULTNS 2018:2521716
AB The title fat emulsion injection of aprepitant for treating chemotherapy-induced nausea and vomiting is prepd. from aprepitant, egg yolk lecithin , oil for injection (coconut oil, soybean oil, or olive oil), glycine, polyvinylpyrrolidone, water for injection, sodium oleate, and C1-5 short-chain alc. (ethanol or propanediol). The inventive prepn. has improved stability and reduced vascular irritation.

IPCI A61K0009-107; A61K0031-5377; A61K0047-18; A61K0047-32; A61K0031-439;
A61K0009-08; A61P0001-08
IPCR A61K0009-107 [I]; A61K0009-08 [I]; A61K0031-439 [I]; A61K0031-5377 [I];
A61K0047-18 [I]; A61K0047-32 [I]; A61P0001-08 [I]
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Lipoid E 80; fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat emulsion injection of aprepitant with improved stability for treating chemotherapy-induced nausea and vomiting)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 109010269 A	CN 2018-10979074	Register|Global Dossier
CN 109010269 B	CN 2018-10979074	Register|Global Dossier

L4 ANSWER 23 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2018:1210583 CAPLUS Full-text
DOCUMENT NUMBER: 169:118657
TITLE: Novel formulations of aprepitant
INVENTOR(S): Titley, Paul Charlton
PATENT ASSIGNEE(S): N4 Pharma UK Limited, UK
ULTIMATE OWNER: N4 PHARMA UK; N4 PHARMA
ULTIMATE OWNER STANDARD: N4 PHARMA UK; N4 PHARMA
SOURCE: PCT Int. Appl., 85pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2018115888	A1	20180628	WO 2017-GB53864		20171221
PRIORITY APPLN. INFO.:			GB 2016-21867	A	20161221
			GB 2017-16293	A	20171005

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE

WO 2018115888	A1	Dead		20210826

OTHER SOURCE(S): CASFORMULTNS 2018:1210583

AB The invention provides a pharmaceutical compn. which comprises: a first fraction comprising aprepitant; and a controlled-release fraction comprising aprepitant.

IPCI A61K0009-20 [I]; A61K0009-24 [I]; A61K0031-00 [I]

IPCR A61K0009-20 [I]; A61K0009-24 [I]; A61K0031-00 [I]

CC 63-1 (Pharmaceuticals)

IT Acrylic polymers
Activated charcoal
Alkali metal bicarbonates
Alkali metal carbonates
Carnauba wax
Fatty acids
Gelatins
Hydrogenated vegetable oils
Lecithins
Paraffin waxes
Polyoxyalkylenes
Polysaccharides
Shellac
Silica gel
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel formulations of aprepitant)

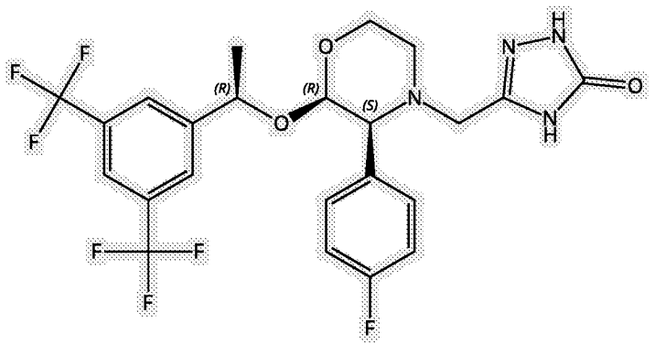
IT 50-02-2, Dexamethasone 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-35-1, Synovir 50-44-2, Mercaptopurine 50-69-1, Ribose 50-76-0, Dactinomycin 52-24-4, Thiotepa 53-03-2, Prednisone 55-86-7, Mechlorethamine hydrochloride 56-40-6, Glycine, biological studies 57-11-4, Stearic acid, biological studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-88-5, Cholesterol, biological studies 59-23-4, Galactose, biological studies 61-90-5, Leucine, biological studies 63-42-3, Lactose 67-68-5, Sclerosol, biological studies 69-65-8, Mannitol 69-79-4, Maltose 70-00-8, Trifluridine 77-92-9, Citric acid, biological studies 79-41-4, biological studies 106-60-5, Aminolevulinic acid 112-92-5, Stearyl alcohol 127-07-1, Hydrea 134-62-3, OFF 143-67-9, Vinblastine sulfate 144-55-8, Sodium bicarbonate, biological studies 147-81-9, Arabinose 148-82-3, Alkeran 151-21-3, Sodium lauryl sulphate, biological studies 154-42-7, Tabloid 154-93-8, Carmustine 305-03-3, Ambochlorin 320-67-2, Azacitidine 366-70-1, Procarbazine hydrochloride 555-44-2, Glyceryl tripalmitate 557-04-0, Magnesium stearate 585-88-6, Maltitol 595-33-5, Megestrol acetate 1323-83-7, Glyceryl distearate 1327-43-1, Aluminum Magnesium silicon oxide 1327-53-3, Arsenic Trioxide 1492-18-8, Leucovorin calcium 2068-78-2, Vincristine sulfate 2068-78-2D, Vincristine sulfate, liposomes 2353-33-5, Dacogen 2921-88-2, Cyfos 3543-75-7, Treanda 4105-38-8, Uridine triacetate 4342-03-4, Dacarbazine 7447-40-7, Potassium chloride, biological studies 7447-41-8, Lithium chloride, biological studies 7487-88-9, Magnesium sulphate, biological studies 7631-86-9, Silica, biological studies 7647-14-5, Sodium chloride, biological studies 7757-82-6, Sodium sulphate, biological studies 7778-80-5, Potassium sulphate, biological studies 7786-30-3, Magnesium chloride, biological studies 9000-30-0, Guar gum 9000-69-5, Pectin 9000-92-4, Amylase 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Carboxymethylcellulose 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, ethers 9004-35-7 9004-38-0, Cellulose acetate phthalate 9004-57-3, Ethyl cellulose 9004-62-0, Hydroxyethylcellulose 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9004-67-5, Methylcellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-38-3, Sodium alginate 9032-42-2, Hydroxyethyl-methylcellulose 9050-04-8 9050-31-1, Hydroxypropylmethylcellulose phthalate 9063-38-1, Sodium starch glycolate 10377-48-7, Lithium sulphate 11056-06-7, Bleomycin 11138-66-2, Xanthan gum 13010-47-4, Lomustine 13311-84-7, Flutamide 14807-96-6, Talc, biological studies 18641-57-1 19171-19-8, Pomalidomide 19767-45-4, Mesna 20830-81-3, Rubidomycin 23214-92-8, Doxil 24584-09-6, Totect 25086-15-1, Methacrylic acid-methyl methacrylate co-polymer 25212-88-8, Methacrylic acid-ethyl acrylate copolymer 25316-40-9, Doxorubicin hydrochloride 25322-68-3, Polyethylene glycol 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26833-87-4, Omacetaxine mepesuccinate 31566-31-1, Glyceryl monostearate 33419-42-0, Etoposide 37380-42-0, Amberlite XAD

4 37380-43-1, Amberlite XAD 7 41575-94-4, Carboplatin 50935-57-4, Methyl vinyl ether-maleic acid copolymer ethyl ester 53237-50-6 54182-62-6, Polacrilin potassium 54578-91-5, Methyl vinyl ether-maleic acid copolymer butyl ester 56038-13-2, Sucralose 56390-09-1, Ellence 57248-88-1, Aredia 57852-57-0, Idamycin 61825-94-3, Eloxatin 64519-82-0, Isomalt 70476-82-3, Mitoxantrone hydrochloride 70535-77-2, Hydroxypropylmethylcellulose acetate succinate 74381-53-6, Leuprolide acetate 74811-65-7, Croscarmellose sodium 75607-67-9, Fludara 82640-04-8, Evista 83712-60-1, Defibrotide Sodium 84449-90-1, Keoxifene 85622-93-1, Methazolastone 89778-26-7, Fareston 90357-06-5, Bicalutamide 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 98530-12-2, Interferon Alfa-2b 99011-02-6, Aldara 99614-01-4, Ondansetron hydrochloride 100286-90-6, Camptosar 100286-90-6D, Irinotecan hydrochloride, liposomes 104219-63-8, Amberlite XAD 16 108736-35-2, Somatuline Depot 110942-02-4, Aldesleukin 112809-51-5, Femara 114899-77-3, Trabectedin 114977-28-5, Docetaxel 117091-64-2, Etopophos 118072-93-8, Zoledronic acid 119413-54-6, Hycamtin 120511-73-1, Anastrozole 121181-53-1, Filgrastim 122111-03-9, Gemcitabine hydrochloride 122312-54-3 123119-31-3 123318-82-1, Clofarabine 125317-39-7, Navelbine 127984-74-1, Lanreotide acetate 128517-07-7, Istodax 129453-61-8, Faslodex 130167-69-0, Oncaspar 134774-45-1, Elitek 135729-62-3, Palonosetron hydrochloride 145781-92-6, Goserelin acetate 146464-95-1, Folotyn 148618-33-1, Ambersorb 572 148879-45-2, Ambersorb 563 149003-01-0, Dexrazoxane hydrochloride 149647-78-9, Vorinostat 150399-23-8, Alimta 153559-49-0, Bexarotene 154229-18-2, Abiraterone Acetate 154361-50-9, Capecitabine 159351-69-6, Everolimus 162394-19-6, Kepivance 162635-04-3, Temsirolimus 170729-80-3, Aprepitant 173146-27-5, Denileukin Diftitox 179324-69-7, Bortezomib 180288-69-1, Herceptin 183133-96-2, Cabazitaxel 183204-72-0, Tipiracil hydrochloride 183319-69-9, Erlotinib hydrochloride 184475-35-2, Gefitinib 191732-72-6, Lenalidomide 192391-48-3, Bexxar 205923-56-4, Cetuximab 206181-63-7, Ibritumomab Tiuxetan 208921-02-2, Tositumomab 208921-02-2D, Tositumomab, Iodine I-131 214766-78-6, Degarelix 215647-85-1, Peginterferon Alfa-2b 216503-57-0, Alemtuzumab 216974-75-3, Avastin 219989-84-1, Ixabepilone 220127-57-1, Gleevec 220578-59-6, Gemtuzumab 290297-26-6, Akynzeo 302962-49-8, Dasatinib 319460-85-0, Axitinib 339177-26-3, Panitumumab 341031-54-7, Sunitinib malate 380610-27-5, Perjeta 380843-75-4, Bosulif 388082-77-7, Lapatinib ditosylate 400046-53-9, Ozogamicin 404950-80-7, Farydak 417716-92-8, Lenvima 441045-17-6, Eribulin mesylate 443913-73-3, Vandetanib 477202-00-9, Ipilimumab 496775-62-3, Eltrombopag Olamine 541502-14-1, Siltuximab 571190-30-2, Ibrance 615258-40-7, Denosumab 635702-64-6, Pazopanib hydrochloride 641571-10-0, Nilotinib 679818-59-8, Arzerra 733030-01-8, Lonsurf 755037-03-7, Regorafenib 763113-22-0, Lynparza 843613-19-4, Ambersorb 348F 849217-68-1, Cabometyx 850140-72-6, Gilotrif 850140-73-7, Afatinib dimaleate 853426-35-4, Blinatumomab 857890-39-2, Lenvatinib mesylate 858102-79-1, Rolapitant hydrochloride 866323-14-0, Beleodaq 868540-17-4, Carfilzomib 870281-82-6, Idelalisib 871700-17-3, Mekinist 877399-52-5, Crizotinib 879085-55-9, Erivedge 906805-06-9, Necitumumab 910046-32-1, Gardasil 912337-47-4, Cervarix 914088-09-8, Adcetris 915087-33-1, Enzalutamide 915296-00-3, Elotuzumab 917381-47-6, Provenge 918504-65-1, Vemurafenib 930113-49-8, CAPOX
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel formulations of aprepitant)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel formulations of aprepitant)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
WO 2018115888 A1	WO 2017-GB53864	Register|Global Dossier

L4 ANSWER 24 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2017:1728289 CAPLUS Full-text
DOCUMENT NUMBER: 168:9512
TITLE: Nanocrystal composition for improving oral absorption of insoluble drug
INVENTOR(S): Liu, Yan; Li, Xueping; Li, Xinru; Zhou, Yanxia
PATENT ASSIGNEE(S): Peking University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

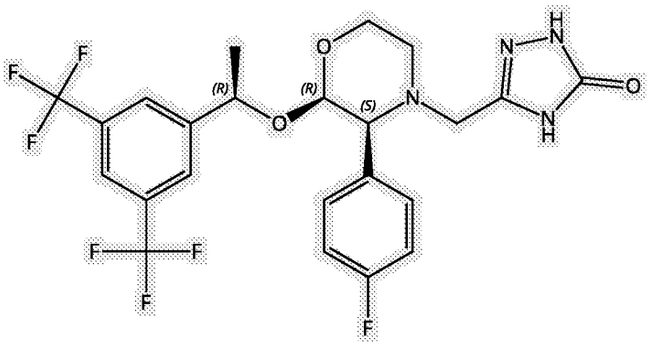
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 107303272	A	20171031	CN 2016-10239333	20160418

PRIORITY APPLN. INFO.: CN 2016-10239333 20160418
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 107303272	A	Dead	20220527

OTHER SOURCE(S): CASFORMULTNS 2017:1728289
AB The title compn. is composed of an insol. drug, a stabilizer, the ligand of the specific receptor expressed by intestinal epithelial cell and/or substrate of transporter and optional pharmaceutically acceptable auxiliary, and is prepd. by prepg. into a suspension and lyophilizing. The expt. proves that the compn. can remarkably improve the oral absorption of the insol. drug so as to provide the prepn. strategy for insol. drug oral administration.
IPCI A61K0009-10; A61K0009-19; A61K0047-10; A61K0047-42; A61K0047-22; A61K0047-26; A61K0047-18; A61K0047-24; A61K0047-38; A61K0047-32; A61K0031-4745; A61K0031-337; A61K0031-7048; A61K0031-436; A61K0031-5377; A61K0031-357
IPCR A61K0009-10 [I]; A61K0009-19 [I]; A61K0031-337 [I]; A61K0031-357 [I]; A61K0031-436 [I]; A61K0031-4745 [I]; A61K0031-5377 [I]; A61K0031-7048 [I]; A61K0047-10 [I]; A61K0047-18 [I]; A61K0047-22 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-32 [I]; A61K0047-38 [I]; A61K0047-42 [I]
CC 63-6 (Pharmaceuticals)
IT Amino acids
Dipeptides
Ethoxylated hydrogenated castor oil
Lecithins
Polyoxyalkylenes
Soya phospholipids
Transferrins

Tripeptides
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanocrystal compn. for improving oral absorption of insol. drug)
IT 50-02-2, Dexamethasone 50-04-4, Cortisone acetate 426-13-1, Fluorometholone 458-37-7, Curcumin 15687-27-1, Ibuprofen 19685-09-7, 10-Hydroxycamptothecin 22888-70-6, Silibinin 25316-40-9, Adriamycin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34368-04-2, Dobutamine 35354-74-6, Honokiol 49562-28-9, Fenofibrate 51333-22-3, Budesonide 59865-13-3, Cyclosporin A 65666-07-1, Silymarin 80474-14-2, Fluticasone propionate 84625-61-6, Itraconazole 91421-42-0, 9-Nitrocamptothecin 104987-11-3, Tacrolimus 114977-28-5, Docetaxel 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanocrystal compn. for improving oral absorption of insol. drug)
IT 170729-80-3, Aprepitant
RL: NANO (Nanomaterial); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanocrystal compn. for improving oral absorption of insol. drug)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 107303272 A	CN 2016-10239333	Register|Global Dossier

L4 ANSWER 25 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2017:1554024 CAPLUS Full-text
DOCUMENT NUMBER: 168:18112
TITLE: Biorelevant Drug Solubility Enhancement Modeled by a Linear Solvation Energy Relationship
AUTHOR(S): Niederquell, Andreas; Kuentz, Martin
CORPORATE SOURCE: Institute of Pharma Technology, University of Applied Sciences and Arts Northwestern Switzerland, Muttenz, 4132, Switz.
SOURCE: Journal of Pharmaceutical Sciences (Philadelphia, PA, United States) (2018), 107(1), 503-506
CODEN: JPMSAE; ISSN: 0022-3549
DIGITAL OBJECT ID: 10.1016/j.xphs.2017.08.017
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB It is for the pharmaceutical sciences of vital importance to understand how drugs are solubilized in biorelevant media. However, the complexity

of fasted state simulated intestinal fluid (FaSSIF) has so far hampered adequate soly. modeling. The present study focuses on apparently neutral compds. at physiol. pH and a linear free energy relationship is introduced for biorelevant drug solubilization. Based on literature data of 40 compds., the Abraham solvation descriptors were calcd. from chem. structure to then predict the ratio of soly. enhancement log(SE) in FaSSIF compared to aq. buffer soly. at pH 6.5. A suitable model was obtained with R2 of 0.810 and notable were esp. the pos. effect of McGowan's characteristic vol. and the neg. effect of drug basicity. A neg. influence on log(SE) was further evidenced for dipolarity/polarizability and for the excess molar refraction descriptor. A pos. solubilization effect was obtained for drug acidity and hence the tendency for proton donation, which was likely due to the different proton-accepting moieties of taurocholic acid and lecithin that are both present in the mixed colloids of FaSSIF. Overall, an improved understanding was achieved regarding the mol. features that are driving drug solubilization in biorelevant media.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

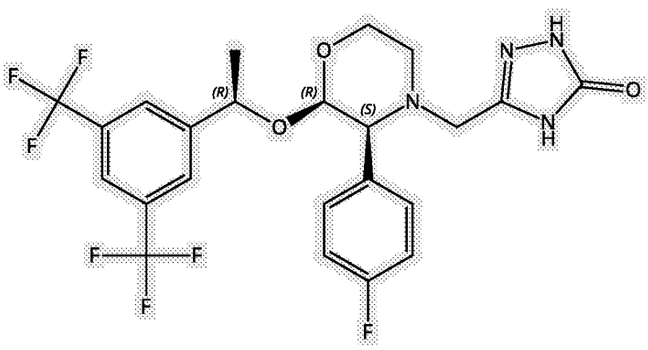
IT Lecithins
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biorelevant drug soly. enhancement modeled by a linear solvation energy relationship)

IT 50-02-2, Dexamethasone 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies 52-01-7, Spironolactone 53-03-2, Prednisone 53-16-7, Estrone, biological studies 57-41-0, Phenytoin 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 58-32-2, Dipyridamole 58-94-6, Chlorothiazide 81-24-3, Taurocholic acid 81-81-2, Warfarin 84-17-3, Dienestrol 126-07-8, Griseofulvin 298-46-4, Carbamazepine 439-14-5, Diazepam 846-49-1, Lorazepam 17230-88-5 23288-49-5, Probucol 39562-70-4, Nitrendipine 49562-28-9, Fenofibrate 51803-78-2, Nimesulide 54965-21-8, Albendazole 55268-74-1 59865-13-3, Cyclosporine 65646-68-6, Fenretinide 70288-86-7, Ivermectin 72509-76-3 73963-72-1, Cilostazole 75330-75-5, Lovastatin 95233-18-4, Atovaquone 103577-45-3, Lansoprazole 124423-84-3, Panadiplon 138402-11-6 154598-52-4 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 170729-80-3, Aprepitant 192725-17-0, Lopinavir 262352-17-0, Torcetrapib
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biorelevant drug soly. enhancement modeled by a linear solvation energy relationship)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biorelevant drug soly. enhancement modeled by a linear solvation energy relationship)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)

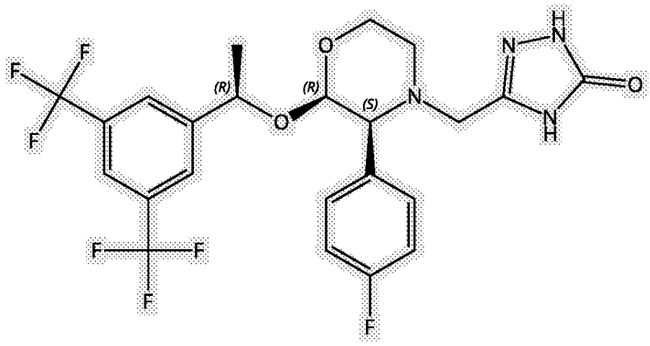


Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2017:1232902 CAPLUS Full-text
DOCUMENT NUMBER: 167:591636
TITLE: Influence of Physiological Gastrointestinal Surfactant Ratio on the Equilibrium Solubility of BCS Class II Drugs Investigated Using a Four Component Mixture Design
AUTHOR(S): Zhou, Zhou; Dunn, Claire; Khadra, Ibrahim; Wilson, Clive G.; Halbert, Gavin W.
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK
SOURCE: Molecular Pharmaceutics (2017), 14(12), 4132-4144
CODEN: MPOHBP; ISSN: 1543-8384
DIGITAL OBJECT ID: 10.1021/acs.molpharmaceut.7b00354
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The absorption of poorly water-sol. drugs is influenced by the luminal gastrointestinal fluid content and compn. which controls soly. Simulated intestinal fluids have been introduced into dissoln. testing including endogenous amphiphiles and digested lipids at physiol. levels; however, in vivo individual variation exists in the concns. of these components, which will alter drug absorption through an effect on soly. The use of a factorial design of expt. and varying media by introducing different levels of bile, lecithin and digested lipids has been previously reported, but here we investigate the soly. variation of poorly-sol. drugs through more complex biorelevant amphiphile interactions. A four component mixt. design was conducted to understand the solubilization capacity and interactions of bile salt, lecithin, oleate and monoglyceride with a const. total concn. (11.7 mM) but varying molar ratios. The equil. soly. of seven low soly. acidic (zafirlukast), basic (aprepitant, carvedilol) and neutral (fenofibrate, felodipine, griseofulvin and spironolactone) drugs was investigated. Soly. results are comparable with literature values and also our own previously published design of expt. studies. Results indicate that solubilization is not a sum accumulation of individual amphiphile concns., but a drug specific effect through interactions of mixed amphiphile compns. with the drug. This is probably due to a combined interaction of drug characteristics for example lipophilicity, mol. shape and ionization with amphiphile components, which can generate specific drug-micelle affinities. The proportion of each component can have a remarkable influence on soly. with in some cases the highest and lowest points close to each other. A single point soly. measurement in a fixed compn. simulated media or human intestinal fluid sample will therefore provide a value without knowledge of the surrounding soly. topog. meaning that variability may be overlooked. This study has demonstrated how the amphiphile ratios influence drug soly. and highlights the importance of the envelope of physiol. variation when simulating in vivo drug behavior.
CC 63-6 (Pharmaceuticals)
IT 52-01-7, Spironolactone 126-07-8, Griseofulvin 49562-28-9, Fenofibrate 72509-76-3, Felodipine 72956-09-3, Carvedilol 107753-78-6, Zafirlukast 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of physiol. gastrointestinal surfactant ratio on equil. soly. of BCS class II drugs investigated using a four component mixt. design)
IT 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of physiol. gastrointestinal surfactant ratio on equil. soly. of BCS class II drugs investigated using a four component mixt. design)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX

NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 28 THERE ARE 28 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:2157637 CAPLUS Full-text
DOCUMENT NUMBER: 166:118691
TITLE: Cosmeceutical compositions comprising polyalkylene glycols
INVENTOR(S): Schmaus, Gerhard; Lange, Sabine
PATENT ASSIGNEE(S): Symrise AG, Germany
ULTIMATE OWNER: SYMRISE AG
ULTIMATE OWNER STANDARD: Symrise
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016207084	A1	20161229	WO 2016-EP64109	20160619
EP 3108941	A1	20161228	EP 2015-173373	20150623
EP 3108941	B1	20180509		
KR 2018015265	A	20180212	KR 2018-7002058	20160619
KR 2117171	B1	20200601		
MX 2017016226	A	20180223	MX 2017-16226	20160619
CN 107847772	A	20180327	CN 2016-80045857	20160619
CN 107847772	B	20220104		
JP 2018518496	T	20180712	JP 2017-565942	20160619
JP 6945458	B2	20211006		
BR 112017027546	A2	20180821	BR 2017-112017027546	20160619
BR 112017027546	B1	20220426		
IN 201717044256	A	20180105	IN 2017-17044256	20171208
US 20180185301	A1	20180705	US 2017-15736494	20171214

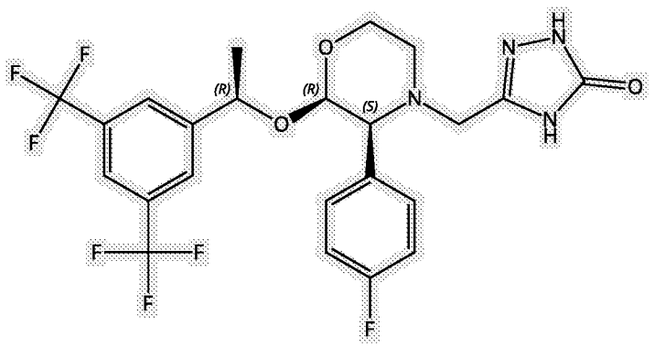
PRIORITY APPLN. INFO.:
EP 2015-173373 A 20150623
WO 2016-EP64109 W 20160619

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2016207084	A1	Dead	20201201
EP 3108941	A1	Indeterminate	20201106
EP 3108941	B1	Indeterminate	20201107
KR 2018015265	A	Alive	20201121
KR 2117171	B1	Alive	20201121
MX 2017016226	A	Alive	20201121
CN 107847772	A	Alive	20201121
CN 107847772	B	Alive	20220120

JP 2018518496 T Alive 20201120
JP 6945458 B2 Alive 20211118
BR 112017027546 A2 Alive 20220519
BR 112017027546 B1 Alive 20220519
US 20180185301 A1 Dead 20220818
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2016:2157637
AB Suggested are compns. comprising or consisting of specific polyalkylene glycol deriv. as pharmaceutical actives for preventing, treating and/or curing itchy conditions of human skin and scalp, and/or providing a PAR-2 antagonistic effect to human skin and scalp.
IPCI A61Q0019-00 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]; A61Q0015-00 [I]; A61K0008-39 [I]; A61K0008-33 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]
IPCR A61K0008-33 [I]; A61Q0019-00 [I]; A61K0008-39 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0015-00 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 63
IT Amino acids
Cannabinoids
Carbohydrates
Ceramides
Collagens
Corticosteroids
Disaccharides
Elastins
Glycosphingolipids
Hydroxy fatty acids
Hydroxycarboxylic acids
Lanolin
Lecithins
Oligosaccharides
Petrolatum
Phytosterols
Polyoxyalkylenes
Pyrazoles
Steroids
Tocopherols
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)
IT 50-02-2 50-21-5, biological studies 50-23-7 50-33-9, biological studies 50-78-2 50-99-7, D-Glucose, biological studies 53-06-5 53-86-1 56-81-5, 1,2,3-Propanetriol, biological studies 57-13-6, Urea, biological studies 57-48-7, D-Fructose, biological studies 57-55-6, 1,2-Propanediol, biological studies 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies 58-95-7 59-23-4, D-Galactose, biological studies 61-68-7 63-42-3 69-46-5 72-17-3 77-52-1 77-92-9, biological studies 81-13-0 83-43-2 89-78-1 89-79-2 97-59-6 98-52-2 104-98-3 124-04-9D, Hexanedioic acid, acyl derivs. 129-20-4 312-93-6 472-15-1 502-65-8, ψ,ψ-Carotene 515-69-5 520-36-5 530-78-9 544-31-0 552-94-3 555-66-8 578-74-5 644-62-2 873-94-9 1117-77-7 1117-86-8, 1,2-Octanediol 1405-86-3, Glycyrrhizin 1406-18-4, Vitamin E 2304-80-5 3458-28-4, D-Mannose 3804-01-1 4394-00-7 5343-92-0, 1,2-Pentanediol 6915-15-7 6920-22-5, 1,2-Hexanediol 9004-61-9, Hyaluronic acid 9007-28-7 9012-76-4, Chitosan 9041-22-9, β-D-Glucan 13539-59-8 13609-67-1 15307-86-5 15687-27-1 22204-53-1 24938-91-8 26171-23-3 27113-22-0 30748-29-9 34645-84-6 36322-90-4 36945-98-9 38194-50-2 41736-92-9 51115-67-4 51234-28-7 53254-77-6 53597-27-6 55965-23-6 58253-27-3, Gingerol 58749-22-7 59804-37-4 59870-68-7 61723-78-2 63187-91-7 74563-64-7 77341-67-4 106729-72-0 108766-16-1 110483-07-3 170729-80-3 185740-18-5 185915-25-7 189128-20-9 207792-35-6 211184-47-3 220621-22-7 381224-15-3 506412-91-5 521981-60-2 637336-79-9 697235-49-7 857557-19-8 1122460-01-8
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)
IT 170729-80-3
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
BR 112017027546 A2	BR 2017-112017027546	Register
BR 112017027546 B1	BR 2017-112017027546	Register
CN 107847772 A	CN 2016-80045857	Register|Global Dossier
CN 107847772 B	CN 2016-80045857	Register|Global Dossier
EP 3108941 A1	EP 2015-173373	Register|Federated Reg.
EP 3108941 B1	EP 2015-173373	Register|Federated Reg.
IN 201717044256 A	IN 2017-17044256	Register
JP 2018518496 T	JP 2017-565942	Register|Global Dossier
JP 6945458 B2	JP 2017-565942	Register|Global Dossier
KR 2018015265 A	KR 2018-7002058	Register|Global Dossier
KR 2117171 B1	KR 2018-7002058	Register|Global Dossier
MX 2017016226 A	MX 2017-16226	Register
US 20180185301 A1	US 2017-15736494	Register|Global Dossier
WO 2016207084 A1	WO 2016-EP64109	Register|Global Dossier

L4 ANSWER 28 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:2152998 CAPLUS Full-text
DOCUMENT NUMBER: 166:112176
TITLE: Cosmeceutical compositions comprising polyalkylene glycols
INVENTOR(S): Schmaus, Gerhard; Lange, Sabine
PATENT ASSIGNEE(S): Symrise AG, Germany
ULTIMATE OWNER: SYMRISE AG
ULTIMATE OWNER STANDARD: Symrise
SOURCE: Eur. Pat. Appl., 46pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 3108941	A1	20161228	EP 2015-173373	20150623
EP 3108941	B1	20180509		
WO 2016207084	A1	20161229	WO 2016-EP64109	20160619
KR 2018015265	A	20180212	KR 2018-7002058	20160619
KR 2117171	B1	20200601		
MX 2017016226	A	20180223	MX 2017-16226	20160619

CN 107847772	A	20180327	CN 2016-80045857		20160619
CN 107847772	B	20220104			
JP 2018518496	T	20180712	JP 2017-565942		20160619
JP 6945458	B2	20211006			
BR 112017027546	A2	20180821	BR 2017-112017027546		20160619
BR 112017027546	B1	20220426			
IN 201717044256	A	20180105	IN 2017-17044256		20171208
US 20180185301	A1	20180705	US 2017-15736494		20171214

PRIORITY APPLN. INFO.:

EP 2015-173373	A	20150623
WO 2016-EP64109	W	20160619

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
EP 3108941	A1	Indeterminate	20201106
EP 3108941	B1	Indeterminate	20201107
WO 2016207084	A1	Dead	20201201
KR 2018015265	A	Alive	20201121
KR 2117171	B1	Alive	20201121
MX 2017016226	A	Alive	20201121
CN 107847772	A	Alive	20201121
CN 107847772	B	Alive	20220120
JP 2018518496	T	Alive	20201120
JP 6945458	B2	Alive	20211118
BR 112017027546	A2	Alive	20220519
BR 112017027546	B1	Alive	20220519
US 20180185301	A1	Dead	20220818

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2016:2152998

AB Suggested are compns. comprising or consisting of specific polyalkylene glycol deriv. as pharmaceutical actives for preventing, treating and/or curing itchy conditions of human skin and scalp, and/or providing a PAR-2 antagonistic effect to human skin and scalp.

IPCI A61Q0019-00 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]; A61Q0015-00 [I]; A61K0008-39 [I]; A61K0008-33 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]

IPCR A61Q0019-00 [I]; A61K0008-33 [I]; A61K0008-39 [I]; A61K0031-08 [I]; A61K0031-25 [I]; A61P0017-04 [I]; A61Q0005-00 [I]; A61Q0005-12 [I]; A61Q0015-00 [I]; A61Q0017-04 [I]; A61Q0019-02 [I]

CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 63

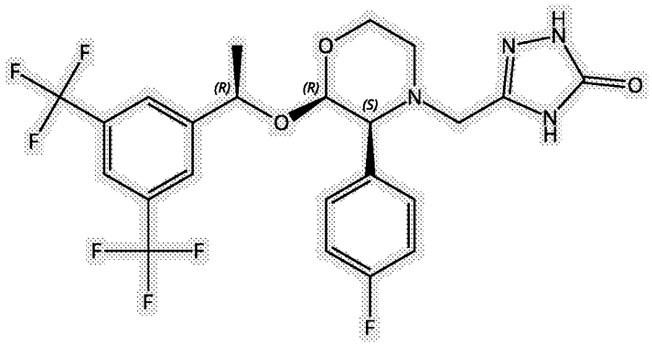
IT Amino acids
Cannabinoids
Carbohydrates
Ceramides
Collagens
Corticosteroids
Disaccharides
Elastins
Glycosphingolipids
Hydroxy fatty acids
Hydroxycarboxylic acids
Lanolin
Lecithins
Oligosaccharides
Petrolatum
Phytosterols
Polyoxyalkylenes
Pyrazoles
Steroids
Tocopherols
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

IT 50-02-2, Dexamethasone 50-21-5, Lactic acid, biological studies 50-23-7, Hydrocortisone 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 50-99-7, D-Glucose, biological studies 53-06-5, Cortisone 53-86-1, Indomethacin 56-81-5, Glycerol, biological studies 57-13-6, Urea, biological studies 57-48-7, D-Fructose, biological studies 57-55-6, Propylene glycol, biological studies 57-88-5, Cholesterol, biological studies 58-95-7, Tocopheryl acetate 59-23-4, D-Galactose, biological studies 61-68-7, Mefenamic acid 63-42-3, Lactose 69-46-5, Solprin 72-17-3, Sodium lactate 77-52-1, Ursolic

acid 77-92-9, Citric acid, biological studies 81-13-0 83-43-2,
Methylprednisolone 89-78-1, Menthol 89-79-2 97-59-6 98-52-2
104-98-3 124-04-9D, Adipic acid, acyl derivs. 129-20-4,
Oxyphenylbutazone 312-93-6, Dexamethasone phosphate 472-15-1, Betulic
acid 502-65-8, ψ,ψ-Carotene 515-69-5, α-Bisabolol
520-36-5, Apigenin 530-78-9, Flufenamic acid 544-31-0, N-Palmitoyl
Ethanolamine 552-94-3, Disalcid 555-66-8 578-74-5 629-54-9,
Hexadecanamide 644-62-2, Meclofenamic acid 873-94-9 1117-77-7
1117-86-8, 1,2-Octanediol 1405-86-3, Glycyrrhizin 1406-18-4, Vitamin E
2304-80-5 3458-28-4, D-Mannose 3804-01-1 4394-00-7, Niflumic acid
5343-92-0, 1,2-Pentanediol 6915-15-7, Malic acid 6920-22-5,
1,2-Hexanediol 9004-61-9, Hyaluronic acid 9007-28-7, Chondroitin
sulfate 9012-76-4, Chitosan 9041-22-9, β-Glucan 13539-59-8
13609-67-1, Hydrocortisone 17-butyrate 15307-86-5, Diclofenac
15687-27-1, Ibuprofen 22204-53-1, Naproxen 24938-91-8, Polyethylene
glycol Tridecyl ether 26171-23-3, Tolmetin 27113-22-0 30748-29-9,
Feprazone 34645-84-6, Fenclofenac 36322-90-4, Piroxicam 36945-98-9,
Icilin 38194-50-2, Sulindac 41736-92-9 51115-67-4,
2-Isopropyl-N-2,3-trimethylbutanamide 51234-28-7, Benoxaprofen
53254-77-6 53597-27-6, Fendosal 55965-23-6 58253-27-3, Gingerol
58749-22-7 59804-37-4, Tenoxicam 59870-68-7 61723-78-2 63187-91-7
74563-64-7 77341-67-4 106729-72-0 108766-16-1 170729-80-3
185740-18-5 185915-25-7, L-Menthyl lactate 189128-20-9 207792-35-6,
3-Menthoxypropane-1,2-diol 211184-47-3 220621-22-7 381224-15-3
506412-91-5 521981-60-2 637336-79-9 697235-49-7 857557-19-8
1122460-01-8
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

IT 170729-80-3
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(cosmeceutical compns. comprising polyalkylene glycols)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
BR 112017027546 A2	BR 2017-112017027546	Register
BR 112017027546 B1	BR 2017-112017027546	Register
CN 107847772 A	CN 2016-80045857	Register|Global Dossier
CN 107847772 B	CN 2016-80045857	Register|Global Dossier
EP 3108941 A1	EP 2015-173373	Register|Federated Reg.

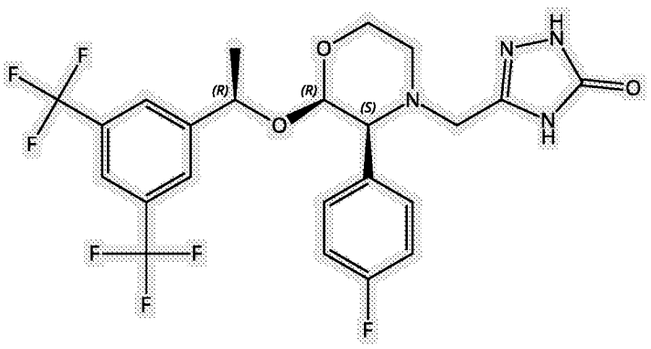
EP 3108941 B1	EP 2015-173373	Register|Federated Reg.
IN 201717044256 A	IN 2017-17044256	Register
JP 2018518496 T	JP 2017-565942	Register|Global Dossier
JP 6945458 B2	JP 2017-565942	Register|Global Dossier
KR 2018015265 A	KR 2018-7002058	Register|Global Dossier
KR 2117171 B1	KR 2018-7002058	Register|Global Dossier
MX 2017016226 A	MX 2017-16226	Register
US 20180185301 A1	US 2017-15736494	Register|Global Dossier
WO 2016207084 A1	WO 2016-EP64109	Register|Global Dossier

L4 ANSWER 29 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:2116494 CAPLUS Full-text
DOCUMENT NUMBER: 172:545657
TITLE: Statistical investigation of simulated fed intestinal media composition on the equilibrium solubility of oral drugs
AUTHOR(S): Zhou, Zhou; Dunn, Claire; Khadra, Ibrahim; Wilson, Clive G.; Halbert, Gavin W.
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK
SOURCE: European Journal of Pharmaceutical Sciences (2017), 99, 95-104
CODEN: EPSCED; ISSN: 0928-0987
DIGITAL OBJECT ID: 10.1016/j.ejps.2016.12.008
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Gastrointestinal fluid is a complex milieu and it is recognized that gut drug soly. is different to that obsd. in simple aq. buffers. Simulated gastrointestinal media have been developed covering fasted and fed states to facilitate in vitro prediction of gut soly. and product dissoln. However, the combination of bile salts, phospholipids, fatty acids and proteins in an aq. buffered system creates multiple phases and drug soly. is therefore a complex interaction between these components, which may create unique environments for each API. The impact on soly. can be assessed through a statistical design of expt. (DoE) approach, to det. the influence and relationships between factors. In this paper DoE has been applied to fed simulated gastrointestinal media consisting of eight components (pH, bile salt, lecithin, sodium oleate, monoglyceride, buffer, salt and pancreatin) using a two level D-optimal design with forty-four duplicate measurements and four center points. The equil. soly. of a range of poorly sol. acidic (indomethacin, ibuprofen, phenytoin, valsartan, zafirlukast), basic (aprepitant, carvedilol, tadalafil, bromocriptine) and neutral (fenofibrate, felodipine, probucol, itraconazole) drugs was investigated. Results indicate that the DoE provides equil. soly. values that are comparable to literature results for other simulated fed gastrointestinal media systems or human intestinal fluid samples. For acidic drugs the influence of pH predominates but other significant factors related to oleate and bile salt or interactions between them are present. For basic drugs pH, oleate and bile salt have equal significance along with interactions between pH and oleate and lecithin and oleate. Neutral drugs show diverse effects of the media components particularly with regard to oleate, bile salt, pH and lecithin but the presence of monoglyceride, pancreatin and buffer have significant but smaller effects on soly. There are fourteen significant interactions between factors mainly related to the surfactant components and pH, indicating that the soly. of neutral drugs in fed simulated media is complex. The results also indicate that the equil. soly. of each drug can exhibit individualistic behavior assocd. with the drug's chem. structure, physicochem. properties and interaction with media components. The utility of DoE for fed simulated media has been demonstrated providing equil. soly. values comparable with similar in vitro systems while also providing greater information on the influence of media factors and their interactions. The detn. of a drug's gastrointestinal soly. envelope provides useful limits that can potentially be applied to in silico modeling and in vivo expts.

CC 63-5 (Pharmaceuticals)
IT 53-86-1, Indomethacin 57-41-0, Phenytoin 15687-27-1, Ibuprofen 23288-49-5, Probucol 25614-03-3, Bromocriptine 49562-28-9, Fenofibrate 72509-76-3, Felodipine 72956-09-3, Carvedilol 84625-61-6, Itraconazole 107753-78-6, Zafirlukast 137862-53-4, Valsartan 170729-80-3,

Aprepitant 171596-29-5, Tadalafil
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated fed intestinal media compn. effect on equil. soly. of oral drugs)
IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated fed intestinal media compn. effect on equil. soly. of oral drugs)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

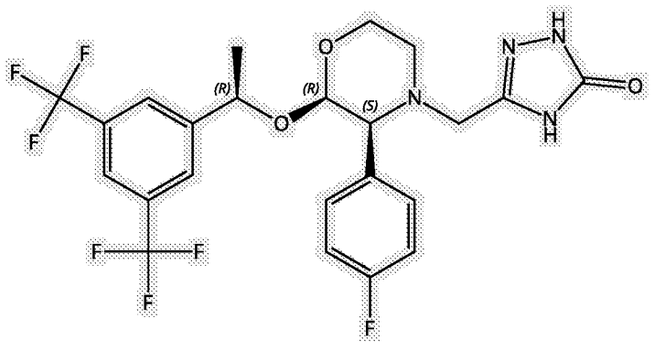
L4 ANSWER 30 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:2039523 CAPLUS Full-text
DOCUMENT NUMBER: 167:295158
TITLE: Stable injectable pharmaceutical composition of neurokinin 1 receptor antagonist and process for preparation thereof
INVENTOR(S): Karavas, Evangelos; Koutris, Efthimios; Bikiaris, Dimitrios; Chatidou, Sotiria; Diakidou, Amalia; Barmpalexis, Panagiotis; Konstanti, Louiza; Minioti, Katerina
PATENT ASSIGNEE(S): Pharmathen S.A., Greece
ULTIMATE OWNER: PARTNERS GROUP HOLDING AG
ULTIMATE OWNER STANDARD: Partners Group
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20150165045	A1	20150618	US 2014-14412147		20141230
WO 2014005606	A1	20140109	WO 2012-EP2854		20120706
US 20200237920	A1	20200730	US 2020-16851779		20200417
PRIORITY APPLN. INFO.:			WO 2012-EP2854	W	20120706
			US 2014-14412147	A1	20141230

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20150165045	A1	Dead	20220105
WO 2014005606	A1	Dead	20201202

US 20200237920 A1 Dead 20231109
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2016:2039523
AB The present invention relates to a controlled release sterile injectable formulation in the form of soln., suspension or sol-gel formulation for i.m. or s.c. administration comprising a therapeutically effective amt. of a neurokinin 1 receptor antagonist, in particular Aprepitant or Fosaprepitant or pharmaceutical acceptable salt, deriv. or metabolite thereof. It also relates to a process for developing such formulations.
IPCI A61K0047-38 [I]; A61K0031-675 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0047-14 [I]; A61K0047-46 [I]; A61K0031-5377 [I]; A61K0009-00 [I]
IPCR A61K0047-38 [I]; A61K0009-00 [I]; A61K0031-5377 [I]; A61K0031-675 [I]; A61K0047-14 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0047-46 [I]
NCL 514/090.000; 514/230.800
CC 63-6 (Pharmaceuticals)
IT Castor oil
Cottonseed oil
Gelatins
Lecithins
Polymers
Polyoxyalkylenes
Sesame oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)
IT 170729-80-3 172673-20-0 265121-04-8
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)
IT 170729-80-3
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
US 20150165045 A1	US 2014-14412147	Register|Global Dossier
US 20200237920 A1	US 2020-16851779	Register|Global Dossier
WO 2014005606 A1	WO 2012-EP2854	Register|Global Dossier

L4 ANSWER 31 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:1859837 CAPLUS Full-text
DOCUMENT NUMBER: 166:232413

TITLE: Evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital

AUTHOR(S): Bourdon, F.; Lecoeur, M.; Leconte, L.; Ultre, V.; Kouach, M.; Odou, P.; Vaccher, C.; Foulon, C.

CORPORATE SOURCE: EA GRITA-7365-Groupe de Recherche sur les formes Injectables et les Technologies Associees, Univ. Lille, Lille, F-59000, Fr.

SOURCE: International Journal of Pharmaceutics (Amsterdam, Netherlands) (2016), 515(1-2), 774-787
CODEN: IJPHDE; ISSN: 0378-5173

DIGITAL OBJECT ID: 10.1016/j.ijpharm.2016.11.014

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

OTHER SOURCE(S): CASFORMULTNS 2016:1859837

AB The objective of this study was to evaluate five com. ready-to-use transdermal vehicles (Phytobase, Lipovan, Pentravan, Pentravan Plus and Pluronic Lecithin Organogel (PLO)), for the compounding of three antiemetic drugs (ondansetron, dexamethasone and aprepitant) and their administration in combination to treat chemotherapy-induced nausea and vomiting (CINV) at the hospital. Drugs were individually formulated in these vehicles and in mixt. in Pentravan Plus using different penetration enhancers. Quality control of the forms has demonstrated that formulation process was mastered and convenient for the hospital (time required: 20 min). Diffusion expts. through synthetic membranes and pig ear epidermis performed using Franz-type diffusion cells, have shown that the release and permeation process were greater for ondansetron than for dexamethasone and aprepitant, with a release step not limiting. As permeation of aprepitant was too low, it was discarded of the study. When ondansetron and dexamethasone were compounded in combination in Pentravan Plus, the most efficient vehicle, a permeation decrease was obsd. Finally, the use of tween 20 instead of EtOH as chem. enhancer has led to 2-fold factor increase in the flux of dexamethasone, resulting in fluxes convenient for transdermal administration of ondansetron to a child, but insufficient for an adult and for dexamethasone.

CC 63-6 (Pharmaceuticals)

ST antiemitic Pentravan Plus Phytobase Lipovan Pluronic Lecithin Organogel skin

IT Antiemetics
Biological permeation
Chemotherapy
Child
Combination chemotherapy
Drug delivery systems
Drug toxicity
Homo sapiens
Human
Nausea
Organogels
Permeation enhancers
Skin
Solubility
Transdermal drug delivery systems
Vomiting
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)

IT 1610779-74-2, Pentravan 1610779-77-5, Pluronic Lecithin Organogel 2074721-57-4, Pentravan Plus 2074721-58-5, Phytobase 2074721-59-6, Lipovan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)

IT 50-02-2, Dexamethasone 99614-01-4, Ondansetron hydrochloride 170729-80-3, Aprepitant

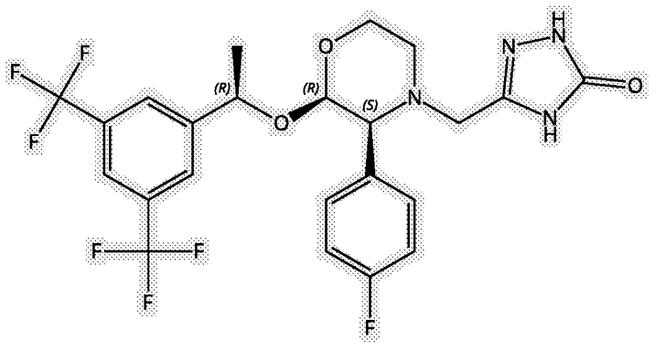
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)

IT 9005-64-5, Tween 20
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)

IT 170729-80-3, Aprepitant
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of Pentravan, Pentravan Plus, Phytobase, Lipovan and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:1723954 CAPLUS Full-text
DOCUMENT NUMBER: 172:411315
TITLE: Optimization of the Ussing chamber setup with excised rat intestinal segments for dissolution/permeation experiments of poorly soluble drugs
AUTHOR(S): Forner, Kristin; Roos, Carl; Dahlgren, David; Kesisoglou, Filippos; Konerding, Moritz A.; Mazur, Johanna; Lennernaes, Hans; Langguth, Peter
CORPORATE SOURCE: Department of Pharmaceutical Technology and Biopharmaceutics, Johannes Gutenberg University, Mainz, Germany
SOURCE: Drug Development and Industrial Pharmacy (2017), 43(2), 338-346
CODEN: DDIPD8; ISSN: 0363-9045
DIGITAL OBJECT ID: 10.1080/03639045.2016.1251449
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Prediction of the in vivo absorption of poorly sol. drugs may require simultaneous dissoln./permeation expts. In vivo predictive media have been modified for permeation expts. with Caco-2 cells, but not for excised

rat intestinal segments. The present study aimed at improving the setup of dissoln./permeation expts. with excised rat intestinal segments by assessing suitable donor and receiver media. The regional compatibility of rat intestine in Ussing chambers with modified Fasted and Fed State Simulated Intestinal Fluids (Fa/FeSSIFmod) as donor media was evaluated via several parameters that reflect the viability of the excised intestinal segments. Receiver media that establish sink conditions were investigated for their foaming potential and toxicity. Dissoln./permeation expts. with the optimized conditions were then tested for two particle sizes of the BCS class II drug aprepitant. Fa/FeSSIFmod were toxic for excised rat ileal sheets but not duodenal sheets, the compatibility with jejunal segments depended on the bile salt concn. A non-foaming receiver medium contg. bovine serum albumin (BSA) and Antifoam B was nontoxic. With these conditions, the permeation of nanosized aprepitant was higher than of the unmilled drug formulations. The compatibility of Fa/FeSSIFmod depends on the excised intestinal region. The chosen conditions enable dissoln./permeation expts. with excised rat duodenal segments. The expts. correctly predicted the superior permeation of nanosized over unmilled aprepitant that is obsd. in vivo. The optimized setup uses FaSSIFmod as donor medium, excised rat duodenal sheets as permeation membrane and a receiver medium contg. BSA and Antifoam B.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 9

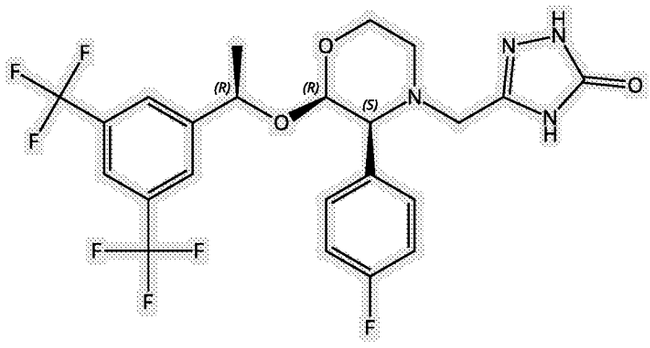
IT Lecithins
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)

IT 81-81-2, Warfarin 15307-86-5, Diclofenac 29122-68-7, Atenolol 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of Ussing chamber setup with excised rat intestinal segments for dissoln./permeation expts. of poorly sol. drugs)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:1057307 CAPLUS Full-text
DOCUMENT NUMBER: 165:169358

TITLE: Difficultly-soluble drug-containing nanostructure lipid carrier pharmaceutical composition with good solubility and high bioavailability and preparation method thereof
INVENTOR(S): Jin, Yinxiu; Wang, Yuxin; Tao, Xuefen; Shi, Lei; Shen, Peipei; Xia, Nianyou
PATENT ASSIGNEE(S): Taizhou Vocational & Technical College, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 21pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105708799	A	20160629	CN 2016-10056874	20160127

PRIORITY APPLN. INFO.: CN 2016-10056874 20160127
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 105708799	A	Dead	20201120

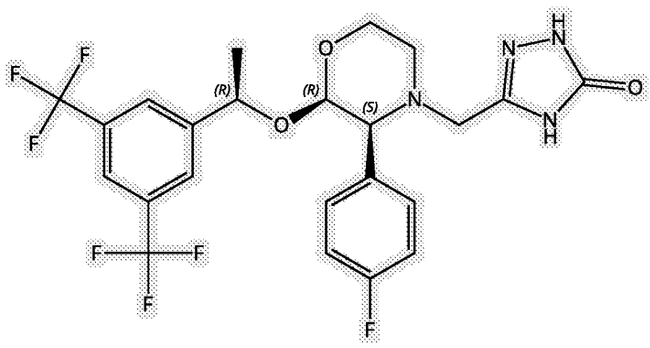
OTHER SOURCE(S): CASFORMULTNS 2016:1057307
AB The title nanostructure lipid carrier pharmaceutical compn. is prepd. from (by wt.%) difficultly-sol. drug (bezafibrate, oxcarbazepine, etc.) 0.02-1, solid lipid material (glyceryl monostearate, etc.) 0.3-15, liq. lipid material (soybean oil, etc.) 0.5-20, lipid-sol. emulsifier (lecithin and/or soybean phospholipid) 0.8-10, water-sol. emulsifier (Tween-20, etc.) 1-15 and water-sol. solvent (water, phosphate buffer soln., etc.) 39-97.38. The invention also provides a prepn. method of the nanostructure lipid carrier pharmaceutical compn. The inventive prepn. method has simple process, and good controllability and repeatability; and the inventive nanostructure lipid carrier pharmaceutical compn. contains difficultly-sol. drug, has good soly., degradability, physiol. compatibility and stability, and high bioavailability and entrapment rate, and no org. solvent residues, and can be used as drug delivery system for difficultly-sol. drug.
IPCI A61K0009-127; A61K0009-19; A61K0047-44; A61K0031-192; A61K0031-55; A61P0003-06; A61P0009-10
IPCR A61K0009-127 [I]; A61K0009-19 [I]; A61K0031-192 [I]; A61K0031-55 [I]; A61K0047-44 [I]; A61P0003-06 [I]; A61P0009-10 [I]
CC 63-6 (Pharmaceuticals)
IT Corn oil
Lecithins
Lipids
Peanut oil
Soya phospholipids
Soybean oil
Sunflower oil
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(difficultly-sol. drug-contg. nanostructure lipid carrier pharmaceutical compn. with good soly. and high bioavailability and prepn. method thereof)
IT 50-14-6, Ergocalciferol 50-24-8, Prednisolone 50-28-2, Oestradiol, biological studies 51-48-9, L-Thyroxine, biological studies 52-01-7, Spironolactone 52-86-8, Haloperidol 53-43-0, Dehydroepiandrosterone 53-86-1, Indomethacin 55-98-1, Busulfan 57-83-0, Progesterone, biological studies 66-76-2, Bishydroxycoumarin 67-20-9, Furadantin 67-45-8, Furazolidone 67-96-9, Dihydrotachysterol 67-97-0, Cholecalciferol 68-26-8, Vitamin A 76-57-3, Codeine 76-99-3, Methadone 90-82-4, Pseudoephedrine 104-31-4, Benzonatate 113-15-5, Ergotamine 113-92-8 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 127-40-2, Xanthophyll 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-57-7, Cinnarizine 298-81-7, Methoxsalen 300-62-9, Amfetamine 302-79-4, Tretinoin 303-49-1, Clomipramine 303-53-7, Cyclobenzaprine 303-98-0, Coenzyme Q10 303-98-0D, Ubidecarenone, salt deriv. 321-64-2, Tacrine 359-83-1, Pentazocine 378-44-9, Betamethasone 404-86-4, Capsaicin 437-38-7, Fentanyl 443-48-1, Metronidazole 502-65-8, Lycopene 511-12-6, Dihydroergotamine 520-85-4, Medroxyprogesterone 652-67-5, Isosorbitol 911-45-5, Clomifene 1134-47-0, Baclofen 1397-89-3,

Amphotericin B 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1665-48-1, Metaxalone 1951-25-3, Amiodarone 1972-08-3, Tetrahydrocannabinol 3562-63-8 4419-39-0, Beclomethasone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 7261-97-4, Dantrolene 7689-03-4, Camptothecin 10238-21-8, Glibenclamide 10238-21-8D, Glibenclamide, salt deriv. 10540-29-1, Tamoxifen 12001-79-5, Vitamin K 15307-86-5, Diclofenac 15574-96-6, Pizotifen 15686-51-8, Clemastine 17230-88-5, Danazol 17230-88-5D, Danazol, salt deriv. 18559-94-9, Salbutamol 19356-17-3, Calcifediol 20594-83-6, Nalbuphine 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22916-47-8, Miconazole 23288-49-5, Probucol 25523-97-1, Dexchlorpheniramine 25812-30-0, Gemfibrozil 27203-92-5, Tramadol 28721-07-5, Oxcarbazepine 29094-61-9, Glipizide 29767-20-2, Teniposide 32222-06-3, Calcitriol 33069-62-4, Taxol 33419-42-0, Etoposide 34911-55-2, Bupropion 38304-91-5, Minoxidil 41340-25-4, Etodolac 41859-67-0, Bezafibrate 42924-53-8, Nabumetone 43200-80-2, Zopiclone 49562-28-9, Fenofibrate 49697-38-3, Rimexolone 51322-75-9, Tizanidine 51333-22-3, Budesonide 51481-61-9, Cimetidine 53123-88-9, Sirolimus 53179-11-6, Loperamide 53230-10-7, Mefloquine 54965-21-8, Albendazole 55079-83-9, Acitretin 55142-85-3, Ticlopidine 57469-82-6, Ibuprofen arginine 59467-70-8, Midazolam 59865-13-3, Cyclosporine 60142-96-3, Gabapentin 61379-65-5, Rifapentine 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 63590-64-7, Terazosin 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 68506-86-5, Vigabatrin 69756-53-2, Halofantrine 70288-86-7, Ivermectin 72432-03-2, Miglitol 72559-06-9, Rifabutine 73590-58-6, Omeprazole 73963-72-1, Cilostazol 74103-06-3, Ketorolac 75330-75-5, Lovastatin 75706-12-6, Leflunomide 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 80621-81-4, Rifaximin 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82626-48-0, Zolpidem 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84371-65-3, Mifepristone 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 88150-42-9, Amlodipine 89778-26-7, Toremifene 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan 98319-26-7, Finasteride 101828-21-1, Butenafine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104987-11-3, Tacrolimus 106133-20-4, Tamsulosin 106650-56-0, Sibutramine 107753-78-6, Zafirlukast 111025-46-8, Pioglitazone 111406-87-2, Zileuton 112965-21-6, Calcipotriene 113665-84-2, Clopidogrel 114977-28-5, Docetaxel 115103-54-3, Tiagabine 117976-89-3, Rabeprazole 118292-40-3, Tazarotene 120014-06-4, Donepezil 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan 127779-20-8, Saquinavir 129497-78-5, Verteporfin 131918-61-1, Paricalcitol 133040-01-4, Eprosartan 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 139755-83-2, Sildenafil 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145941-26-0, Oprevelkin 146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 153559-49-0, Targretin 154229-19-3, Abiraterone 154598-52-4, Efavirenz 155213-67-5, Ritonavir 158747-02-5, Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 170729-80-3, Aprepitant 290297-26-6, Netupitant 366789-02-8, Rivaroxaban 394730-60-0, Boceprevir 402957-28-2, Telaprevir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(difficultly-sol. drug-contg. nanostructure lipid carrier pharmaceutical compn. with good soly. and high bioavailability and prepn. method thereof)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(difficultly-sol. drug-contg. nanostructure lipid carrier pharmaceutical compn. with good soly. and high bioavailability and prepn. method thereof)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105708799 A	CN 2016-10056874	Register|Global Dossier

L4 ANSWER 34 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:725430 CAPLUS Full-text
DOCUMENT NUMBER: 164:573948
TITLE: Self-microemulsifying drug delivery system for improving bioavailability of poorly soluble drug and its application
INVENTOR(S): Li, Suhua; Li, Jixi
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 23pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105535979	A	20160504	CN 2015-10819197	20151122
CN 105535979	B	20190625		
PRIORITY APPLN. INFO.:			CN 2015-10819197	20151122

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 105535979	A	Alive	20201121
CN 105535979	B	Alive	20201121

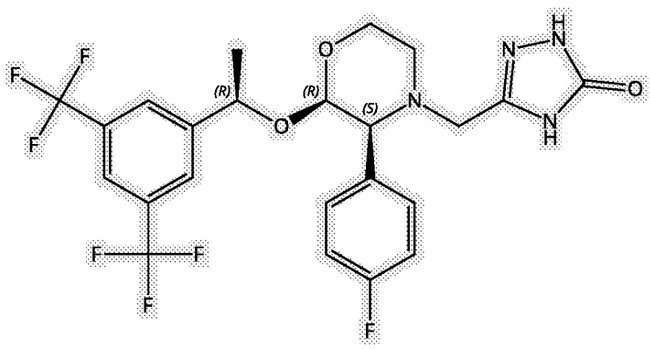
AB The present invention provides a novel self-microemulsifying drug delivery system (SEDDS), wherein the SEDDS carrier material comprises Capmul MCMs and medium-chain fatty acid-contg. oil phase and surfactant. It is suitable for loading two classes of poorly sol. drugs, including pH-dependent (weak acid, weak base drug) and non-pH-dependent (neutral drugs), greatly increases the soly. of the drug to achieve the optimal bioavailability, and has important application value in the formulation development of insol. drugs.
IPCI A61K0047-14 [I]; A61K0047-12 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0031-405 [I]; A61K0031-4515 [I]; A61K0031-58 [I]; A61K0047-14; A61K0047-12; A61K0047-10; A61K0047-44; A61K0031-405; A61K0031-4515; A61K0031-58
IPCR A61K0047-14 [I]; A61K0031-405 [I]; A61K0031-4515 [I]; A61K0031-58 [I]; A61K0047-12 [I]; A61K0047-34 [I]; A61K0047-44 [I]; A61K0047-14 [I]; A61K0047-10 [I]; A61K0047-44 [I]

CC 63-6 (Pharmaceuticals)
IT Acylcarnitines
Alcohols
Amino acids
Bile acids
Bile salts
Cephalins
Ceramides
Dipeptides
Ethoxylated hydrogenated castor oil
Gangliosides
Glycerides
Glycerophospholipids
Glycosphingolipids
Lecithins
Lysophosphatides
Lysophosphatidylcholines
Lysophosphatidylserines
Medium-chain fatty acids
Monoglycerides
Phosphatidic acids
Phosphatidylcholines
Phosphatidylserines
Phospholipids
Polyoxyalkylenes
Pyranosides
Sphingomyelins
Tripeptides
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self-microemulsifying drug delivery system for improving bioavailability of poorly sol. drug and its application)
IT 50-14-6, Ergocalciferol 50-24-8, Prednisolone 50-28-2, Oestradiol, biological studies 51-48-9, L-Thyroxine, biological studies 52-01-7, Spironolactone 52-86-8, Haloperidol 53-43-0, Dehydroepiandrosterone 53-86-1, Indomethacin 55-98-1, Busulfan 57-83-0, Progestin, biological studies 66-76-2, Dicoumarol 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-96-9, Dihydrotachysterol 67-97-0, Cholecal ciferol 68-26-8, Vitamin A 76-57-3, Codeine 76-99-3, Methadone 83-43-2, Methylprednisolone 90-82-4, Pseudoephedrine 104-31-4, Benzonatate 113-15-5, Ergotamine 113-92-8, Chlorphenamine maleate 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 127-40-2 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-57-7, Cinnarizine 298-81-7, Methoxsalen 300-62-9, Amphetamine 302-79-4, Retinoic acid 303-49-1, Clomipramine 303-53-7, Cyclobenzaprine 303-98-0, Coenzyme Q10 321-64-2, Tacrine 359-83-1, Pentazocine 378-44-9, Betamethasone 404-86-4, Capsaicin 437-38-7, Fentanyl 443-48-1, Metronidazole 502-65-8, Lycopene 511-12-6, Dihydroergotamine 652-67-5, Isosorbitol 911-45-5, Clomifene 1134-47-0, Baclofen 1397-89-3, Amphotericin B 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1665-48-1, Metaxalone 1951-25-3, Amiodarone 1972-08-3, Tetrahydrocannabinol 3562-63-8 4419-39-0, Beclomethasone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 7261-97-4, Dantrolene 7689-03-4, Camptothecin 10238-21-8, Glyburide 10540-29-1, Tamoxifen 12001-79-5, Vitamin K 15307-86-5, Diclofenac 15574-96-6, Pizotifen 15686-51-8, Clemastine 15687-27-1, Ibuprofen 17230-88-5, Danazol 18559-94-9, Salbutamol 19356-17-3, Calcifediol 20594-83-6, Nalbuphine 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22916-47-8, Miconazole 23288-49-5, Probucol 25523-97-1, Dexchlorpheniramine 25812-30-0, Gemfibrozil 27203-92-5, Tramadol 29094-61-9, Glipizide 29767-20-2, Teniposide 32222-06-3, Calcitriol 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34911-55-2, Bupropion 38304-91-5, Minoxidil 41340-25-4, Etodolac 42924-53-8, Nabumetone 43200-80-2, Zopiclone 49562-28-9, Fenofibrate 49697-38-3, Rimexolone 51322-75-9, Tizanidine 51333-22-3, Budesonide 51481-61-9, Cimetidine 53123-88-9, Sirolimus 53179-11-6, Loperamide 53230-10-7, Mefloquine 54965-21-8, Albendazole 55079-83-9, Acitretin 55142-85-3, Ticlopidine 59467-70-8, Midazolam 60142-96-3, Gabapentin 61379-65-5, Rifapentine 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 63590-64-7, Terazosin 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 68506-86-5, Vigabatrin 69756-53-2, Halofantrine 70288-86-7, Ivermectin 72432-03-2, Miglitol

72559-06-9, Rifabutine 73590-58-6, Omeprazole 73963-72-1, Cilostazole
74103-06-3, Ketorolac 75330-75-5, Lovastatin 75706-12-6, Leflunomide
76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine
79217-60-0, Cyclosporin 79617-96-2, Sertraline 79794-75-5, Loratadine
79902-63-9, Simvastatin 80621-81-4, Rifaximin 81093-37-0, Pravastatin
81098-60-4, Cisapride 81103-11-9, Clarithromycin 82626-48-0, Zolpidem
83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5,
Azithromycin 84057-84-1, Lamotrigine 84371-65-3, Mifepristone
84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1,
Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril
88150-42-9, Amlodipine 89778-26-7, Toremifene 90357-06-5, Bicalutamide
91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5,
Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin
95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone
97682-44-5, Irinotecan 98319-26-7, Finasteride 101828-21-1, Butenafine
103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104987-11-3,
Tacrolimus 106133-20-4, Tamsulosin 106650-56-0, Sibutramine
107753-78-6, Zafirlukast 111025-46-8, Pioglitazone 111406-87-2,
Zileuton 112965-21-6, Calcipotriene 113665-84-2, Clopidogrel
114977-28-5, Docetaxel 115103-54-3, Tiagabine 117976-89-3, Rabeprazole
118292-40-3, Tazarotene 120014-06-4, Donepezil 121679-13-8,
Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan
127779-20-8, Saquinavir 129497-78-5, Verteporfin 131918-61-1,
Paricalcitol 133040-01-4, Eprosartan 134523-00-5, Atorvastatin
135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6,
Irbesartan 139264-17-8, Zolmitriptan 139481-59-7, Candesartan
139755-83-2, Sildenafil 144034-80-0, Rizatriptan 144494-65-5,
Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin
146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 153559-49-0,
Targretin 154229-19-3, Abiraterone 154598-52-4, Efavirenz
155213-67-5, Ritonavir 158747-02-5, Frovatriptan 158966-92-8,
Montelukast 159989-64-7, Nelfinavir 162011-90-7, Rofecoxib
169590-42-5, Celecoxib 170729-80-3, Aprepitant 290297-26-6,
Netupitant 366789-02-8, Rivaroxaban 394730-60-0, Boceprevir
402957-28-2, Telaprevir
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(self-microemulsifying drug delivery system for improving
bioavailability of poorly sol. drug and its application)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(self-microemulsifying drug delivery system for improving
bioavailability of poorly sol. drug and its application)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105535979 A	CN 2015-10819197	Register|Global Dossier
CN 105535979 B	CN 2015-10819197	Register|Global Dossier

L4 ANSWER 35 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2016:535017 CAPLUS Full-text
DOCUMENT NUMBER: 164:512967
TITLE: Aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy
INVENTOR(S): Zhu, Songlin; Xiao, Yan; Meng, Qingyue; Zhao, Yongxing; Cui, Hao; Chen, Yongqiang; Fang, Shuixia; Pan, Na; Chen, Shuiku; Liang, Qian; Luo, Feng; Liu, Jinxia; Yue, Xiaohui
PATENT ASSIGNEE(S): Furen Medicines Group Co., Ltd., Peop. Rep. China; Kaifeng Pharmaceutical (Group) Co., Ltd.; Henan Furen Pharmaceutical Technology Development Co., Ltd.
ULTIMATE OWNER: FUREN MEDICINE GROUP; KAIFENG PHARMACEUTICAL GROUP; HENAN FUREN MEDICAL TECH DEV
ULTIMATE OWNER STANDARD: FUREN MEDICINE GROUP; KAIFENG PHARMACEUTICAL GROUP; HENAN FUREN MEDICAL TECH DEV
SOURCE: Faming Zhuanli Shenqing, 7pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105456228	A	20160406	CN 2015-10928963	20151211
CN 105456228	B	20180605		

PRIORITY APPLN. INFO.: CN 2014-10814246 A 20141224
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 105456228	A	Alive	20201121
CN 105456228	B	Alive	20201121

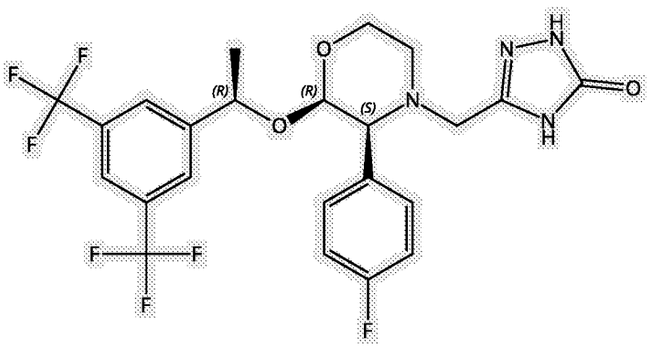
OTHER SOURCE(S): CASFORMULTNS 2016:535017
AB The present invention provides an aprepitant loaded nanocrystal lipid microcapsule, and its prepn. method is as follows: prepg. aprepitant nanocrystals with av. particle size ranging from 50 nm to 400 nm with aprepitant and stabilizer through grinding, high-speed air-jet milling or high-pressure homogenization, dispersing in water and forming a suspension; after then, after dissolving phospholipid in an org. solvent, mixing and emulsifying with the aprepitant nanocrystals suspension, subsequently removing liq. phase, drying and obtaining prepd. the aprepitant nanocrystal lipid microcapsule; wherein the particle size distribution of aprepitant nanocrystal lipid microcapsules is 10-500 μm; the stabilizer is a mixt. of one or two and more of polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft copolymer, polyvinyl pyrrolidone, hydroxypropylmethyl cellulose, poloxamer and the like; the phospholipid is a mixt. of one or two and more of soybean phospholipid, lecithin and hydrogenated phospholipid. The above-mentioned aprepitant nanocrystal lipid microcapsule has stable properties, good in vivo absorption, high bioavailability and rapid drug efficacy functions; it can be used for treating nausea and vomiting after chemotherapy.
IPCI A61K0009-50; A61K0031-5377; A61K0047-24; A61P0001-08; A61P0025-24
IPCR A61K0009-50 [I]; A61K0031-5377 [I]; A61K0047-24 [I]; A61P0001-08 [I]; A61P0025-24 [I]
CC 63-6 (Pharmaceuticals)
IT Lecithins
Phospholipids
Soya phospholipids
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aprepitant loaded nanocrystal lipid microcapsule for treating nausea and vomiting after chemotherapy)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105456228 A	CN 2015-10928963	Register|Global Dossier
CN 105456228 B	CN 2015-10928963	Register|Global Dossier

L4 ANSWER 36 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN

ACCESSION NUMBER: 2016:473657 CAPLUS Full-text
DOCUMENT NUMBER: 164:387016
TITLE: Emulsion formulations of aprepitant
INVENTOR(S): Ottoboni, Thomas B.; Han, Han
PATENT ASSIGNEE(S): Heron Therapeutics, Inc., USA
ULTIMATE OWNER: HERON THERAPEUTICS, INC.
ULTIMATE OWNER STANDARD: HERON THERAPEUTICS, INC.
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016044784	A1	20160324	WO 2015-US51050	20150918
US 20160082013	A1	20160324	US 2015-14859013	20150918
US 9808465	B2	20171107		
KR 2017056575	A	20170523	KR 2017-7008598	20150918
KR 2424837	B1	20220725		
CN 106852118	A	20170613	CN 2015-80050449	20150918
EP 3193830	A1	20170726	EP 2015-772163	20150918
EP 3193830	B1	20231101		
EP 3193830	C0	20231101		
JP 2017533183	T	20171109	JP 2017-514863	20150918
JP 6741655	B2	20200819		
US 20160206622	A1	20160721	US 2016-15083071	20160328
US 9561229	B2	20170207		
US 20170112847	A1	20170427	US 2017-15398928	20170105
US 10500208	B2	20191210		
US 20180000828	A1	20180104	US 2017-15705201	20170914
US 9974793	B2	20180522		

US 20180000829	A1	20180104	US 2017-15705208		20170914
US 9974794	B2	20180522			
JP 2019196398	A	20191114	JP 2019-137539		20190726
US 20200197404	A1	20200625	US 2019-16669262		20191030
US 10953018	B2	20210323			
US 20210186981	A1	20210624	US 2021-17194114		20210305
JP 2022092040	A	20220621	JP 2022-66236		20220413

PRIORITY APPLN. INFO.:

US 2014-62052948	P	20140919
JP 2017-514863	A3	20150918
US 2015-14859013	A1	20150918
WO 2015-US51050	W	20150918
US 2016-15083071	A1	20160328
US 2017-15398928	A1	20170105
JP 2019-137539	A3	20190726
US 2019-16669262	A1	20191030

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2016044784	A1	Dead	20201202
US 20160082013	A1	Alive	20201121
US 9808465	B2	Alive	20201120
KR 2017056575	A	Alive	20220602
KR 2424837	B1	Alive	20220811
CN 106852118	A	Transitional	20240307
EP 3193830	A1	Alive	20201201
EP 3193830	C0	Alive	20240104
JP 2017533183	T	Alive	20201121
JP 6741655	B2	Alive	20201121
US 20160206622	A1	Alive	20201120
US 9561229	B2	Alive	20201120
US 20170112847	A1	Alive	20201120
US 10500208	B2	Alive	20201120
US 20180000828	A1	Alive	20201121
US 9974793	B2	Alive	20201120
US 20180000829	A1	Alive	20201121
US 9974794	B2	Alive	20201120
JP 2019196398	A	Dead	20231026
US 20200197404	A1	Alive	20201121
US 10953018	B2	Alive	20210401
US 20210186981	A1	Alive	20231012
JP 2022092040	A	Dead	20231207

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2016:473657

AB Disclosed herein are novel pharmaceutical formulations of aprepitant suitable for parenteral administration including i.v. administration. Also included are formulations including both aprepitant and dexamethasone sodium phosphate. The pharmaceutical formulations are stable oil-in-water emulsions for non-oral treatment of emesis and are particularly useful for treatment of subjects undergoing cancer chemotherapy.

IPCI A61K0009-00 [I]; A61K0047-10 [I]; A61K0047-44 [I]; A61K0047-24 [I]; A61K0047-12 [I]; A61K0047-26 [I]

IPCR A61K0009-00 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-24 [I]; A61K0047-26 [I]; A61K0047-44 [I]

CC 63-6 (Pharmaceuticals)

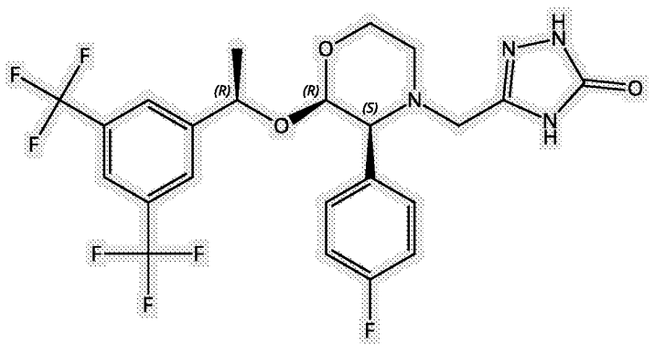
IT Alcohols
Egg yolk lecithins
Phospholipids
Soybean oil
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

IT 2392-39-4 170729-80-3
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

IT 170729-80-3
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion formulations of aprepitant)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 106852118 A	CN 2015-80050449	Register|Global Dossier
EP 3193830 A1	EP 2015-772163	Register|Federated Reg.
EP 3193830 B1	EP 2015-772163	Register|Federated Reg.
EP 3193830 C0	EP 2015-772163	Register|Federated Reg.
JP 2017533183 T	JP 2017-514863	Register|Global Dossier
JP 6741655 B2	JP 2017-514863	Register|Global Dossier
JP 2019196398 A	JP 2019-137539	Register|Global Dossier
JP 2022092040 A	JP 2022-66236	Register|Global Dossier
KR 2017056575 A	KR 2017-7008598	Register|Global Dossier
KR 2424837 B1	KR 2017-7008598	Register|Global Dossier
US 20160082013 A1	US 2015-14859013	Register|Global Dossier
US 9808465 B2	US 2015-14859013	Register|Global Dossier
US 20160206622 A1	US 2016-15083071	Register|Global Dossier
US 9561229 B2	US 2016-15083071	Register|Global Dossier
US 10500208 B2	US 2017-15398928	Register|Global Dossier
US 20170112847 A1	US 2017-15398928	Register|Global Dossier
US 20180000828 A1	US 2017-15705201	Register|Global Dossier
US 9974793 B2	US 2017-15705201	Register|Global Dossier
US 20180000829 A1	US 2017-15705208	Register|Global Dossier
US 9974794 B2	US 2017-15705208	Register|Global Dossier
US 10953018 B2	US 2019-16669262	Register|Global Dossier
US 20200197404 A1	US 2019-16669262	Register|Global Dossier
US 20210186981 A1	US 2021-17194114	Register|Global Dossier
WO 2016044784 A1	WO 2015-US51050	Register|Global Dossier

L4 ANSWER 37 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2015:1470836 CAPLUS Full-text
DOCUMENT NUMBER: 163:403366
TITLE: Method for manufacture of nano suspension
INVENTOR(S): Wang, Yongjun; Han, Xiangfei; Xue, Peng; Wang, Jing; Jiang, Mengjuan; He, Zhonggui
PATENT ASSIGNEE(S): Shenyang Pharmaceutical University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104887626	A	20150909	CN 2015-10287997	20150529

PRIORITY APPLN. INFO.: CN 2015-10287997 20150529

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
CN 104887626	A	Dead	20201120

AB The present invention relates to a method for manuf. of nano suspension, belonging to the field of pharmaceutical prepns. The present invention utilizes an effervescent method to generate bubbles for dispersion and mixing to obtain nano-suspensions, and includes the following specific steps : mixing drug, stabilizer, the org. acid and other pharmaceutically acceptable excipients as org. phase, dissolving carbonate and other pharmaceutically acceptable excipients in water as carbonate phase, mixing the two phases, or shaking or vortex, to obtain nano suspension. The drug contg. prescription comprises drugs 1, stabilizer 0. 01-20, org. acids 0. 01 -10, carbonate 0. 01 -10 wt. parts. The carbonate is sodium carbonate, potassium carbonate, KHCO3, CaCO3, calcium bicarbonate, ammonium carbonate, etc. The org. acid is malic acid, citric acid, succinic acid, sorbic acid, formic acid, acetic acid, propionic acid. The stabilizer is PEG 1000 vitamin E succinate, Tween, Span, poloxamer, etc. The drug is insol. anticancer drug, insol. antifungal drug, insol. antimicrobial agent, hypotensive drug, etc. The present invention significantly improves the soly. and dissoln. rate of poorly sol. drugs, thereby increases the bioavailability of poorly sol. drugs.

IPCI A61K0009-10 [I]; A61K0047-12 [I]; A61K0047-04 [I]; A61K0045-00 [I]

IPCR A61K0009-10 [I]; A61K0045-00 [I]; A61K0047-04 [I]; A61K0047-12 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

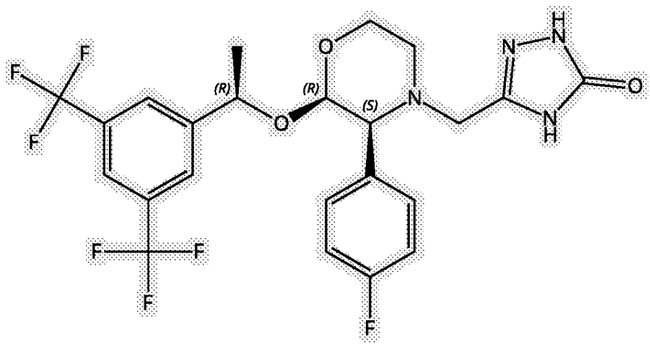
IT Amino acids
Carbonates
Ethoxylated hydrogenated castor oil
Fatty acids
Fatty alcohols
Gelatins
Lecithins
Organic acids
Phospholipids
Polyoxyalkylenes
Taxanes
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for manuf. of pharmaceutical nano suspension)

IT 50-02-2, Dexamethasone 52-01-7, Spirolactone 443-48-1, Metronidazole 595-33-5, Megestrol acetate 1397-89-3, Amphotericin B 7689-03-4, Camptothecin 9002-96-4, TPGS 10238-21-8, Glibenclamide 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16773-42-5, Ornidazole 23593-75-1, Clotrimazole 29767-20-2, Teniposide 33069-62-4, Taxol 33419-42-0, Etoposide 39562-70-4, Nitrendipine 53123-88-9, Sirolimus 55985-32-5, Nicardipine 66085-59-4, Nimodipine 79794-75-5, Loratadine 84625-61-6, Itraconazole 93479-97-1, Glimepiride 103577-45-3, Lansoprazole 104987-11-3, Tacrolimus 170729-80-3, Aprepitant 183133-96-2, Cabazitaxel 199739-10-1, Paliperidone palmitate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for manuf. of pharmaceutical nano suspension)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for manuf. of pharmaceutical nano suspension)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 104887626 A	CN 2015-10287997	Register|Global Dossier

L4 ANSWER 38 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2015:1390403 CAPLUS Full-text
DOCUMENT NUMBER: 163:369597
TITLE: Compositions of pentosan polysulfate salts for oral administration and methods of use
INVENTOR(S): Parsons, C. Lowell; Goldberg, Michael; Meenan, Christopher P.
PATENT ASSIGNEE(S): Urigen Pharmaceuticals, Inc., USA
ULTIMATE OWNER: PLATINUM MONTAUR LIFE SCIENCES
ULTIMATE OWNER STANDARD: PLATINUM MONTAUR LIFE SCIENCES
SOURCE: PCT Int. Appl., 248pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2015127416	A1	20150827	WO 2015-US17205		20150224
CA 2949480	A1	20150827	CA 2015-2949480		20150224
AU 2015218642	A1	20161006	AU 2015-218642		20150224
EP 3110427	A1	20170104	EP 2015-751441		20150224
KR 2017003527	A	20170109	KR 2016-7026610		20150224
CN 106456662	A	20170222	CN 2015-80022057		20150224
JP 2017512757	T	20170525	JP 2016-554267		20150224
US 20170189443	A1	20170706	US 2016-15121312		20160824
PRIORITY APPLN. INFO.:			US 2014-61943824	P	20140224
			WO 2015-US17205	W	20150224

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2015127416	A1	Dead	20201201
CA 2949480	A1	Dead	20220428
AU 2015218642	A1	Dead	20210318
EP 3110427	A1	Dead	20210729
KR 2017003527	A	Alive	20201121
CN 106456662	A	Dead	20201121
JP 2017512757	T	Alive	20201120
US 20170189443	A1	Dead	20210324

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 163:369597; CASFORMULTNS 2015:1390403
AB The invention is directed to a pharmaceutical compn. comprising: (1) a therapeutically effective quantity of sodium pentosan polysulfate; (2) a quantity of a penetration enhancer sufficient to improve the bioavailability of the sodium pentosan polysulfate; and (3) optionally, a

pharmaceutically acceptable carrier and to methods for the oral administration of sodium pentosan polysulfate with improved bioavailability for the treatment of interstitial cystitis and other urinary tract diseases and conditions. Such compns. and methods allow the administration of sodium pentosan polysulfate at lower dosages to reduce the frequency and severity of side effects.

IPCI A61K0031-715 [I]; C07H0005-10 [I]; A61K0047-14 [I]; A61P0019-02 [I]

IPCR A61K0031-715 [I]; A61K0047-14 [I]; A61P0019-02 [I]; C07H0005-10 [I]

CC 1-12 (Pharmacology)

IT Acrylic polymers
Acylcarnitines
Amino acids
Bile salts
Bone morphogenetic protein 7
Bone sialoproteins
Cartilage oligomeric matrix protein
Collagen type I
Collagen type II
Collagen type IX
Collagen type XI
Collagens
Crown compounds
Dendrimers
Diglycerides
Estrogens
Fatty acids
Insulin-like growth factor-binding protein 3
Lecithins
Matrix proteins
Medium-chain fatty acids
Monoclonal antibodies
Monoglycerides
Opioids
Osteocalcins
Osteonectin
Osteopontin
Peptides
Polyanhydrides
Polyoxyalkylenes
Proteins
Salicylates
Steroidal hormones
Sulfonanilides
Terpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and methods of use)

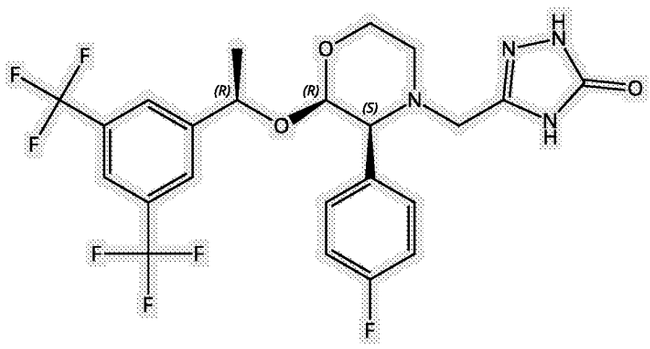
IT 15866-90-7, Metastat 15880-03-2 16011-96-4, 2-Iminopiperidine hydrochloride 16067-69-9, Strontium benzenesulfonate 16088-89-4, Strontium maleate 16139-18-7, Aminoguanidine hydrochloride 18847-18-2 19767-45-4, Mesna 19878-22-9 19982-08-2, Memantine 20093-91-8 20594-83-6, Nalbuphine 21084-57-1, 8-(Phthalimido)caprylic acid 21256-18-8, Oxaprozin 21463-31-0, 2-Amino-5,6-dihydro-6-methyl-4H-1,3-thiazine hydrochloride 22059-21-8, 1-Aminocyclopropane-1-carboxylic acid 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22410-94-2 22494-42-4, Diflunisal 22834-47-5 24314-23-6 24339-95-5 25087-26-7 25087-26-7D, derivs. 25322-68-3 25496-72-4 25518-54-1 25587-34-2 26009-03-0, Poly[oxy(1-oxo-1,2-ethanediyl)] 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26171-23-3, Tolmetin 26615-21-4, Zotepine 26864-56-2, Penfluridol 27203-92-5, Tramadol 27261-86-5 27540-07-4 27638-00-2 28945-89-3, 3-(3-Ethoxyphenyl)propanoic acid 28945-91-7, 3-(3-Butoxyphenyl)propanoic acid 29679-58-1, Fenoprofen 30762-02-8, 4-(Cyclopentyloxy)benzoic acid 31477-60-8, Ormeloxifene 33369-31-2, Zomepirac 34346-01-5 34816-55-2, Moxestrol 35197-20-7 36322-90-4, Piroxicam 36330-86-6 36440-58-1 36978-49-1 38194-50-2, Sulindac 39860-99-6, Pipotiazine 40182-75-0, Strontium citrate 40391-99-9 40472-00-2, Strontium succinate 41340-25-4, Etodolac 41839-80-9 42408-82-2, Butorphanol 42907-92-6 42907-93-7 43218-50-4 47739-98-0, Clocapramine 49594-75-4 50700-72-6,

Vecuronium 51036-98-7 51333-22-3, Budesonide 51803-78-2, Nimesulide
52240-14-9 52349-26-5 52485-79-7, Buprenorphine 52888-70-7,
3-(3-Phenoxyphenyl)propanoic acid 53583-79-2, Sultopride 53597-27-6,
Fendosal 53648-55-8, Dezocine 53716-49-7, Carprofen 53772-83-1,
Zuclopenthixol 57648-21-2, Timiperone 57821-78-0 59122-46-2,
Misoprostol 59227-89-3 59804-37-4, Tenoxicam 59865-13-3,
Cyclosporine 60118-07-2, Endorphin 61126-74-7 61126-76-9
63471-88-5 64228-79-1, Atracurium 64779-07-3 64779-14-2
65576-45-6, Asenapine 66644-81-3, Veralipride 67763-96-6, Insulin like
growth factor-1 68047-06-3, 4-Hydroxy-tamoxifen 68134-81-6,
Gacyclidine 71125-38-7, Meloxicam 71675-85-9, Amisulpride
74103-06-3, Ketorolac 75221-40-8, [4-(Cyclohexylmethoxy)phenyl]acetic
acid 75221-43-1 75272-39-8, Nemonapride 75706-12-6, Leflunomide
77086-21-6, Dizocilpine 77599-17-8, Panomifene 78994-23-7,
Levormeloxifene 79055-68-8 79669-11-7, 3-(4-Isopropoxyphenyl)propanoic
acid 79778-41-9, Neridronate 80125-14-0, Remoxipride 81093-37-0,
Pravastatin 81109-85-5 82413-20-5, Droloxifene 83015-26-3,
Atomoxetine 84449-90-1, Raloxifene 86111-26-4, Zindoxifene
89326-69-2, 5-(4-Ethylphenyl)pentanoic acid 89419-40-9, Mosapramine
89750-15-2, Glucagon like peptide-2 89778-26-7, Toremifene 89987-06-4,
Tiludronate 93957-54-1, Fluvastatin 98007-99-9 98774-23-3,
Tesmilifene 100759-29-3 100944-08-9 101253-68-3 102676-47-1,
Fadrozole 103735-76-8, erythro-MEA 103987-16-2 105462-24-6,
Risedronate 106266-06-2, Risperidone 106516-24-9, Sertindole
107868-30-4, Exemestane 108179-99-3 110347-85-8, Selfotel
110931-77-6 111974-69-7, Quetiapine 112809-51-5, Letrozole
114084-78-5, Ibandronate 115767-74-3, TAT-59 116057-68-2
116057-75-1, Idoxifene 117910-70-0 117928-94-6, Rapastinel
118072-93-8, Zoledronic acid 119431-25-3, Eliprodil 120511-73-1,
Anastrozole 121368-58-9, Olpadronate 122004-99-3 123663-49-0, T-614
124937-51-5, Tolterodine 124937-52-6, Detrol 128298-28-2, Remacemide
128607-22-7, Ospemifene 129318-43-0 129453-61-8, Fulvestrant
129612-87-9, Miproxifene 129722-12-9, Aripiprazole 129731-10-8,
Vorozole 129948-69-2 130370-59-1, GI-129471 130370-60-4, Batimastat
131123-76-7, 5,7-Dichlorokynurenic acid 131692-21-2 132539-06-1,
Olanzapine 132810-10-7, Blonanserin 133454-47-4, Iloperidone
133814-18-3, Doxacurium 134523-00-5, Atorvastatin 135459-87-9,
Strontium ranelate 136013-76-8, 2-(Cyclopropylmethoxy)benzoic acid
136553-81-6, BQ-123 136982-36-0, CP-99994 137159-92-3, Aptiganel
137945-48-3, CT-3 138330-18-4, Incadronate 141620-66-8 142880-36-2,
Ilomastat 144598-75-4, Paliperidone 145599-86-6, Cerivastatin
146490-38-2 146939-27-7, Ziprasidone 147536-97-8, Bosentan
148215-77-4, 2-(Cyclopentyloxy)benzoic acid 148700-85-0, L-733060
150403-89-7 150915-41-6, Perospirone 153322-05-5, Lanicemine
153438-49-4, RPR-100893 154039-60-8, Marimastat 155383-07-6, SDZ-PTS
893 156161-89-6, BQ-788 156806-79-0 157116-68-2 157116-71-7
158089-95-3, S-2474 158860-95-8, 3-(Cyclohexylmethoxy)benzoic acid
158860-99-2, 3-(Cyclopentyloxy)benzoic acid 159190-44-0 162011-90-7,
Rofecoxib 162752-13-8, 3-(4-Propylphenyl)propanoic acid 165536-41-4,
MDL-103323 168158-16-5, KB-R-7785 168266-90-8, Vofopitant
168980-06-1 168980-07-2 168980-08-3 168980-09-4 168980-10-7
168980-12-9 168980-13-0 169590-41-4, Deracoxib 169590-42-5,
Celecoxib 169799-04-6, MMI-270 169799-44-4, Keratin sulfate
170277-31-3, Infliximab 170566-84-4, Lanepitant 170713-75-4
170729-80-3, Aprepitant 172673-20-0, Fosaprepitant
173937-91-2, Atrasentan 175033-36-0, NCX4016 177036-94-1, Ambrisentan
177172-49-5 177653-18-8 177653-31-5 177653-36-0 177653-53-1
177653-62-2 177653-65-5 179545-77-8, Tanomastat 180064-38-4
180384-57-0, Tezosentan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and
methods of use)

IT 170729-80-3, Aprepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(compns. of pentosan polysulfate salts for oral administration and
methods of use)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2015218642 A1	AU 2015-218642	Register
CA 2949480 A1	CA 2015-2949480	Register
CN 106456662 A	CN 2015-80022057	Register|Global Dossier
EP 3110427 A1	EP 2015-751441	Register|Federated Reg.
JP 2017512757 T	JP 2016-554267	Register|Global Dossier
KR 2017003527 A	KR 2016-7026610	Register|Global Dossier
US 20170189443 A1	US 2016-15121312	Register|Global Dossier
WO 2015127416 A1	WO 2015-US17205	Register|Global Dossier

L4 ANSWER 39 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2015:865407 CAPLUS Full-text
DOCUMENT NUMBER: 162:663467
TITLE: Orally disintegrating porous film comprising pharmacological active ingredient and method for preparing the same
INVENTOR(S): Oh, Dong Hoon; Lee, Jin Hoo; Lee, So Yi; Kang, Jun Hyuk; Lim, Chae Yun; Jung, Kyung Tae; Yeon, Kyu Jeong; Park, Jin Gyu
PATENT ASSIGNEE(S): Seoul Pharma. Co., Ltd., S. Korea
ULTIMATE OWNER: SEOUL PHARMA. CO., LTD.
ULTIMATE OWNER STANDARD: SEOUL PHARMA. CO., LTD.
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

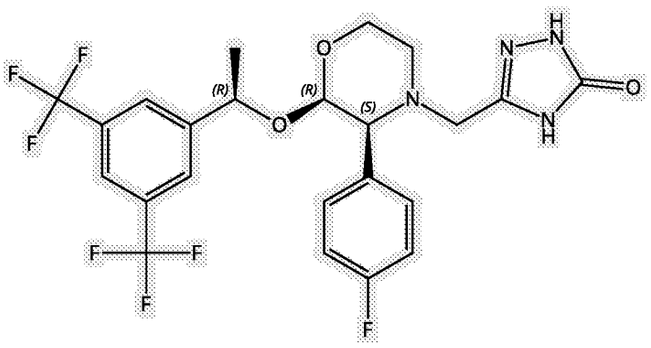
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2015072684	A1	20150521	WO 2014-KR10293		20141030
KR 1407922	B1	20140617	KR 2013-138040		20131114
CN 105873572	A	20160817	CN 2014-80071821		20141030
EP 3069716	A1	20160921	EP 2014-861454		20141030
US 20160279071	A1	20160929	US 2016-15036784		20160513
PRIORITY APPLN. INFO.:			KR 2013-138040	A	20131114
			WO 2014-KR10293	W	20141030

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2015072684	A1	Dead	20201202
KR 1407922	B1	Dead	20201121
CN 105873572	A	Dead	20201121

EP 3069716 A1 Dead 20201203
US 20160279071 A1 Dead 20201121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2015:865407
AB The present invention relates to an orally disintegrating porous film and a method for prepg. the same, the film comprising a foaming agent, a foam stabilizing agent, a plasticizer, and pharmacol. active ingredient. The orally disintegrating porous film according to the present invention has micropores within the film and phys. properties suitable for a film, so that the film has an effect of significantly improving the dissoln. rate of a drug and has good processability since the film can be easily prepd. at low cost and through a simplified prepn. method.
IPCI A61K0009-70 [I]; A61P0003-10 [I]; A61P0003-04 [I]
IPCR A61K0009-70 [I]; A61P0003-04 [I]; A61P0003-10 [I]
CC 63-6 (Pharmaceuticals)
IT Alditols
Enzymes
Hormones, animal
Lecithins
Medium-chain fatty acids
Polyoxyalkylenes
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active substance and its manufg. method)
IT 50-02-2, Dexamethasone 50-58-8, Phendimetrazine tartrate 50-81-7, L-Ascorbic acid, biological studies 54-11-5, Nicotine 55-63-0, Nitroglycerin 56-81-5, Glycerin, biological studies 56-81-5D, Glycerin, fatty acid esters 57-50-1D, Sucrose, fatty acid esters 57-55-6, Propylene glycol, biological studies 58-08-2, Caffeine, biological studies 61-76-7, Phenylephrine hydrochloride 90-84-6, Diethylpropion 94-09-7, Benzocaine 102-76-1, Triacetin 103-90-2, Acetaminophen 113-92-8 123-03-5, Cetylpyridinium chloride 124-90-3, Oxycodone hydrochloride 125-69-9, Dextromethorphan bromide 147-24-0, Diphenhydramine hydrochloride 345-78-8, Pseudoephedrine hydrochloride 357-08-4, Naloxone hydrochloride 437-38-7, Fentanyl 562-10-7 569-65-3, Meclizine 797-63-7, Levonorgestrel 1134-47-0, Baclofen 1197-21-3, Phentermine hydrochloride 1508-65-2, Oxybutynin hydrochloride 2216-51-5, L-Menthol 7232-21-5, Metoclopramide hydrochloride 7384-98-7, Propylene glycol dicaprylate 8050-81-5, Simethicone 9000-30-0, Guar gum 9000-40-2, Locust bean gum 9000-69-5, Pectin 9003-20-7, Polyvinyl acetate 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 9005-32-7, Alginic acid 9057-02-7, Pullulan 11138-66-2, Xanthan gum 12441-09-7D, Sorbitan, fatty acid esters 14611-52-0, Selegiline hydrochloride 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16679-58-6, Desmopressin 22071-15-4, Ketoprofen 22232-71-9, Mazindol 23828-92-4, Ambroxol hydrochloride 25322-68-3, Polyethylene oxide 27848-84-6, Nicergoline 28911-01-5, Triazolam 28981-97-7, Alprazolam 31565-12-5, Propylene glycol monocaprylate 34552-83-5, Loperamide hydrochloride 37220-82-9, Glycerol oleate 41100-52-1, Memantine hydrochloride 51481-61-9, Cimetidine 52485-79-7, Buprenorphine 56211-40-6, Torasemide 59729-32-7, Citalopram hydrobromide 64461-82-1, Tizanidine hydrochloride 66357-59-3, Ranitidine hydrochloride 71125-38-7, Meloxicam 72797-41-2, Tianeptine 73590-58-6, Omeprazole 76824-35-6, Famotidine 77883-43-3, Doxazosin mesylate 79794-75-5, Loratadine 82248-59-7, Atomoxetine hydrochloride 82626-48-0, Zolpidem 83480-29-9, Voglibose 83881-52-1, Cetirizine hydrochloride 84057-84-1, Lamotrigine 87333-19-5, Ramipril 90729-43-4, Ebastine 93479-97-1, Glimepiride 97240-79-4, Topiramate 99614-01-4, Ondansetron hydrochloride 99614-02-5, Ondansetron 100299-08-9, Pemirolast potassium 100643-71-8, Desloratadine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 106133-20-4, Tamsulosin 106266-06-2, Risperidone 109889-09-0, Granisetron 112885-41-3, Mosapride 119356-77-3, Dapoxetine 120011-70-3, Donepezil hydrochloride 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 132907-72-3, Ramosetron hydrochloride 139264-17-8, Zolmitriptan 139755-83-2, Sildenafil 140462-76-6, Olopatadine hydrochloride 144034-80-0, Rizatriptan 144689-63-4, Olmesartan medoxomil 151767-02-1, Montelukast sodium 153439-40-8, Fexofenadine hydrochloride 158966-92-8, Montelukast 170729-80-3, Aprepitant 171596-29-5, Tadalafil 171599-83-0, Sildenafil citrate 219861-08-2, Escitalopram oxalate

224785-91-5, Vardenafil hydrochloride 242478-38-2, Solifenacin succinate
246852-12-0, Amlodipine mesylate 268203-93-6, Udenafil 286930-03-8,
Fesoterodine fumarate 385367-47-5, Tarafenacin 823178-28-5
862189-96-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active
substance and its manufg. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active
substance and its manufg. method)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105873572 A	CN 2014-80071821	Register|Global Dossier
EP 3069716 A1	EP 2014-861454	Register|Federated Reg.
KR 1407922 B1	KR 2013-138040	Register|Global Dossier
US 20160279071 A1	US 2016-15036784	Register|Global Dossier
WO 2015072684 A1	WO 2014-KR10293	Register|Global Dossier

L4 ANSWER 40 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2014:2053394 CAPLUS Full-text
DOCUMENT NUMBER: 162:85982
TITLE: Lipid, protein, and/or cationic molecule coated pharmaceutically active particles and compositions comprising same
INVENTOR(S): Chawrai, Suresh; Prasad, Sudhanand; Bajaj, Kirti
PATENT ASSIGNEE(S): Vyome Biosciences Pvt. Ltd., India
ULTIMATE OWNER: VYOME THERAPEUTICS LIMITED
ULTIMATE OWNER STANDARD: Vyome
SOURCE: PCT Int. Appl., 221pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014195872	A1	20141211	WO 2014-IB61925	20140603
CA 2914583	A1	20141211	CA 2014-2914583	20140603
CA 2914583	C	20190618		

AU 2014276460	A1	20151224	AU 2014-276460		20140603
IL 242916	A	20160131	IL 2014-242916		20140603
KR 2016015335	A	20160212	KR 2015-7037272		20140603
KR 1814895	B1	20180104			
CN 105407718	A	20160316	CN 2014-80042031		20140603
CN 105407718	B	20190104			
EP 3003031	A1	20160413	EP 2014-739231		20140603
JP 2016523232	T	20160808	JP 2016-517716		20140603
BR 112015030501	A2	20170725	BR 2015-112015030501		20140603
NZ 714817	A	20170728	NZ 2014-714817		20140603
US 20160128944	A1	20160512	US 2015-14895738		20151203
MX 2015016675	A	20160715	MX 2015-16675		20151203
IN 2015CN07967	A	20160831	IN 2015-CN7967		20151224
AU 2017203374	A1	20170608	AU 2017-203374		20170519
AU 2018282407	A1	20190117	AU 2018-282407		20181221
PRIORITY APPLN. INFO.:			IN 2013-DE1684	A	20130604
			AU 2014-276460	A3	20140603
			WO 2014-IB61925	W	20140603
			AU 2017-203374	A3	20170519

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2014195872	A1	Dead	20201201
CA 2914583	A1	Dead	20221013
CA 2914583	C	Dead	20221013
AU 2014276460	A1	Dead	20201121
KR 2016015335	A	Alive	20201121
KR 1814895	B1	Alive	20201121
CN 105407718	A	Dead	20221117
CN 105407718	B	Dead	20221117
EP 3003031	A1	Dead	20210715
JP 2016523232	T	Alive	20201121
BR 112015030501	A2	Alive	20210729
NZ 714817	A	Dead	20210820
US 20160128944	A1	Dead	20210408
MX 2015016675	A	Alive	20201120
AU 2017203374	A1	Alive	20201121
AU 2018282407	A1	Dead	20210708

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2014:2053394

AB The invention provides species of lipid, protein, and/or cationic mol. coated active agents and compns. comprising the coated particles. The compns. can be personal care compns. such as anti-dandruff shampoo or conditioner, skin care compns., creams, gels, toothpastes, mouth washes, and chewing gums.

IPCI A01N0025-12 [I]; A01N0025-34 [I]; A01N0037-06 [I]; A01N0043-12 [I]; A01N0043-40 [I]; A01N0057-12 [I]; A01N0059-16 [I]; A61K0008-11 [I]; A61K0008-49 [I]; A61Q0005-00 [I]; A61K0031-44 [I]; A61Q0019-00 [I]; A61K0009-00 [I]; A61K0031-496 [I]

IPCR A01N0025-34 [I]; A01N0025-12 [I]; A01N0037-06 [I]; A01N0043-12 [I]; A01N0043-40 [I]; A01N0057-12 [I]; A01N0059-16 [I]; A61K0008-11 [I]; A61K0008-49 [I]; A61K0009-00 [I]; A61K0031-44 [I]; A61K0031-496 [I]; A61Q0005-00 [I]; A61Q0019-00 [I]

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 62

IT Actins
Albumins
Alkaloids
Aminoglycosides
Androgens
Antibodies and Immunoglobulins
Apricot kernel oil
Avocado oil
Blood proteins
Carbapenems
Carbohydrates
Caseins
Citronella oil
Coal tar
Coconut oil
Collagen hydrolyzates
Collagens

Conchiolins
Corticosteroids
Curcuminoids
Echinocandins
Egg yolk lecithins
Elastins
Estrogens
Ethoxylated hydrogenated castor oil
Fibroin
Fibronectins
Flavanoids
Flavonoids
Fructooligosaccharides
Galactooligosaccharides
Gelatin hydrolyzates
Glycerolipids
Glycerophospholipids
Glycopeptides
Glycosaminoglycans
Hemoglobins
Hydrocarbon oils
Immunoglobulin fragments
Indoles
Integrins
Keratins
Ketolides
Lactalbumins
Lipids
Macrolides
Milk proteins
Neem oil
Oligosaccharides
Oxazolidinones
Palmarosa oil
Paraffin oils
Peppermint oil
Peptide analogs
Peptides
Phosphatidic acids
Phosphatidylcholines
Phosphatidylethanolamines
Phosphatidylinositol 4,5-bisphosphate
Phosphatidylinositol 4-phosphate
Phosphatidylinositols
Phosphatidylinositols
Phosphatidylserines
Phospholipids
Podophyllum (resin)
Polyamines
Polyamines (nonpolymeric)
Polyketides
Polyoxyalkylenes
Polysaccharides
Progestogens
Pyrethroids
Reticulin
Retinoids
Sericin hydrolyzates
Sericins
Soya lecithins
Soybean proteins
Sphingolipids
Sterols
Sulfonamides
Sunflower oil
Sweet orange peel oil
Tetracyclines
Tocopherols
Zeins
β-Lactams
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)

(lipid and protein and/or cationic mol. coated pharmaceutically active particles and compns. comprising same)

IT 84625-61-6, Itraconazole 84957-29-9, Cefpirome 85233-19-8, 1,2-Bis(o-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid 85441-61-8, Quinapril 85622-93-1, Temozolomide 85650-52-8, Mirtazapine 85721-33-1, Ciprofloxacin 86003-55-6, Nikkomycin 86386-73-4, Fluconazole 86541-75-5, Benazepril 86697-97-4, Sensomer CT-250 87061-04-9 87239-81-4, Cefpodoxime proxetil 87848-99-5, Acrivastine 88040-23-7, Cefepime 88150-42-9, Amlodipine 89365-50-4, Salmeterol 91161-71-6, Terbinafine 91374-21-9, Ropinirole 91832-40-5, Cefdinir 92348-62-4, Hydroxycaprylic acid 92665-29-7, Cefprozil 93413-69-5, Venlafaxine 95058-81-4, Gemcitabine 96036-03-2, Meropenem 97321-87-4 97519-39-6, Ceftibuten 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 99011-02-6, Imiquimod 99592-32-2, Sertaconazole 99614-02-5, Ondansetron 100643-71-8, Desloratadine 100986-85-4, Levofloxacin 101828-21-1, Butenafine 103060-53-3, Daptomycin 103577-45-3, Lansoprazole 103775-14-0, Moexiprilat 104227-87-4, Famciclovir 104632-26-0, Pramipexole 105462-24-6, Risedronic acid 105956-97-6, Clinafloxacin 106133-20-4, Tamsulosin 106266-06-2, Risperidone 106392-12-5, Poloxamer 407 106516-24-9, Sertindole 106650-56-0, Sibutramine 106685-40-9, Adapalene 107233-08-9, Cevimeline 107753-78-6, Zafirlukast 108319-06-8, Temafloxacin 110871-86-8, Sparfloxacin 111025-46-8, Pioglitazone 111974-69-7, Quetiapine 112362-50-2, Dalfopristin 112809-51-5, Letrozole 112811-59-3, Gatifloxacin 112965-21-6, Calcipotriene 113170-55-1 113665-84-2, Clopidogrel 113775-47-6, Dexmedetomidine 113806-05-6, Olopatadine 114798-26-4, Losartan 115103-54-3, Tiagabine 115256-11-6, Dofetilide 115956-12-2, Dolasetron 116539-59-4, Duloxetine 117467-28-4, Cefditoren pivoxil 117976-89-3, Rabeprazole 118292-40-3, Tazarotene 119141-88-7, Esomeprazole 119914-60-2, Grepafloxacin 120014-06-4, Donepezil 120138-50-3, Quinupristin 120279-96-1, Dorzolamide 120511-73-1, Anastrozole 121028-76-0 121708-81-4 123441-03-2, Rivastigmine 124937-51-5, Tolterodine 127045-41-4, Pazufloxacin 127254-12-0, Sitafloxacin 128196-01-0, Escitalopram 129618-40-2, Nevirapine 129639-79-8 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 132781-92-1 134678-17-4, Lamivudine 135729-61-2, Palonosetron 136470-78-5, Abacavir 136817-59-9, Delavirdine 137234-62-9, Voriconazole 138402-11-6, Irbesartan 139264-17-8, Zolmitriptan 139755-83-2, Sildenafil 141388-76-3, Besifloxacin 142340-99-6, Adefovir dipivoxil 143322-58-1, Eletriptan 143491-57-0, Emtricitabine 144034-80-0, Rizatriptan 144377-73-1, Linoleamidopropyl PG-dimonium chloride phosphate 144494-65-5, Tirofiban 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 145158-71-0, Tegaserod 146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 150378-17-9, Indinavir 151096-09-2, Moxifloxacin 151319-34-5, Zaleplon 151581-81-6, Pradimicin 152459-95-5, Imatinib 154323-57-6, Almotriptan 154592-20-8, Copper pyrithione 156259-68-6, Capmul MCM 159989-64-7, Nelfinavir 161465-32-3, Elaidolinolenyl alcohol 162011-90-7, Rofecoxib 162808-62-0, Caspofungin 165800-03-3, Linezolid 166663-25-8, Anidulafungin 169590-42-5, Celecoxib 170729-80-3, Aprepitant 171228-49-2, POsaconazole 171596-29-5, Tadalafil 175357-18-3 175463-14-6, Gemifloxacin 177933-73-2D, AMP (acrylate polymer), allyl methacrylate copolymer 179463-17-3, Cancidas 182760-06-1, Ravuconazole 184475-35-2, Gefitinib 187949-02-6, Albaconazole 188627-80-7, Eptifibatide 191114-48-4, Telithromycin 194804-75-6 195868-36-1, Phenyl trimethicone 198904-31-3, Atazanavir 201341-05-1, Tenofovir disoproxil 201531-68-2D, Pyridazinone, dimorpholino deriv. 220222-14-0, Lithium pyrithione 220222-18-4, Strontium pyrithione 224785-90-4, Vardenafil 226256-56-0, Cinacalcet 235114-32-6, Micafungin 241479-67-4, Isavuconazole 313998-09-3, Gold pyrithione 351420-48-9 351420-50-3 374629-79-5 433711-29-6, Carbopol Aqua SF 1 463965-85-7, Behentrimonium methosulfate 506412-91-5 577746-42-0 608514-56-3 830331-83-4 881038-57-9, Zinc selenide sulfide 915764-71-5 951216-62-9 1477911-63-9, Dimethicone PEG-7 Isostearate 1639929-04-6

RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lipid and protein and/or cationic mol. coated pharmaceutically active particles and compns. comprising same)

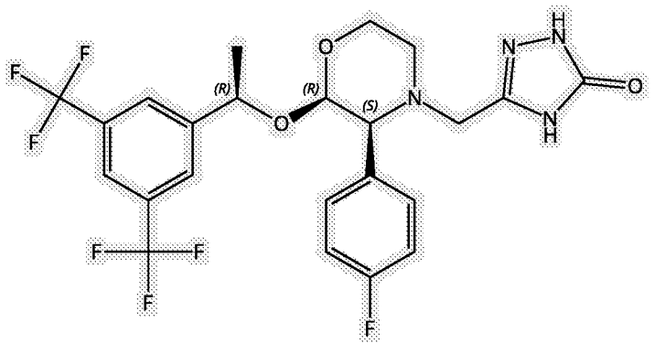
IT 170729-80-3, Aprepitant

RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)
(lipid and protein and/or cationic mol. coated pharmaceutically active particles and compns. comprising same)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2014276460 A1	AU 2014-276460	Register
AU 2017203374 A1	AU 2017-203374	Register
AU 2018282407 A1	AU 2018-282407	Register
BR 112015030501 A2	BR 2015-112015030501	Register
CA 2914583 A1	CA 2014-2914583	Register
CA 2914583 C	CA 2014-2914583	Register
CN 105407718 A	CN 2014-80042031	Register|Global Dossier
CN 105407718 B	CN 2014-80042031	Register|Global Dossier
EP 3003031 A1	EP 2014-739231	Register|Federated Reg.
IL 242916 A	IL 2014-242916	Register
IN 2015CN07967 A	IN 2015-CN7967	Register
JP 2016523232 T	JP 2016-517716	Register|Global Dossier
KR 1814895 B1	KR 2015-7037272	Register|Global Dossier
KR 2016015335 A	KR 2015-7037272	Register|Global Dossier
MX 2015016675 A	MX 2015-16675	Register
NZ 714817 A	NZ 2014-714817	Register
US 20160128944 A1	US 2015-14895738	Register|Global Dossier
WO 2014195872 A1	WO 2014-IB61925	Register|Global Dossier

L4 ANSWER 41 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN

ACCESSION NUMBER: 2014:1944702 CAPLUS Full-text

DOCUMENT NUMBER: 164:453599

TITLE: Statistical investigation of simulated intestinal fluid composition on the equilibrium solubility of biopharmaceutics classification system class II drugs

AUTHOR(S): Khadra, Ibrahim; Zhou, Zhou; Dunn, Claire; Wilson, Clive G.; Halbert, Gavin

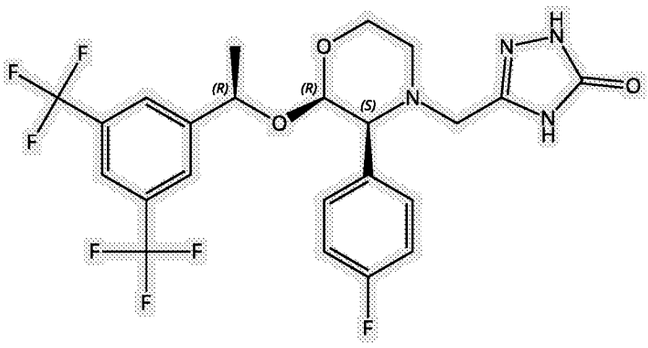
CORPORATE SOURCE: Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G4 0RE, UK

SOURCE: European Journal of Pharmaceutical Sciences (2015), 67, 65-75
CODEN: EPSCED; ISSN: 0928-0987

DIGITAL OBJECT ID: 10.1016/j.ejps.2014.10.019

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB A drug's soly. and dissoln. behavior within the gastrointestinal tract is a key property for successful administration by the oral route and one of the key factors in the biopharmaceutics classification system. This property can be detd. by investigating drug soly. in human intestinal fluid (HIF) but this is difficult to obtain and highly variable, which has led to the development of multiple simulated intestinal fluid (SIF) recipes. Using a statistical design of expt. (DoE) technique this paper has investigated the effects and interactions on equil. drug soly. of seven typical SIF components (sodium taurocholate, lecithin, sodium phosphate, sodium chloride, pH, pancreatin and sodium oleate) within concn. ranges relevant to human intestinal fluid values. A range of poorly sol. drugs with acidic (naproxen, indomethacin, phenytoin, and piroxicam), basic (aprepitant, carvedilol, zafirlukast, tadalafil) or neutral (fenofibrate, griseofulvin, felodipine and probucol) properties have been investigated. The equil. soly. results detd. are comparable with literature studies of the drugs in either HIF or SIF indicating that the DoE is operating in the correct space. With the exception of pancreatin, all of the factors individually had a statistically significant influence on equil. soly. with variations in magnitude of effect between the acidic and basic or neutral compds. and drug specific interactions were evident. Interestingly for the neutral compds. pH was the factor with the second largest soly. effect. Around one third of all the possible factor combinations showed a significant influence on equil. soly. with variations in interaction significance and magnitude of effect between the acidic and basic or neutral compds. The least no. of significant media component interactions were noted for the acidic compds. with three and the greatest for the neutral compds. at seven, with again drug specific effects evident. This indicates that a drug's equil. soly. in SIF is influenced depending upon drug type by between eight to fourteen individual or combinations of media components with some of these drug specific. This illustrates the complex nature of these fluids and provides for individual drugs a visualisation of the possible soly. envelope within the gastrointestinal tract, which may be of importance for modeling in vivo behavior. In addn. the results indicate that the design of expt. approach can be employed to provide greater detail of drug soly. behavior, possible drug specific interactions and influence of variations in gastrointestinal media components due to disease. The approach is also feasible and amenable to adaptation for high throughput screening of drug candidates.
CC 63-5 (Pharmaceuticals)
IT 53-86-1, Indomethacin 57-41-0, Phenytoin 126-07-8, Griseofulvin 22204-53-1, Naproxen 23288-49-5, Probucol 36322-90-4, Piroxicam 49562-28-9, Fenofibrate 72509-76-3, Felodipine 72956-09-3, Carvedilol 107753-78-6, Zafirlukast 170729-80-3, Aprepitant 171596-29-5, Tadalafil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated intestinal fluid compn. on equil. soly. of biopharmaceutics classification system class II drugs)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statistical investigation of simulated intestinal fluid compn. on equil. soly. of biopharmaceutics classification system class II drugs)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 53 THERE ARE 53 CAPLUS RECORDS THAT CITE THIS RECORD (53 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2014:1014062 CAPLUS Full-text
DOCUMENT NUMBER: 161:132468
TITLE: Orally disintegrating film comprising pharmacologically active substance and its manufacturing method
INVENTOR(S): Oh, Dong Hun; Lee, Jin Hu; Lee, So I.; Kang, Jun Hyeok; Lim, Chae Yun; Jung, Gyeong Tae; Yeon, Gyu Jeong; Park, Jin Gyu
PATENT ASSIGNEE(S): Seoul Pharmaceutical Co., Ltd., S. Korea
ULTIMATE OWNER: SEOUL PHARMA. CO., LTD.
ULTIMATE OWNER STANDARD: SEOUL PHARMA. CO., LTD.
SOURCE: Repub. Korea, 15pp.
CODEN: KRXXFC
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 1407922	B1	20140617	KR 2013-138040	20131114
WO 2015072684	A1	20150521	WO 2014-KR10293	20141030
CN 105873572	A	20160817	CN 2014-80071821	20141030
EP 3069716	A1	20160921	EP 2014-861454	20141030
US 20160279071	A1	20160929	US 2016-15036784	20160513

PRIORITY APPLN. INFO.: KR 2013-138040 A 20131114
WO 2014-KR10293 W 20141030

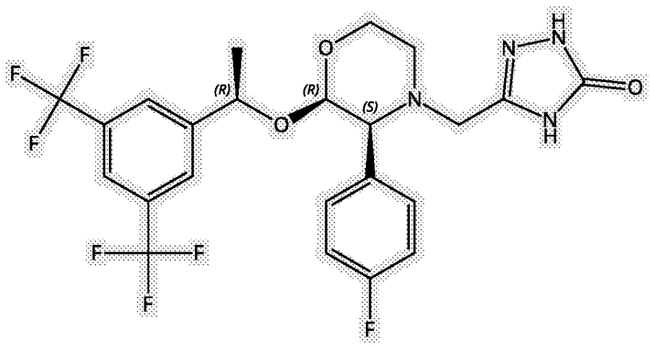
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
KR 1407922	B1	Dead	20201121
WO 2015072684	A1	Dead	20201202
CN 105873572	A	Dead	20201121
EP 3069716	A1	Dead	20201203
US 20160279071	A1	Dead	20201121

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASFORMULTNS 2014:1014062
AB The title film has porosity of 10-35%, and contains more than one bubbling agent selected from nonionic surfactant, cationic surfactant, anionic surfactant and zwitterionic surfactant, more than one bubble stabilizer selected from pullulan, hydroxypropyl Me cellulose, polyvinyl acetate, polyethylene oxide, xanthan gum, guar gum, locust bean gum, starch, starch deriv., pectin, pectin hydrolyzate, alginic acid and alginic acid hydrolyzate, more than one plasticizer selected from glycerin, glycerol oleate, medium chain fatty acid, polyethylene glycol, propylene glycol, propylene glycol monocaprylate, propylene glycol dicaprylate, sugar, sugar

alc. and triacetin, and pharmacol. active substance.
IPCI A61K0009-70 [I]; A61P0003-10 [I]; A61P0003-04 [I]
IPCR A61K0009-70 [I]; A61P0003-04 [I]; A61P0003-10 [I]
CC 63-6 (Pharmaceuticals)
IT Alditols
Enzymes
Hormones, animal
Lecithins
Medium-chain fatty acids
Polyoxyalkylenes
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active substance and its manufg. method)
IT 50-02-2, Dexamethasone 50-58-8, Phendimetrazine tartrate 50-81-7, L-Ascorbic acid, biological studies 54-11-5, Nicotine 55-63-0, Nitroglycerin 56-81-5, Glycerin, biological studies 56-81-5D, Glycerin, fatty acid esters 57-50-1, Sugar, biological studies 57-50-1D, Sucrose, fatty acid esters 57-55-6, Propylene glycol, biological studies 58-08-2, Caffeine, biological studies 61-76-7, Phenylephrine hydrochloride 90-84-6, Diethylpropion 94-09-7, Benzocaine 102-76-1, Triacetin 103-90-2, Acetaminophen 113-92-8 123-03-5, Cetylpyridinium chloride 124-90-3, Oxycodone hydrochloride 125-69-9, Dextromethorphan bromide 147-24-0, Diphenhydramine hydrochloride 345-78-8, Pseudoephedrine hydrochloride 357-08-4, Naloxone hydrochloride 437-38-7, Fentanyl 562-10-7 569-65-3, Meclizine 797-63-7, Levonorgestrel 1134-47-0, Baclofen 1197-21-3, Phentermine hydrochloride 1508-65-2, Oxybutynin hydrochloride 2216-51-5, L-Menthol 7232-21-5, Metoclopramide hydrochloride 7384-98-7, Propylene glycol dicaprylate 8050-81-5, Simethicone 9000-30-0, Guar gum 9000-40-2, Locust bean gum 9000-69-5, Pectin 9003-20-7, Polyvinyl acetate 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 9005-32-7, Alginic acid 9057-02-7, Pullulan 11138-66-2, Xanthan gum 12441-09-7D, Sorbitan, fatty acid esters 14611-52-0, Selegiline hydrochloride 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16679-58-6, Desmopressin 22071-15-4, Ketoprofen 22232-71-9, Mazindol 23828-92-4, Ambroxol hydrochloride 25322-68-3, Polyethylene oxide 27848-84-6, Nicergoline 28911-01-5, Triazolam 28981-97-7, Alprazolam 31565-12-5, Propylene glycol monocaprylate 34552-83-5, Loperamide hydrochloride 37220-82-9, Glycerol oleate 41100-52-1, Memantine hydrochloride 51481-61-9, Cimetidine 52485-79-7, Buprenorphine 56211-40-6, Torasemide 59729-32-7, Citalopram hydrobromide 64461-82-1, Tizanidine hydrochloride 66357-59-3, Ranitidine hydrochloride 71125-38-7, Meloxicam 72797-41-2, Tianeptine 73590-58-6, Omeprazole 76824-35-6, Famotidine 77883-43-3, Doxazosin mesylate 79794-75-5, Loratadine 82248-59-7, Atomoxetine hydrochloride 83480-29-9, Voglibose 83881-52-1, Cetirizine hydrochloride 84057-84-1, Lamotrigine 87333-19-5, Ramipril 90729-43-4, Ebastine 93479-97-1, Glimepiride 97240-79-4, Topiramate 99614-01-4, Ondansetron hydrochloride 99614-02-5, Ondansetron 100299-08-9, Pemirolast potassium 100643-71-8, Desloratadine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 106133-20-4, Tamsulosin 106266-06-2, Risperidone 109889-09-0, Granisetron 112885-41-3, Mosapride 119356-77-3, Dapoxetine 120011-70-3, Donepezil hydrochloride 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 132907-72-3, Ramosetron hydrochloride 139264-17-8, Zolmitriptan 139755-83-2, Sildenafil 140462-76-6, Olopatadine hydrochloride 144034-80-0, Rizatriptan 144689-63-4, Olmesartan medoxomil 151767-02-1, Montelukast sodium 153439-40-8, Fexofenadine hydrochloride 158966-92-8, Montelukast 170729-80-3, Aprepitant 171596-29-5, Tadalafil 171599-83-0, Sildenafil citrate 219861-08-2, Escitalopram oxalate 224785-91-5, Vardenafil hydrochloride 242478-38-2, Solifenacin succinate 246852-12-0, Amlodipine mesylate 268203-93-6, Udenafil 286930-03-8, Fesoterodine fumarate 385367-47-5, Tarafenacin 823178-28-5 862189-96-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active substance and its manufg. method)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating porous film comprising pharmacol. active

substance and its manufg. method)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CN 105873572 A	CN 2014-80071821	Register|Global Dossier
EP 3069716 A1	EP 2014-861454	Register|Federated Reg.
KR 1407922 B1	KR 2013-138040	Register|Global Dossier
US 20160279071 A1	US 2016-15036784	Register|Global Dossier
WO 2015072684 A1	WO 2014-KR10293	Register|Global Dossier

L4 ANSWER 43 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2014:38255 CAPLUS Full-text
DOCUMENT NUMBER: 160:166366
TITLE: Preparation of stable injectable pharmaceutical compositions of neurokinin 1 receptor antagonist
INVENTOR(S): Karavas, Evangelos; Koutris, Efthimos; Bikiaris, Dimitrios; Chatidou, Sotiria; Diakidou, Amalia; Barmpalexis, Panagiotis; Konstanti, Louiza; Minioti, Katerina
PATENT ASSIGNEE(S): Pharmathen S.A., Greece
ULTIMATE OWNER: PARTNERS GROUP HOLDING AG
ULTIMATE OWNER STANDARD: Partners Group
SOURCE: PCT Int. Appl., 24pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014005606	A1	20140109	WO 2012-EP2854	20120706
EP 2866797	A1	20150506	EP 2012-756353	20120706
EP 2866797	B1	20200429		
RS 60599	B1	20200831	RS 2020-846	20120706
ES 2798103	T3	20201209	ES 2012-756353	20120706
US 20150165045	A1	20150618	US 2014-14412147	20141230
US 20200237920	A1	20200730	US 2020-16851779	20200417

PRIORITY APPLN. INFO.:

EP 2012-756353	A3	20120706
WO 2012-EP2854	W	20120706
US 2014-14412147	A1	20141230

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE

WO 2014005606	A1	Dead	20201202
EP 2866797	A1	Indeterminate	20201106
EP 2866797	B1	Indeterminate	20201107
RS 60599	B1	Alive	20201121
ES 2798103	T3	Alive	20201217
US 20150165045	A1	Dead	20220105
US 20200237920	A1	Dead	20231109

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2014:38255

AB The present invention relates to a controlled release sterile injectable formulation in the form of soln., suspension or sol-gel formulation for i.m. or s.c. administration comprising a therapeutically effective amt. of a neurokinin 1 receptor antagonist, in particular aprepitant or fosaprepitant or pharmaceutical acceptable salts, derivs. or metabolites thereof. It also relates to a process for developing such formulations. Thus, an aq. ready-to-use soln. comprised fosaprepitant dimeglumine 142.7, and HPMC-K100 6.7 g/L and water for injection qs to 1 L.

IPCI A61K0031-165 [I]; A61K0009-00 [I]

IPCR A61K0009-00 [I]; A61K0031-165 [I]

CC 63-6 (Pharmaceuticals)

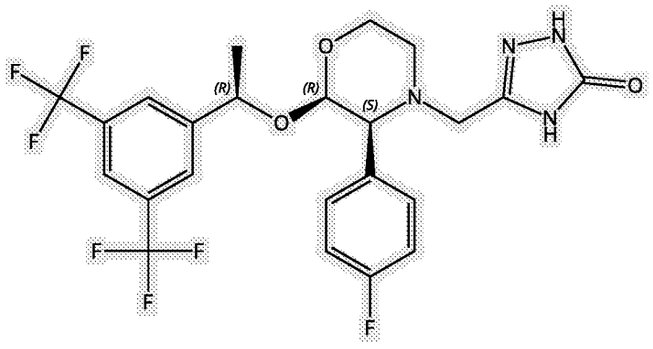
IT Castor oil
Cottonseed oil
Gelatins
Lecithins
Polymers
Polyoxyalkylenes
Sesame oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)

IT 170729-80-3, Aprepitant 172673-20-0 265121-04-8, Fosaprepitant dimeglumine
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)

IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable injectable pharmaceutical compns. of neurokinin 1 receptor antagonist)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

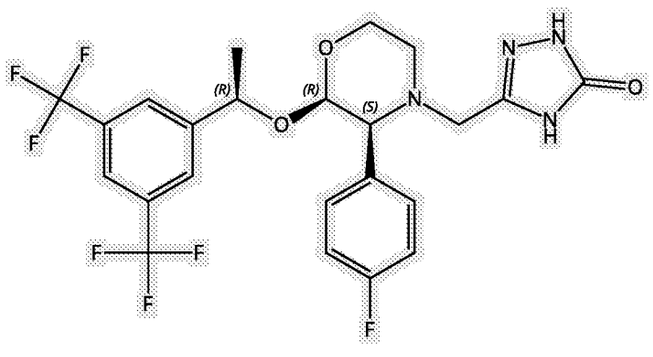
LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
EP 2866797 A1	EP 2012-756353	Register|Federated Reg.
EP 2866797 B1	EP 2012-756353	Register|Federated Reg.
ES 2798103 T3	ES 2012-756353	Register
RS 60599 B1	RS 2020-846	Register
US 20150165045 A1	US 2014-14412147	Register|Global Dossier
US 20200237920 A1	US 2020-16851779	Register|Global Dossier
WO 2014005606 A1	WO 2012-EP2854	Register|Global Dossier

L4 ANSWER 44 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2013:496643 CAPLUS Full-text
DOCUMENT NUMBER: 159:140262
TITLE: Preparation of aprepitant emulsion for intravenous injection
AUTHOR(S): Zhou, Wei; Chen, Fei; Chen, Ning; Mao, Ke
CORPORATE SOURCE: School of Pharmaceutical, Jiangsu Provincial Institute of Materia Medica, Nanjing University of Technology, Nanjing, Jiangsu Province, 211816, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2012), 43(12), 1003-1006
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The formulation of aprepitant emulsion for i.v. injection was optimized by single factor test and orthogonal design. The properties, such as appearance, particle size, ζ potential and stability of the product were investigated. The results showed that the type and amt. of emulsifier as well as the amt. of oleic acid had the greater effect on stability. The optimal formulation of aprepitant emulsion was as follows: aprepitant was 0.25%, soybean oil was 15%, egg yolk lecithin ESO was 2.5% and oleic acid was 0.125%. The appearance of the product was ivory. The av. particle size, PDI, centrifugal stability const. (Ke), ζ potential, pH value and drug content of the product before and after sterilization were (215.71±1.26) and (220.3±0.53) nm, 0.203±0.016 and 0.210±0.009, 0.21±0.01 and 0.34±0.01, (-37.5±0.2) and (-37.6±0.5) mV, 7.21±0.23 and 7.31±0.30, (101.03±0.89)% and (101.12±1.20)%, resp.

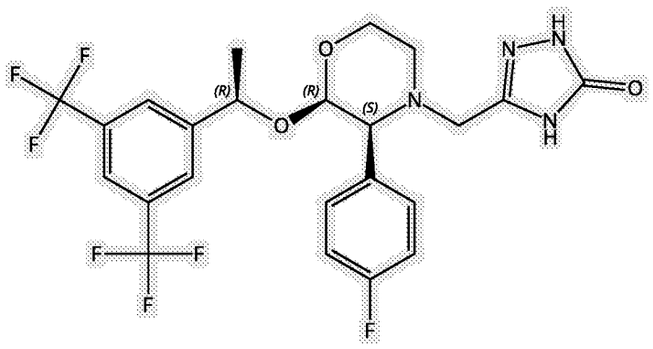
CC 63-6 (Pharmaceuticals)
IT Egg yolk lecithins
Soybean oil
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of aprepitant emulsion for i.v. injection)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of aprepitant emulsion for i.v. injection)
IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of aprepitant emulsion for i.v. injection)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

L4 ANSWER 45 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2010:1100829 CAPLUS Full-text
DOCUMENT NUMBER: 153:415489
TITLE: Simulating Fasted Human Intestinal Fluids: Understanding the Roles of Lecithin and Bile Acids
AUTHOR(S): Soederlind, Erik; Karlsson, Eva; Carlsson, Anders; Kong, Rui; Lenz, Anna; Lindborg, Sara; Sheng, Jennifer J.
CORPORATE SOURCE: Pharmaceutical Development, AstraZeneca, Moelndal, Swed.
SOURCE: Molecular Pharmaceutics (2010), 7(5), 1498-1507
CODEN: MPOHBP; ISSN: 1543-8384
DIGITAL OBJECT ID: 10.1021/mp100144v
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this work is to evaluate the roles of lecithin and bile salts in a new generation of fasted simulated small intestinal fluid (FaSSIF-II), thus enhancing the closer mimic of simulated fluids to the real human intestinal fluids (HIF) in drug discovery and drug product development. To assess the effects of lecithin in FaSSIF-II, soly. studies were conducted at 37 °C using four media including first generation simulated intestinal fluid (FaSSIF-I), FaSSIF-II, phosphate pH 6.5 buffer, and HIF. A total of 24 model compds. representing a wide range of biopharmaceutic properties were included. The drug soly. values measured in the FaSSIF-II were compared with those in FaSSIF-I, pH 6.5 buffer and HIF. To assess the effects of bile acids, soly. was measured for 4 compds. in the FaSSIF-I contg. five different bile acids of various concns. The lecithin concn. in the FaSSIF-II is lowered from 0.75 mM to 0.2 mM. The results suggested that the FaSSIF-II is a better medium to reflect HIF, compared with pH 6.5 phosphate buffer and FaSSIF-I. Soly. of neutral compds. including atovaquone, carbamazepine, cyclosporine, danazol, diethylstilbestrol, felodipine, griseofulvin and probucol in FaSSIF-II showed improvement in predicting the in vivo soly. The relative std. deviation (SD) of soly. measurement in FaSSIF-II is comparable with FaSSIF-I. For the acidic and basic tested compds., the FaSSIF-II performs similarly to the FaSSIF-I. Exptl. results showed that the level of bile salts typically is less than 5 mM under fasted state. Among the five studied bile acids, the conjugation (glycine or taurine) has no impact on the drug solubilization, while there may be a minimal effect of the degree of hydroxylation of the steroid ring system on solubilization. The lecithin concn. of 0.2 mM in FaSSIF-II has been demonstrated to closely represent HIF, for both neutral and ionizable compds. In the compn. of simulated intestinal fluids, the structure of bile acids has minimal effect, providing the flexibility of choosing one bile salt to represent complex in vivo bile acids.
CC 63-5 (Pharmaceuticals)
ST intestine fluid human lecithin bile acid drug soly
IT Artificial intestinal juice
Dissolution
Human
Hydroxylation
Intestinal juice
Solubility
Solubilization
(simulating fasted human intestinal fluids, roles of lecithin and bile acids)
IT Bile acids
Egg yolk lecithins
Phosphatidylcholines
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(simulating fasted human intestinal fluids, roles of lecithin and bile acids)
IT 81-24-3, Taurocholic acid 145-42-6, Sodium taurocholate 360-65-6, Glycodeoxycholic acid 475-31-0, Glycocholic acid 516-50-7, Taurodeoxycholic acid 640-79-9, Glycochenodeoxycholic acid
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(simulating fasted human intestinal fluids, roles of lecithin and bile acids)

IT 56-53-1, Diethylstilbestrol 57-66-9, Probenecid 58-32-2, Dipyridamole
68-26-8, Retinol 81-81-2, Warfarin 126-07-8, Griseofulvin 298-46-4,
Carbamazepine 530-78-9, Flufenamic acid 599-79-1, Sulfasalazine
1951-25-3, Amiodarone 15307-86-5, Diclofenac 17230-88-5, Danazol
23288-49-5, Probucol 29094-61-9, Glipizide 36322-90-4, Piroxicam
50679-08-8, Terfenadine 51803-78-2, Nimesulide 59865-13-3, Cyclosporin
A 65277-42-1, Ketoconazole 72509-76-3, Felodipine 72956-09-3,
Carvedilol 95233-18-4, Atovaquone 138402-11-6, Irbesartan
168273-06-1, Rimonabant 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(simulating fasted human intestinal fluids, roles of lecithin
and bile acids)
IT 170729-80-3, Aprepitant
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(simulating fasted human intestinal fluids, roles of lecithin
and bile acids)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX
NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS
RECORD (24 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 46 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2006:142759 CAPLUS Full-text
DOCUMENT NUMBER: 144:239925
TITLE: Solid carriers for improved delivery of active
ingredients containing surfactants and glycerides
INVENTOR(S): Patel, Mahesh
PATENT ASSIGNEE(S): USA
ULTIMATE OWNER: LIPOCINE INC.
ULTIMATE OWNER STANDARD: Lipocine
SOURCE: U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S.
Ser. No. 428,341.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060034937	A1	20060216	US 2005-196805	20050802
US 6248363	B1	20010619	US 1999-447690	19991123
CA 2706113	A1	20010531	CA 2000-2706113	20001122
US 20030064097	A1	20030403	US 2001-800593	20010306
US 6569463	B2	20030527		

US 20030215496	A1	20031120	US 2003-428341		20030501
US 6923988	B2	20050802			
WO 2007018943	A2	20070215	WO 2006-US27159		20060712
WO 2007018943	A3	20090507			
US 20090074859	A1	20090319	US 2008-326711		20081202
JP 2012116863	A	20120621	JP 2012-29635		20120214
US 20140357586	A1	20141204	US 2014-14460188		20140814
US 20150224130	A9	20150813			
US 20150273067	A1	20151001	US 2015-14713692		20150515
US 20180125978	A1	20180510	US 2017-15625764		20170616
US 20200061191	A1	20200227	US 2019-16289565		20190228
US 20210008212	A1	20210114	US 2020-16917731		20200630
PRIORITY APPLN. INFO.:			US 1999-447690	A3	19991123
			US 2001-800593	A1	20010306
			US 2003-428341	A2	20030501
			CA 2000-2391923	A3	20001122
			JP 2001-539423	A3	20001122
			US 2002-159601	A2	20020530
			US 2005-196805	A	20050802
			US 2008-326711	A1	20081202
			US 2014-14460188	A1	20140814
			US 2017-15625764	A1	20170616
			US 2019-16289565	A1	20190228

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20060034937	A1	Dead	20201107
US 6248363	B1	Dead	20201107
CA 2706113	A1	Dead	20201121
US 20030064097	A1	Dead	20201106
US 6569463	B2	Dead	20201106
US 20030215496	A1	Dead	20201106
US 6923988	B2	Dead	20201107
WO 2007018943	A2	Dead	20201201
WO 2007018943	A3	Dead	20201201
US 20090074859	A1	Dead	20201107
JP 2012116863	A	Alive	20201121
US 20140357586	A1	Dead	20201107
US 20150224130	A9	Dead	20201107
US 20150273067	A1	Dead	20201107
US 20180125978	A1	Dead	20201106
US 20200061191	A1	Dead	20201106
US 20210008212	A1	Dead	20210128

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2006:142759

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritional agents, cosmeceuticals and diagnostic agents. For example, particles contained glyburide, PEG stearate, glycerol monolaurate, and Nonpareil seed.

INCL 424497000

IPCI A61K0009-50 [I]; A61K0009-16 [I]

IPCR A61K0009-50 [I]; A61K0009-16 [I]

NCL 424/497.000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 18, 62

IT Lecithins
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

IT Diglycerides

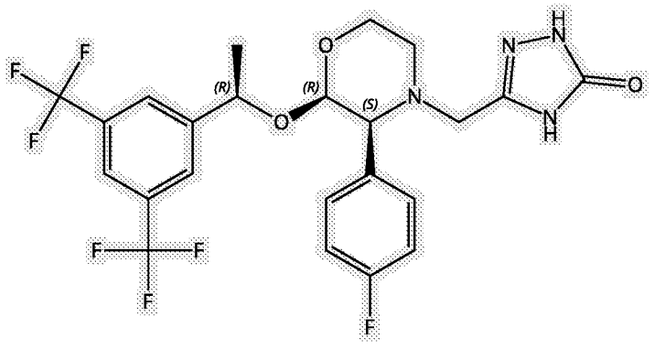
Ethoxylated hydrogenated castor oil
Glycerides
Lecithins
Oligopeptides
Peptides
Polyoxyalkylenes
Safflower oil
Sterols
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

IT 50-35-1, Thalidomide 50-49-7, Imipramine 52-01-7, Spironolactone
52-86-8, Haloperidol 53-03-2, Prednisone 53-39-4, Oxandrolone
57-83-0, Progesterone, biological studies 67-20-9, Nitrofurantoin
81-24-3 83-44-3, Deoxycholic acid 87-69-4D, Tartaric acid, esters
112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 124-07-2,
Octanoic acid, biological studies 145-42-6, Sodium taurocholate
151-41-7, Lauryl sulfate 302-79-4, Tretinoin 303-98-0, Coenzyme Q10
321-64-2, Tacrine 334-48-5, Decanoic acid 357-70-0, Galantamine
511-12-6, Dihydroergotamine 541-15-1D, Carnitine, analogs and derivs.
577-11-7, Sodium docusate 595-33-5, Megestrol acetate 1622-61-3,
Clonazepam 1972-08-3, Dronabinol 2644-64-6, DPPC 5633-20-5,
Oxybutynin 5786-21-0, Clozapine 5949-44-0, Testosterone undecanoate
9002-96-4 9003-39-8, PVP K30 9004-65-3, Hydroxypropyl methylcellulose
9004-96-0, Crodet O 100 9005-32-7D, Alginic acid, salts 9005-37-2,
Propylene glycol alginate 9005-38-3, Sodium alginate 9005-63-4,
Polyoxyethylene sorbitan 9005-64-5, PEG sorbitan monolaurate
9005-65-6, PEG sorbitan monooleate 9009-32-9, Polyglyceryl stearate
10041-19-7 10238-21-8, Glyburide 10540-29-1, Tamoxifen 11140-04-8,
Imwitor 988 14440-80-3, Stearyl lactylate 18656-38-7, DMPC
21256-18-8, Oxaprozin 25086-15-1, Eudragit L100 25322-68-3,
Polyethylene glycol 25322-68-3D, esters 25618-55-7, Polyglycerol
26545-74-4 27215-38-9, Monomuls 90-45 28721-07-5, Oxacarbazepine
29975-16-4, Estazolam 31566-31-1, Imwitor 191 34911-55-2, Bupropion
37220-82-9, Peceol 47931-85-1, Salmon calcitonin 49562-28-9,
Fenofibrate 51322-75-9, Tizanidine 51333-22-3, Budesonide
53123-88-9, Sirolimus 55142-85-3, Ticlopidine 63675-72-9, Nisoldipine
68475-42-3, Anagrelide 70458-96-7, Norfloxacin 71125-38-7, Meloxicam
72509-76-3, Felodipine 72956-09-3, Carvedilol 73590-58-6, Omeprazole
73963-72-1, Cilostazol 74504-64-6, Polyglyceryl laurate 75330-75-5,
Lovastatin 75695-93-1, Isradipine 77337-76-9, Acamprosate
79902-63-9, Simvastatin 81103-11-9, Clarithromycin 82410-32-0,
Ganciclovir 84057-84-1, Lamotrigine 84449-90-1, Raloxifene
84625-61-6, Itraconazole 87333-19-5, Ramipril 88150-42-9, Amlodipine
91374-21-9, Ropinirole 100427-26-7, Lercanidipine 100986-85-4,
Levofloxacin 103577-45-3, Lansoprazole 104987-11-3, Tacrolimus
106266-06-2, Risperidone 106308-44-5, Rufinamide 106392-12-5,
Oxyethylene-oxypropylene block copolymer 107724-20-9, Eplerenone
107753-78-6, Zafirlukast 111025-46-8, Pioglitazone 112811-59-3,
Gatifloxacin 115103-54-3, Tiagabine 124937-51-5, Tolterodine
127779-20-8, Saquinavir 127829-97-4, Solulan C-24 129318-43-0,
Alendronate sodium 129722-12-9, Aripiprazole 130929-57-6, Entacapone
132539-06-1, Olanzapine 133040-01-4, Eprosartan 134308-13-7, Tolcapone
134523-00-5, Atorvastatin 137862-53-4, Valsartan 139755-83-2,
Sildenafil 145158-71-0, Tegaserod 146478-45-7, Polyglycerol dioleate
146939-27-7, Ziprasidone 147536-97-8, Bosentan 154598-52-4, Efavirenz
156259-68-6, Capmul MCM 162011-90-7, Rofecoxib 169590-42-5, Celecoxib
170729-80-3, Aprepitant 174392-00-8, Polyglyceryl monooleate
197179-53-6, Nonpareil
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

IT 170729-80-3, Aprepitant
RL: COS (Cosmetic use); FFD (Food or feed use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients contg. surfactants and glycerides)

RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phen
yl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX

NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 162 THERE ARE 162 CAPLUS RECORDS THAT CITE THIS RECORD (272 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
CA 2706113 A1	CA 2000-2706113	Register
JP 2012116863 A	JP 2012-29635	Register|Global Dossier
US 6248363 B1	US 1999-447690	Register
US 20030064097 A1	US 2001-800593	Register
US 6569463 B2	US 2001-800593	Register
US 20030215496 A1	US 2003-428341	Register|Global Dossier
US 6923988 B2	US 2003-428341	Register|Global Dossier
US 20060034937 A1	US 2005-196805	Register|Global Dossier
US 20090074859 A1	US 2008-326711	Register|Global Dossier
US 20140357586 A1	US 2014-14460188	Register|Global Dossier
US 20150224130 A9	US 2014-14460188	Register|Global Dossier
US 20150273067 A1	US 2015-14713692	Register|Global Dossier
US 20180125978 A1	US 2017-15625764	Register|Global Dossier
US 20200061191 A1	US 2019-16289565	Register|Global Dossier
US 20210008212 A1	US 2020-16917731	Register|Global Dossier
WO 2007018943 A2	WO 2006-US27159	Register|Global Dossier
WO 2007018943 A3	WO 2006-US27159	Register|Global Dossier

L4 ANSWER 47 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2005:1311702 CAPLUS Full-text
DOCUMENT NUMBER: 144:57525
TITLE: Coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents
INVENTOR(S): Wilson, Michelle; Desai, Kishorkumar J.; Pauletti, Giovanni M.; Antoon, Mitchell K.; Clendening, Chris E.
PATENT ASSIGNEE(S): UMD, Inc., USA
ULTIMATE OWNER: U M D
ULTIMATE OWNER STANDARD: U M D
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 126,863
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050276836	A1	20051215	US 2005-180076	20050712
US 6197327	B1	20010306	US 1998-79897	19980515
US 6086909	A	20000711	US 1999-249963	19990212
US 6572874	B1	20030603	US 2000-626025	20000727
NZ 508130	A	20020301	NZ 2000-508130	20001113

AU 2001054192	A	20010913	AU 2001-54192		20010703
AU 765269	B2	20030911			
US 20030049302	A1	20030313	US 2002-226667		20020821
US 6982091	B2	20060103			
US 20040005345	A1	20040108	US 2003-349029		20030122
US 6905701	B2	20050614			
US 20040043071	A1	20040304	US 2003-600849		20030620
US 20050249774	A1	20051110	US 2005-126863		20050510
US 7744916	B2	20100629			
PRIORITY APPLN. INFO.:			US 1997-60049325	P	19970611
			US 1998-79897	A2	19980515
			US 1999-249963	A2	19990212
			US 2000-626025	A2	20000727
			US 2002-226667	A2	20020821
			US 2003-349029	A2	20030122
			US 2003-600849	A2	20030620
			US 2004-60587454	P	20040712
			US 2005-126863	A2	20050510
			AU 1998-76976	A3	19980610
			NZ 1998-502120	A1	19980610
			US 1999-249693	A2	19990212
			US 1999-60146218	P	19990728
			US 2001-60315877	P	20010829
			US 2002-60390748	P	20020621

PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
US 20050276836	A1	Dead	20201107
US 6197327	B1	Dead	20201107
US 6086909	A	Dead	20201106
US 6572874	B1	Dead	20201107
NZ 508130	A	Dead	20201121
AU 2001054192	A	Dead	20201107
AU 765269	B2	Dead	20201106
US 20030049302	A1	Dead	20201121
US 6982091	B2	Dead	20201121
US 20040005345	A1	Dead	20201107
US 6905701	B2	Dead	20201107
US 20040043071	A1	Dead	20201121
US 20050249774	A1	Dead	20220310
US 7744916	B2	Dead	20220310

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2005:1311702

AB Disclosed is a vaginal device for delivering therapeutical and/or health-promoting agents. The vaginal device partly or completely coated by, covered by or combined with a coating or covering comprising a film, foam, strip, cap, cup or particles. The coating of the device comprises a mucoadhesive compn. comprising a therapeutical and/or health-promoting agent. For example, sumatriptan vaginal suppository were prepd. from Suppocire AS2X, hydroxypropyl Me cellulose as a mucoadhesive agent, and Transcutol as a permeation enhancer.

INCL 424422000

IPCI A61F0013-00 [ICM,7]

IPCR A61F0013-00 [I]; A61K0009-00 [I]; A61K0009-02 [I]; A61K0009-12 [I]; A61K0009-19 [I]; A61K0009-70 [I]

NCL 424/422.000

CC 63-6 (Pharmaceuticals)

IT Alkaloids
Amino acids
Bile salts
Cellulosic fibers
Coenzymes
Cottonseed oil
Essential oils
Fats and Glyceridic oils
Interleukins
Lecithins
Minerals
Natural products, pharmaceutical
Peptides
Phenols
Polyketides

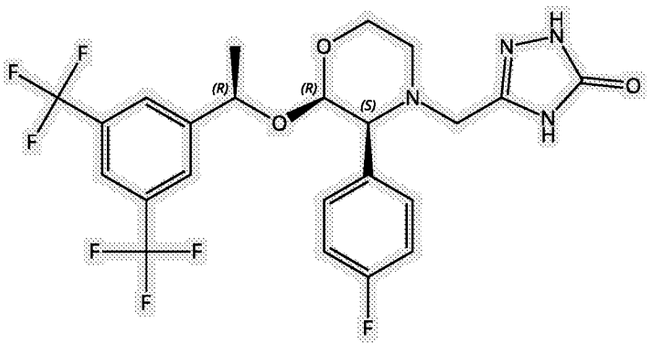
Polyoxyalkylenes
Proteins
Resins
Silicone rubber
Tannins
Terpenes
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents)

IT 68379-02-2, Clofilium 69655-05-6, Didanosine 70458-96-7, Norfloxacin 71048-87-8, Levonantradol 71125-38-7, Meloxicam 72479-26-6, Fenticonazole 72509-76-3, Felodipine 73573-87-2, Formoterol 74103-06-3, Ketorolac 74103-07-4, Ketorolac tromethamine 74191-85-8, Doxazosin 74545-79-2, Aloeresin A 75088-80-1, Manoalide 75330-75-5, Lovastatin 75695-93-1, Isradipine 76584-70-8, Divalproex sodium 79350-37-1, Cefixime 79778-41-9, Neridronate 80210-62-4, Cefpodoxime 80937-31-1, Flosulide 82410-32-0, Ganciclovir 83905-01-5, Azithromycin 83991-25-7, Ambasilide 84625-61-6, Itraconazole 85622-93-1, Temozolomide 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 88150-42-9, Amlodipine 89365-50-4, Salmeterol 89565-68-4, Tropisetron 89778-26-7, Toremifene 89987-06-4, Tiludronate 90357-06-5, Bicalutamide 90961-53-8, Tedisamil 91714-94-2, Bromfenac 92665-29-7, Cefprozil 95058-81-4, Gemcitabine 95298-47-8 95751-30-7, Charybdotoxin 97240-79-4, Topiramate 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 98225-48-0, Brevetoxin 99614-02-5, Ondansetron 101526-83-4, Sematilide 103628-46-2, Sumatriptan 104227-87-4, Famciclovir 105462-24-6 107868-30-4, Exemestane 110042-95-0, Acemannan 112455-84-2, Papuamine 112809-51-5, Letrozole 114084-78-5, Ibandronate 114977-28-5, Docetaxel 115256-11-6, Dofetilide 115956-12-2, Dolasetron 118072-93-8, Zoledronate 120511-73-1, Anastrozole 121368-58-9, Olpadronate 121679-13-8, Naratriptan 122647-31-8, Ibutilide 123948-87-8, Topotecan 127779-20-8, Saquinavir 129618-40-2, Nevirapine 132539-06-1, Olanzapine 134678-17-4, Lamivudine 135729-61-2, Palonosetron 136470-78-5, Abacavir 136817-59-9, Delavirdine 137234-62-9, Voriconazole 139110-80-8, Zanamivir 139226-28-1, Darbufelone 139264-17-8, Zolmitriptan 143322-58-1, Eletriptan 143491-57-0, Emtricitabine 144034-80-0, Rizatriptan 147127-20-6, Tenofovir 149908-53-2, Azimilide 150378-17-9, Indinavir 152459-95-5, Imatinib 153559-49-0, Bexarotene 154323-57-6, Almotriptan 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155213-67-5, Ritonavir 158751-64-5, ClAmikalant 159519-65-0, Enfuvirtide 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 169944-35-8, Bisulfan 170729-80-3, Aprepitant 181695-72-7, Valdecoxib 184475-35-2, Gefitinib 190017-00-6, Correolide 192725-17-0, Lopinavir 196618-13-0, Oseltamivir 198470-84-7, Parecoxib 198904-31-3, Atazanavir 202409-33-4, Etoricoxib 220991-20-8, Lumiracoxib 226700-79-4, Fosamprenavir 260792-29-8, 6β,7β-Diacetoxy-13-hydroxylabda-8,14-diene 264875-61-8, Cimiracemoside A 501938-01-8, 23-epi-26-Deoxyactein 856012-03-8 865111-98-4 865147-59-7, Altissinone 871260-93-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents)

IT 170729-80-3, Aprepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents)

RN 170729-80-3 CAPLUS

CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2001054192 A	AU 2001-54192	Register
AU 765269 B2	AU 2001-54192	Register
NZ 508130 A	NZ 2000-508130	Register
US 6197327 B1	US 1998-79897	Register
US 6086909 A	US 1999-249963	Register
US 6572874 B1	US 2000-626025	Register
US 20030049302 A1	US 2002-226667	Register
US 6982091 B2	US 2002-226667	Register
US 20040005345 A1	US 2003-349029	Register|Global Dossier
US 6905701 B2	US 2003-349029	Register|Global Dossier
US 20040043071 A1	US 2003-600849	Register|Global Dossier
US 20050249774 A1	US 2005-126863	Register|Global Dossier
US 7744916 B2	US 2005-126863	Register|Global Dossier
US 20050276836 A1	US 2005-180076	Register|Global Dossier

L4 ANSWER 48 OF 48 CAPLUS COPYRIGHT 2024 ACS on STN
ACCESSION NUMBER: 2002:695760 CAPLUS Full-text
DOCUMENT NUMBER: 137:237717
TITLE: Inhalant compositions containing anticholinergics and NK1 receptor antagonists
INVENTOR(S): Meade, Christopher John Montague; Pairet, Michel; Pieper, Michael Paul
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069944	A2	20020912	WO 2002-EP1987	20020226
WO 2002069944	A3	20031002		
DE 10111058	A1	20020912	DE 2001-10111058	20010308
CA 2439915	A1	20020912	CA 2002-2439915	20020226
AU 2002251010	A1	20020919	AU 2002-251010	20020226
EP 1370293	A2	20031217	EP 2002-719915	20020226
JP 2004519484	T	20040702	JP 2002-569121	20020226
MX 2003008051	A	20031204	MX 2003-8051	20030905

PRIORITY APPLN. INFO.:
DE 2001-10111058 A 20010308
WO 2002-EP1987 W 20020226

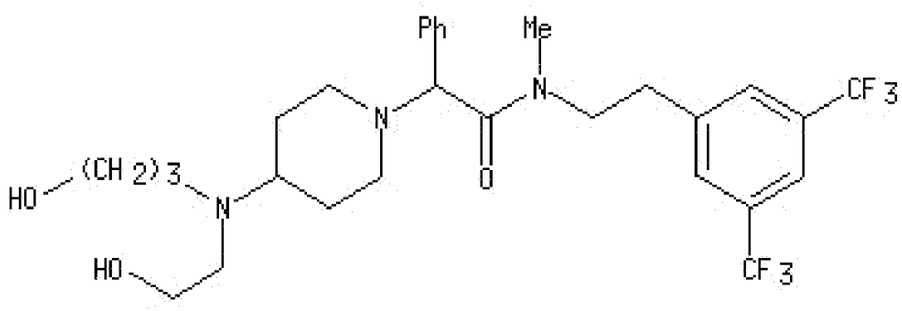
PATENT STATUS PATENT INFORMATION:

PATENT NO.	KIND	STATUS	STATUS DATE
WO 2002069944	A2	Dead	20201201

WO 2002069944	A3	Dead	20201201
DE 10111058	A1	Dead	20201121
CA 2439915	A1	Dead	20201121
AU 2002251010	A1	Dead	20201121
EP 1370293	A2	Dead	20201202
JP 2004519484	T	Dead	20220303
MX 2003008051	A	Dead	20201121

OTHER SOURCE(S): MARPAT 137:237717; CASFORMULTNS 2002:695760

GI



AB The invention relates to drug compns. based on anticholinergics and on NK1 receptor antagonists, to methods for their prodn., and to their use as inhalants for the treatment of respiratory tract diseases. Synthesis of NK1 receptor antagonists from the group of bis-trifluoromethyl-phenyl-piperidine derivs. are described. The products are used in suspension aerosols. Thus a compn. contained (wt./wt.%): tiotropium bromide 0.015; NK1 receptor antagonist 0.066; soy lecithin 0.2; TG11: TG12 = 2:3 to 100.

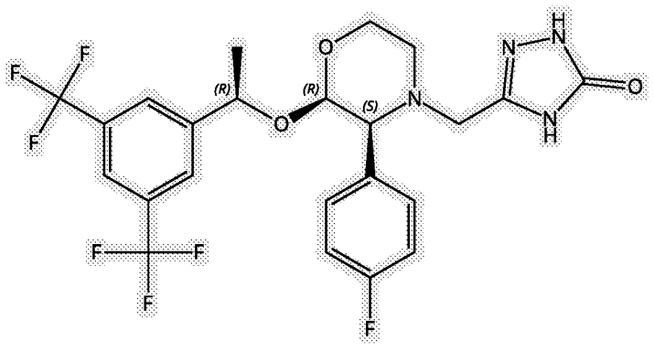
IPCI A61K0031-00 [ICM,7]

IPCR A61K0009-08 [I]; A61K0009-00 [I]; A61K0009-10 [I]; A61K0009-14 [I]; A61K0009-48 [I]; A61K0009-72 [I]; A61K0031-00 [I]; A61K0031-223 [I]; A61K0031-403 [I]; A61K0031-439 [I]; A61K0031-4468 [I]; A61K0031-46 [I]; A61K0031-4745 [I]; A61K0031-535 [I]; A61K0031-55 [I]; A61K0045-06 [I]; A61K0047-04 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-18 [I]; A61K0047-22 [I]; A61K0047-26 [I]; A61P0011-00 [I]; A61P0011-08 [I]; A61P0029-00 [I]; A61P0043-00 [I]

CC 63-6 (Pharmaceuticals)

IT 50-81-7, Ascorbic acid, biological studies 56-81-5, Glycerol, biological studies 57-55-6, Propylene glycol, biological studies 64-02-8 64-17-5, Ethanol, biological studies 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 65-85-0, Benzoic acid, biological studies 74-98-6, n-Propane, biological studies 75-28-5, Isobutane 77-92-9, Citric acid, biological studies 79-09-4, Propionic acid, biological studies 106-97-8, n-Butane, biological studies 110-15-6, Succinic acid, biological studies 110-16-7, Maleic acid, biological studies 110-17-8, Fumaric acid, biological studies 123-03-5, Cetylpyridinium chloride 431-89-0, TG227 526-83-0, Tartaric acid 811-97-2, TG134a 1406-18-4, Vitamin E 6915-15-7, Malic acid 7647-01-0, Hydrochloric acid, biological studies 7664-93-9, Sulfuric acid, biological studies 7697-37-2, Nitric acid, biological studies 10035-10-6, Hydrobromic acid, biological studies 11103-57-4, Vitamin A 25322-68-3, Polyethylene glycol 25322-68-3D, alcs. and fatty acid esters 25322-69-4, Polypropylene glycol 60205-81-4, Ipratropium 99571-64-9, Oxitropium 138449-07-7, FK-888 142001-63-6, Saredutant 145742-28-5, CP-122721 147116-64-1, CJ 11974 155418-05-6, SR 140333 168266-90-8, GR 205171 170566-84-4, Lanepitant 170739-80-3, MK-869 171272-39-2, MEN-10930 172673-20-0, L-758298 173941-19-0, YM 49244 173941-22-5, YM 35375 173941-74-7, YM 44778 174636-32-9, SB 223412 174661-97-3, DA-5018 178370-50-8, MDL 103896 183747-35-5, Nepadutant 188241-50-1, S-19752 193694-35-8, MDL-105172A 201152-86-5, SR-144190 206052-25-7, MEN-11149 209474-01-1, Neuronorm 214487-46-4, MEN-11467 217185-75-6, TAK-637 350610-25-2 350610-26-3, 6b-I 350610-27-4, DNK-33A 350610-29-6, ZM-274773 350610-34-3, DNK 333A 350610-51-4, CGP 60829 350610-61-6, NKP 608A 350610-64-9, NKP 608C 415917-13-4 457910-81-5 458568-84-8, TG 11 458569-01-2, TG 12
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhalant compns. contg. anticholinergics and NK1 receptor antagonists)
IT 170729-80-3, MK-869
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalant compns. contg. anticholinergics and NK1 receptor antagonists)
RN 170729-80-3 CAPLUS
CN 3H-1,2,4-Triazol-3-one, 5-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl]methyl]-1,2-dihydro- (CA INDEX NAME)



Absolute stereochemistry shown
Rotation (+)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LINK INFORMATION

PUBLICATIONS	APPLICATIONS	REGISTER
AU 2002251010 A1	AU 2002-251010	Register
CA 2439915 A1	CA 2002-2439915	Register
DE 10111058 A1	DE 2001-10111058	Register
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WO 2002069944 A3	WO 2002-EP1987	Register|Global Dossier

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METHODS OF USE OF EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. Application No. 18/535,853, filed December 11, 2023, pending, which is a continuation of U.S. Application No. 17/180,593, filed February 19, 2021, now allowed, which is a continuation of U.S. Application No. 16/820,311, filed March 16, 2020, now U.S. Patent No. 11,173,118, which is a continuation of U.S. Application No. 15/965,638, filed April 27, 2018, now U.S. Patent No. 10,624,850, which is a continuation of U.S. Application No. 15/012,532, filed February 1, 2016, now U.S. Patent No. 9,974,742, each of which is incorporated herein in its entirety.

TECHNICAL FIELD

[0002] The disclosure relates generally to emulsion formulations and systems for the intravenous or parenteral administration of an NK-1 receptor antagonist for treatment of emesis. The emulsion formulations are stable for prolonged periods of time. Also described are methods for preparing the stable NK-1 receptor antagonist emulsions and pharmaceutical formulations.

BACKGROUND

[0003] Emesis is a critical problem experienced as a result of anticancer cytotoxic therapy. Up to 80% of patients will experience chemotherapy-induced nausea and vomiting (CINV) without prophylactic therapy (Vieira dos Santos et al., 2012, J Natl Cancer Inst, 104:1280-1292). Navari et al. (1999, N Engl J Med, 340:190-195) showed that neurokinin-1 (NK-1) receptor antagonists improve CINV when used in combination with cisplatin-based chemotherapy. NK-1 receptor antagonists block binding of substance P to the receptor, thereby preventing or limiting induction of vomiting pathways mediated by the NK-1 receptor (Aziz, 2012, Ann Palliat Med, 1:130-136).

[0004] NK-1 receptor antagonists currently approved and marketed include aprepitant and rolapitant HCl, which are both available in oral form. Not surprisingly, oral dosage forms can create a problem for patients suffering from emesis, specifically, for example, on days two and three of chemotherapy. Accordingly, it is desirable to have injectable formulations to simplify treatment for these patients. Described herein are emulsions formulated for administering to a patient by injection. These emulsions are formulated to contain neurokinin-1 receptor antagonists which may be poorly soluble in aqueous solvents or unstable in aqueous-based liquid formulations.

[0005] Liquid formulations containing NK-1 receptor antagonists having poor solubility and/or poor gastrointestinal permeability characteristics can be very challenging to formulate for purposes of long-term storage and for administration. One means of addressing this challenge is to prepare an emulsion which may both allow preparation of an injectable formulation as well as enhance bioavailability of the active agent once administered.

[0006] Intravenous emulsions should have a very small droplet size to circulate in the bloodstream without causing capillary blockage and embolization. These size limits are typified by USP33-NF28 General Chapter <729> for Globule Size Distribution in Lipid Injectable Emulsions, hereinafter referred to as USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm (PFAT5) not exceeding 0.05%, irrespective of the final lipid concentration.

[0007] Emulsion formulations must be physically stable. The droplet size limits defined in USP <729> apply throughout the assigned shelf life. All true emulsions are thermodynamically unstable and may over time undergo a range of processes which tend to increase the droplet size. These include direct droplet coalescence, when two droplets collide and form a single new droplet; and aggregation, in which droplets adhere together to form larger masses. Aggregation may in some cases be a precursor of further coalescence into larger droplets. These processes may result in large aggregates rising to the surface of the container, a phenomenon known as 'creaming', and ultimately to free oil being visible on the emulsion surface, known as ‘cracking’.

[0008] Emulsion formulations must also be chemically stable. The drug substance may degrade; for example, lipophilic drugs will partition into the oil phase, which will confer some degree of protection, but hydrolytic degradation may still occur at the oil-water interface. Possible chemical degradation within parenteral fat emulsions includes oxidation of unsaturated fatty acid residues present in triglyceride and lecithin, and hydrolysis of phospholipids leading to the formation of free fatty acids (FFA) and lysophospholipids. Such degradants lower pH, which may then promote further degradation. Thus, pH should be controlled during manufacture and parenteral emulsion formulations may include a buffering agent to provide additional control. Any decrease in pH over the assigned shelf-life may be indicative of chemical degradation.

[0009] In the present application, emulsion formulations were prepared and characterized to identify a formulation and process that will allow an NK-1 receptor antagonist compound to be

incorporated into an emulsion for intravenous injection and remain stable during the shelf life of the formulation.

BRIEF SUMMARY

[0010] The following aspects and embodiments thereof described and illustrated below are meant to be exemplary and illustrative, not limiting in scope.

[0011] In one aspect, a pharmaceutical composition suitable for intravenous administration is provided which comprises a stable emulsion comprising an oil phase, wherein the oil phase comprises a neurokinin 1 (NK-1) receptor antagonist, a surfactant and a co-surfactant; and an aqueous phase, wherein the aqueous phase comprises water, a tonicity agent, and a pH modifier.

[0012] In some embodiments, the NK-1 receptor antagonist is selected from the group consisting of aprepitant, rolapitant, netupitant, lanepitant, vestipitant, orvepitant maleate, casopitant, ezlopitant, serlopitant, befetupitant and maropitant, or a pharmaceutically acceptable salt thereof. In other embodiments, the NK-1 receptor antagonist is poorly soluble in water.

[0013] In some embodiments, the NK-1 receptor antagonist is selected from the group consisting of rolapitant, netupitant, casopitant, ezlopitant, vestipitant, serlopitant, maropitant, and orvepitant.

[0014] In some embodiments, the NK-1 receptor antagonist is not aprepitant.

[0015] In some embodiments, the composition is an oil-in-water emulsion comprising an oil wherein the oil is selected from the group consisting of coconut oil, olive oil, soybean oil, safflower oil, triglycerides, octyl and decyl glycerate, ethyl oleate, glyceryl linoleate, ethyl linoleate, glyceryl oleate, cholesteryl oleate/linoleate or a mixture thereof. In other embodiments, the oil is hydrolyzed. In still other embodiments, the oil is structurally modified.

[0016] In some embodiments, the emulsifier comprises a phospholipid. In another embodiment, the emulsifier is selected from the group consisting of egg phospholipids, soy phospholipids, phosphatidylcholines, phosphatidylethanolamines, phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids, mixed chain phospholipids, lysophospholipids, hydrogenated phospholipids, partially hydrogenated phospholipids, and mixtures thereof.

[0017] In some embodiments, the co-surfactant comprises an alcohol. In other embodiments, the co-surfactant is ethanol.

[0018] In some embodiments, the pH modifier comprises an oleate or pharmaceutically acceptable salt thereof. In other embodiments, the oleate is sodium, potassium or ammonium oleate. In yet other embodiments, the pH modifier is sodium oleate or a pharmaceutically acceptable salt thereof.

[0019] In some embodiments, the pH modifier comprises a buffer. In other embodiments, the buffer is selected from the group consisting of phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer and borate buffer. In still other embodiments, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer.

[0020] In some embodiments, the pH modifier comprises an oleate and a buffer. In other embodiments, the oleate is sodium oleate and the buffer is Tris buffer.

[0021] In some embodiments, the pH modifier is selected from the group consisting of sodium hydroxide, potassium hydroxide, magnesium hydroxide, sodium carbonate, Tris, sodium linoleate, sodium oleate, potassium oleate, ammonium oleate, potassium carbonate, potassium linoleate, and mixtures thereof.

[0022] In some embodiments, the composition comprises about 5 wt/wt% (weight/weight %) to 15 wt/wt%, 5 wt/wt% to 10 wt/wt%, 7 wt/wt% to 10 wt/wt%, 8 wt/wt% to 9 wt/wt%, or 9 wt/wt% to 10 wt/wt% oil. In another embodiment, the composition comprises about 8 wt/wt5, 8.5 wt/wt%, 9 wt/wt%, 9.5 wt/wt%, 10 wt/wt%, or 10.5 wt/wt% oil. In still other embodiments, the oil is soybean oil.

[0023] In some embodiments, the composition comprises about 10 wt/wt% to 20 wt/wt%, 12 wt/wt% to 17 wt/wt%, 13 wt/wt% to 16 wt/wt%, 13 wt/wt% to 15 wt/wt%, 14 wt/wt% to 15 wt/wt%, or 13 wt/wt% to 14 wt/wt% emulsifier. In other embodiments, the composition comprises about 13 wt/wt%, 13.5 wt/wt%, 14 wt/wt%, 14.5 wt/wt%, 15 wt/wt%, 16 wt/wt%, 17 wt/wt%, 18 wt/wt%, 19 wt/wt% or 20 wt/wt% emulsifier. In still other embodiments, the emulsifier is a lecithin. In other embodiments, the lecithin is an egg yolk lecithin.

[0024] In some embodiments, the composition comprises about 0.05 wt/wt% to 1.5 wt/wt%, 0.1 wt/wt% to 1.0 wt/wt%, 0.2 wt/wt% to 0.8 wt/wt%, 0.3 wt/wt% to 0.7 wt/wt%, 0.4 wt/wt% to 0.6 wt/wt%, 0.4 wt/wt% to 0.5 wt/wt% oleate or salt thereof. In other embodiments, the composition comprises about 0.05 wt/wt%, 0.1 wt/wt%, 0.2 wt/wt%, 0.3 wt/wt%, 0.4 wt/wt%, 0.45 wt/wt%, 0.5 wt/wt%, 0.6 wt/wt%, 0.7 wt/wt%, 0.8 wt/wt%, 0.9 wt/wt%, 1.0 wt/wt% or 1.5 wt/wt% oleate or salt thereof. In still other embodiments, the oleate is sodium oleate. In still another embodiment, the oleate or sodium oleate is the pH modifier.

[0025] In some embodiments, the composition comprises about 20 wt/wt% to 50 wt/wt%, 30 wt/wt% to 50 wt/wt%, 35 wt/wt% to 45 wt/wt%, 30 wt/wt% to 45 wt/wt%, 37 wt/wt% to 42 wt/wt%, 38 wt/wt% to 40 wt/wt%, 30 wt/wt%, 31 wt/wt%, 32 wt/wt%, 33 wt/wt%, 34 wt/wt%, 35 wt/wt%,

36 wt/wt%, 37 wt/wt%, 38 wt/wt%, 39 wt/wt%, 40 wt/wt%, 41 wt/wt%, 42 wt/wt%, 43 wt/wt%, 44 wt/wt%, 45 wt/wt%, 46 wt/wt%, 47 wt/wt%, 48 wt/wt%, 49 wt/wt%, 50 wt/wt% of oil expressed as a percentage of the weight of the oil per the sum of weight of oil, emulsifier and oleate in a unit of the composition. In other embodiments, the oil is soybean oil.

[0026] In some embodiments, the composition comprises about 20 wt/wt% to 50 wt/wt%, 30 wt/wt% to 50 wt/wt%, 35 wt/wt% to 45 wt/wt%, 30 wt/wt% to 45 wt/wt%, 37 wt/wt% to 42 wt/wt%, 38 wt/wt% to 40 wt/wt%, 30 wt/wt%, 31 wt/wt%, 32 wt/wt%, 33 wt/wt%, 34 wt/wt%, 35 wt/wt%, 36 wt/wt%, 37 wt/wt%, 38 wt/wt%, 39 wt/wt%, 40 wt/wt%, 41 wt/wt%, 42 wt/wt%, 43 wt/wt%, 44 wt/wt%, 45 wt/wt%, 46 wt/wt%, 47 wt/wt%, 48 wt/wt%, 49 wt/wt%, 50 wt/wt% of oil expressed as a percentage of the weight of the oil per the sum of weight of oil and emulsifier in a unit of the composition. In other embodiments, the oil is soybean oil.

[0027] In some embodiments, the composition comprises about 40 wt/wt% to 80 wt/wt%, 50 wt/wt% to 70 wt/wt%, 55 wt/wt% to 65 wt/wt%, 57 wt/wt% to 63 wt/wt%, 58 to 60 wt/wt%, 35 wt/wt% to 40 wt/wt%, 30 wt/wt% to 40 wt/wt%, 50 wt/wt%, 51 wt/wt%, 52 wt/wt%, 53 wt/wt%, 54 wt/wt%, 55 wt/wt%, 56 wt/wt%, 57 wt/wt%, 58 wt/wt%, 59 wt/wt%, 60 wt/wt%, 61 wt/wt%, 62 wt/wt%, 63 wt/wt%, 64 wt/wt%, 65 wt/wt%, 66 wt/wt%, 67 wt/wt%, 68 wt/wt%, 69 wt/wt%, 70 wt/wt% of emulsifier expressed as a percentage of the weight of emulsifier per the sum of weight of oil, emulsifier and oleate in a unit of the composition. In other embodiments, the emulsifier is a lecithin. In still other embodiments, the lecithin is an egg yolk lecithin.

[0028] In some embodiments, the composition comprises about 40 wt/wt% to 80 wt/wt%, 50 wt/wt% to 70 wt/wt%, 55 wt/wt% to 65 wt/wt%, 57 wt/wt% to 63 wt/wt%, 58 to 60 wt/wt%, 35 wt/wt% to 40 wt/wt%, 30 wt/wt% to 40 wt/wt%, 50 wt/wt%, 51 wt/wt%, 52 wt/wt%, 53 wt/wt%, 54 wt/wt%, 55 wt/wt%, 56 wt/wt%, 57 wt/wt%, 58 wt/wt%, 59 wt/wt%, 60 wt/wt%, 61 wt/wt%, 62 wt/wt%, 63 wt/wt%, 64 wt/wt%, 65 wt/wt%, 66 wt/wt%, 67 wt/wt%, 68 wt/wt%, 69 wt/wt%, 70 wt/wt% of emulsifier expressed as a percentage of the weight of emulsifier per the sum of weight of oil and emulsifier in a unit of the composition. In other embodiments, the emulsifier is a lecithin. In still other embodiments, the lecithin is an egg yolk lecithin.

[0029] In some embodiments, the ratio of oil to NK-1 receptor antagonist (wt%:wt%) in the composition ranges from about 5:1 to 20:1, 5:1 to 15:1, 5:1 to 10:1, 11:1 to 20:1, 11:1 to 15:1, 12:1 to 16:1, 12:1 to 14:1, 11:1 to 15:1, 12:1 to 14:1, 12.5:1 to 13.5:1, 13:1 to 14:1, or 12:1 to 15:1. In other embodiments, the ratio of oil to NK-1 receptor antagonist (wt%:wt%) in the composition is

about 11:1 to 20:1, 11:1 to 15:1, 12:1 to 16:1, 12:1 to 14:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 11:1, 11.5:1, 12:1, 12.5:1, 13:1, 13.5:1, 14:1, 14.5:1 or 15:1, 15.5:1, 16:1.

[0030] In some embodiments, the ratio of emulsifier to NK-1 receptor antagonist (wt%:wt%) in the composition ranges from about 10:1 to 30:1, 10:1 to 20:1, 15:1 to 30:1, 20:1 to 25:1, 18:1 to 22:1, 19:1 to 20:1, or 10:1 to 30:1. In other embodiments, the ratio of emulsifier:NK-1 receptor antagonist (wt%:wt%) in the composition is about 10:1, 11:1, 13:1, 14:1, 15:1, 18:1, 19:1, 20:1, 21:1, 22:1 23:1, 24:1, 25:1, or 30:1.

[0031] In some embodiments, the ratio of (emulsifier plus oil) to NK-1 receptor antagonist (wt%:wt%) in the composition ranges from about 20:1 to 40:1, 25:1 to 35:1, 30:1 to 35:1, or 32:1 to 34:1. In other embodiments, the ratio of (emulsifier plus oil) to NK-1 receptor antagonist is about 25:1, 26:1, 27:1, 28:1, 29:1 30:1, 31:1, 32:1, 33:1, 34:1, 35:1, 36:1, 37:1, 38:1 or 40:1.

[0032] In some embodiments, the ratio of emulsifier to oil (wt%:wt%) in the composition ranges from about 0.5:1, to 4:1, 1:1 to 2:1, 1.25:1 to 1.75:1, or 1.4:1 to 1.6:1. In other embodiments, the ratio of emulsifier to oil (wt%:wt%) in the composition is about 0.5:1, 0.5:1, 0.6:1, 0.7:1, 0.8:1, 0.9:1, 1:1, 1.1:1, 1.2:1, 1.3:1, 1.4:1, 1.5:1, 1.6:1, 1.7:1, 1.8:1, 1.9:1, 2:1, 1.05:1, 1.15:1, 1.25:1, 1.35:1, 1.45:1, 1.55:1, 1.65:1, 1.75:1, 1.85:1, or 1.95:1.

[0033] In some embodiments, a therapeutic dose of the pharmaceutical composition comprises about 1 to 4 g, 1.5 to 3 g, 1.8 to 2.8 g, 2.3 to 2.8 g, 1.8 to 2.3 g, 1 g, 1.1 g, 1.2 g, 1.3 g, 1.4 g, 1.5 g, 1.6 g, 1.7 g, 1.8 g. 1.9 g, 2 g, 2.1 g, 2.2 g, 2.3 g, 2.4 g, 2.5 g, 2.6 g, 2.7 g, 2.8 g. 2.9 g, 3 g, 3.1 g, 3.2 g, 3.3 g, 3.4 g, 3.5 g, 3.6 g, 3.7 g, 3.8 g. 3.9 g, 4 g emulsifier. In other embodiments, the emulsifier is a lecithin. In still other embodiments, the emulsifier is egg yolk lecithin.

[0034] In some embodiments, a therapeutic dose of the pharmaceutical composition comprises about 0.5 to 3 g, 1 to 2.5 g, 1 to 2 g, 1 to 1.5 g, 1.5 g to 2 g, 0.5g 0.6 g, 0.7 g, 0.8 g, 0.9 g, 1 g, 1.1 g, 1.2 g, 1.3 g, 1.4 g, 1.5 g, 1.6 g, 1.7 g, 1.8 g. 1.9 g, 2 g, 2.1 g, 2.2 g, 2.3 g, 2.4 g, 2.5 g oil. In other embodiments, the oil is soybean oil.

[0035] In some embodiments, a therapeutic dose of the pharmaceutical composition comprises about 50 to 600 mg, 100 to 600 mg, 100 to 500 mg, 100 to 400 mg, 100 to 300 mg, 100 to 200 mg, 200 to 400 mg, 50 to 250 mg, 75 to 200 mg, 100 to 150 mg, 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180 mg, 190 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, or 600 mg of the NK-1 receptor antagonist.

[0036] In some embodiments, the composition comprises about 0 wt/wt% to 10 wt/wt%, 1 wt/wt% to 9 wt/wt%, 2 wt/wt% to 6 wt/wt%, 2 wt/wt% to 4 wt/wt% or 2 wt/wt% to 3 wt/wt% co-surfactant.

In other embodiments, the composition comprises less than 10 wt/wt%, less than 9 wt/wt%, less than 8 wt/wt%, less than 7, less than 6 wt/wt%, less than 5 wt/wt%, less than 4 wt/wt%, less than 3 wt/wt%, less than 2 wt/wt% or less than 1 wt/wt% co-surfactant.

[0037] In some embodiments, the composition comprises about 0 wt/wt% to 10 wt/wt%, 1 wt/wt% to 9 wt/wt%, or 2 wt/wt% to 6 wt/wt% ethanol. In other embodiments, the composition comprises less than 10 wt/wt%, less than 9 wt/wt%, less than 8 wt/wt%, less than 7, less than 6 wt/wt%, less than 5 wt/wt%, less than 4 wt/wt%, less than 3 wt/wt%, less than 2 wt/wt% or less than 1 wt/wt% ethanol.

[0038] In some embodiments, the aqueous phase of the emulsion comprises a tonicity agent, a pH modifier, and water.

[0039] In some embodiments, the aqueous phase of the emulsion comprises an osmotic agent, a pH modifier, and water.

[0040] In some embodiments, the aqueous phase of the emulsion comprises a tonicity agent, an osmotic agent, a pH modifier, and water.

[0041] In some embodiments, the aqueous phase further comprises a buffer.

[0042] In some embodiments, the aqueous phase comprises a buffer but does not comprise a pH modifier which is different from the buffer. In other embodiments, the buffer functions as both a pH modifier agent and a buffer.

[0043] In some embodiments, when the aqueous phase comprises a buffer, the composition contains no tonicity agent.

[0044] In some embodiments, the buffer is selected from the group consisting of phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer and borate buffer. In other embodiments, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer.

[0045] In some embodiments, the aqueous phase comprises a buffer, that when mixed with the oil phase will provide a substantially isotonic oil in water emulsion.

[0046] In some embodiments, the osmotic agent is selected from the group consisting of glycerol, sorbitol, xylitol, mannitol, glucose, trehalose, maltose, sucrose, raffinose, lactose, dextran, polyethylene glycol, or propylene glycol. In other embodiments, the osmotic agent is an inorganic salt such as sodium chloride and mixtures thereof.

[0047] In some embodiments, the composition has a pH of about 6 to 9, 7 to 9, 7.5 to 9, 7.5 to 8.5, 8 to 9, 6 to 8, 7 to 8, or 6, 7, 8 or 9.

[0048] In some embodiments, the composition comprises about 0 wt/wt% to 25 wt/wt%, 2 wt/wt% to 20 wt/wt%, 3 wt/wt% to 15 wt/wt%, or 3 wt/wt% to 8 wt/wt% tonicity agent. In other embodiments, the composition comprises about 1 wt/wt%, 2 wt/wt%, 3 wt/wt%, 4 wt/wt%, 5 wt/wt%, 6 wt/wt%, 7 wt/wt%, 8 wt/wt%, 9 wt/wt%, or 10 wt/wt%, 11 wt/wt%, 12 wt/wt%, 13 wt/wt%, 14 wt/wt%, 15 wt/wt%, 16 wt/wt%, 17 wt/wt%, 18 wt/wt%, 19 wt/wt%, or 20 wt/wt%, 21 wt/wt%, 22 wt/wt%, 23 wt/wt%, 24 wt/wt%, 25 wt/wt% tonicity agent. In still other embodiments, the composition comprises no tonicity agent.

[0049] In some embodiments, the composition comprises about 0 wt/wt% to 25 wt/wt%, 2 wt/wt% to 20 wt/wt%, 3 wt/wt% to 15 wt/wt%, or 3 wt/wt% to 8 wt/wt% osmotic agent. In other embodiments, the composition comprises about 1 wt/wt%, 2 wt/wt%, 3 wt/wt%, 4 wt/wt%, 5 wt/wt%, 6 wt/wt%, 7 wt/wt%, 8 wt/wt%, 9 wt/wt%, or 10 wt/wt%, 11 wt/wt%, 12 wt/wt%, 13 wt/wt%, 14 wt/wt%, 15 wt/wt%, 16 wt/wt%, 17 wt/wt%, 18 wt/wt%, 19 wt/wt%, or 20 wt/wt%, 21 wt/wt%, 22 wt/wt%, 23 wt/wt%, 24 wt/wt%, 25 wt/wt% osmotic agent. In still other embodiments, the composition comprises no osmotic agent.

[0050] In some embodiments, the aqueous phase comprises a dose of dexamethasone sodium phosphate in a therapeutic dose of the pharmaceutical composition. In other embodiments, the dose of dexamethasone sodium phosphate ranges from about 0.5 mg to 30 mg, 0.5 mg to 25 mg, 1 mg to 20 mg, 10 mg to 20 mg, or 3 mg to 16 mg. In still other embodiments, the dose of dexamethasone sodium phosphate is about 9 mg or 16 mg in a therapeutic dose of the pharmaceutical composition. In these embodiments comprising a dose of dexamethasone, the therapeutic dose of the pharmaceutical composition comprises about 50 to 600 mg, 100 to 600 mg, 100 to 500 mg, 100 to 400 mg, 100 to 300 mg, 100 to 200 mg, 200 to 400 mg, 50 to 250 mg, 75 to 200 mg, 100 to 150 mg, 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180 mg, 190 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, or 600 mg of the NK-1 receptor antagonist.

[0051] In some embodiments, the oil phase comprises a dose of dexamethasone in a therapeutic dose of the pharmaceutical composition. In other embodiments, the dose of dexamethasone ranges from about 0.5 mg to 30 mg, 0.5 mg to 20 mg, 1 mg to 18 mg, 10 mg to 20 mg, or 3 mg to 16 mg. In other embodiments, the dose of dexamethasone is about 8 mg or 12 mg in a therapeutic dose of the pharmaceutical composition. In these embodiments comprising a dose of dexamethasone, the therapeutic dose of the pharmaceutical composition comprises about 50 to 600 mg, 100 to 600 mg, 100 to 500 mg, 100 to 400 mg, 100 to 300 mg, 100 to 200 mg, 200 to 400 mg, 50 to 250 mg, 75 to 200 mg, 100 to 150 mg, 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180

mg, 190 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, or 600 mg of the NK-1 receptor antagonist

[0052] In some embodiments, the emulsion comprises about 0.002 wt/wt% to 0.2 wt/wt%, 0.003 wt/wt% to 0.16 wt/wt%, 0.02 wt/wt% to 0.1 wt/wt% dexamethasone sodium phosphate.

[0053] In some embodiments, the composition is a stable system maintaining an intensity-weighted mean particle size as determined by dynamic light scattering (DLS) of about 50 nm to 1000 nm, 50 to 500 nm, 50 nm to 400 nm, 50 nm to 300 nm, 50 nm to 200 nm or 50 nm to 100 nm. In another embodiment, the average droplet size is maintained below 500 nm for a period of at least 1 month, 3 months, 6 months, 9 months, 12 months, 2 years or 3 years at room temperature. In other embodiments, the average droplet size is maintained below 500 nm for a period of at least 1 month, 3 months, 6 months, 9 months, 12 months, 2 years or 3 years at 5 °C.

[0054] In another aspect, a method for preparing an emulsion comprising an NK-1 receptor antagonist compound and suitable for parenteral administration is provided.

[0055] In some embodiments, the administration is intravenous administration.

[0056] In some embodiments, the method comprises: a) preparing an oil phase by dissolving the antagonist compound and an emulsifier in ethanol, then adding in oil to generate an oil-based mixture; b) preparing an aqueous phase by mixing water, optionally with a tonicity agent, optionally with an osmotic agent and optionally with a pH modifier and optionally with a buffer to generate an aqueous mixture; c) combining the oil-based mixture and the aqueous mixture and subjecting this to high speed homogenization to generate a crude emulsion; and d) subjecting the crude emulsion to high pressure homogenization to generate a fine emulsion.

[0057] In some embodiments, preparing the oil phase further comprises dissolving dexamethasone with the antagonist compound and the emulsifier in the ethanol.

[0058] In some embodiments, the method comprises: a) combining a NK-1 receptor antagonist, an emulsifier, and an alcohol with an oil to generate an oil phase; (b) combining water, a tonicity agent, a pH modifier, and optionally a buffer to generate an aqueous phase; (c) homogenizing the oil phase with the aqueous phase to generate the pharmaceutical emulsion; and (d) sterilizing the pharmaceutical emulsion. In other embodiments, the homogenizing comprises high speed homogenization.

[0059] In some embodiments, the method comprises: a) preparing an oil phase by dissolving the antagonist compound and an emulsifier in ethanol and oil to generate an oil-based mixture; b) preparing an aqueous phase by mixing water, optionally with a tonicity agent, optionally with an

osmotic agent and optionally with a pH modifier and optionally with a buffer to generate an aqueous mixture; c) combining the oil-based mixture and the aqueous mixture and subjecting this to homogenization to generate a crude emulsion; and d) subjecting the crude emulsion to homogenization to generate a fine emulsion. In other embodiments, the subjecting the homogenization to generate a crude emulsion is high-speed homogenization. In still other embodiments, the homogenization to generate a fine emulsion is a high pressure homogenization.

[0060] In some embodiments, preparing the oil phase further comprises dissolving dexamethasone with the antagonist compound and the emulsifier in the ethanol and oil.

[0061] In some embodiments, preparing the aqueous phase further comprises mixing dexamethasone with the water, tonicity agent, pH modifier, and a buffer. In other embodiments, the dexamethasone is a salt of dexamethasone. In still other embodiments, the dexamethasone is dexamethasone sodium phosphate.

[0062] In some embodiments, the method further comprises sterilizing the fine emulsion to generate the final emulsion, wherein the final emulsion is suitable for injection into a subject.

[0063] In some embodiments, the dissolution in ethanol is performed at a temperature of about 25 °C to 80 °C, 40 °C to 75 °C, 60 °C to 70 °C, or at about 25 °C, 35 °C, 45 °C, 60 °C, 65 °C, 70 °C or 75 °C.

[0064] In some embodiments, the high-speed homogenization is performed at a speed of about 2,000 rpm (revolutions per minute) to 25,000 rpm. In other embodiments, the high-speed homogenization is performed at a speed of about 20,000 rpm. In still other embodiments, the high-speed homogenization is performed at a speed of about 3600 rpm.

[0065] In some embodiments, the high-speed homogenization is performed for a time period of about 0.5 min to 1 hour, 1 min to 45 min, or 1 min to 30 min. In other embodiments, the high-speed homogenization is performed for a time period of about 20 to 40 min or for about 30 min.

[0066] In some embodiments, the high-speed homogenization is performed at about 10 °C to about 60 °C, 20 °C to about 60 °C, about 30 °C to about 50 °C, or about 35 °C to about 45 °C. In another embodiment, the high-speed homogenization is performed at about 25 °C, 30 °C, 35 °C, 40 °C, 45 °C or 50 °C.

[0067] In some embodiments, the high-pressure homogenization is performed at a pressure of about 10,000 psi (pounds per square inch) to 30,000 psi. In other embodiments, the high-pressure homogenization is performed at a pressure of about 20,000 psi.

[0068] In some embodiments, the high-pressure homogenization is performed with cooling. In another embodiment, the high-pressure homogenization is performed with cooling which is sufficient to bring the temperature of the emulsion at the outlet of the process to about 0 °C to about 60 °C, about 10 °C to about 40 °C, about 20 °C to about 30 °C, or to about 20 °C, 25 °C or 30 °C within the time period.

[0069] In some embodiments, the sterilizing the fine emulsion comprises filtering the fine emulsion through a nylon filter. In other embodiments, the nylon filter is a Posidyne® filter. In yet another embodiment, the filter has a pore size of about 0.2 μm (micrometers).

[0070] In another aspect, the compositions described herein are for treatment of a subject, and the composition is administered via injection to a subject in need.

[0071] In some embodiments, the compositions are for use in a method for the treatment of emesis induced by a chemotherapeutic agent, by radiation-induced nausea and vomiting, and/or by post-operative induced nausea and vomiting in a subject. In other embodiments, the treatment comprises administering to the subject a composition comprising an NK-1 receptor antagonist as described herein. In still other embodiments, the compositions are for use in preventing or treating acute and delayed nausea and vomiting.

[0072] Additional embodiments of the present compositions and methods and the like, will be apparent from the following description, drawings, examples, and claims. As can be appreciated from the foregoing and following description, each and every feature described herein, and each and every combination of two or more of such features, is included within the scope of the present disclosure provided that the features included in such a combination are not mutually inconsistent. In addition, any feature or combination of features may be specifically excluded from any embodiment of the present invention. Additional aspects and advantages of the present invention are set forth in the following description and claims, particularly when considered in conjunction with the accompanying examples and drawings.

BRIEF DESCRIPTION OF DRAWINGS

[0073] FIGS. 1A-1D provides microscope images of samples from Examples 1, 2, 3 and 6 after a freeze-thaw cycle. FIG. 1A: Example 1, FIG. 1B: Example 2, FIG. 1C: Example 3, FIG. 1D: Example 6

[0074] FIG. 2 shows plasma levels of aprepitant after injection of a fosaprepitant solution (●) or an aprepitant emulsion prepared as described herein (▲).

[0075] FIG. 3 shows plasma levels of aprepitant after injection of a solution of fosaprepitant (▲) or after injection of an emulsion containing aprepitant and dexamethasone prepared as described herein (●).

[0076] FIG. 4 shows plasma levels of dexamethasone after injection of a solution of dexamethasone sodium phosphate (●) or after injection of an emulsion containing aprepitant and dexamethasone prepared as described herein (▲).

DETAILED DESCRIPTION

[0077] Various aspects now will be described more fully hereinafter. Such aspects may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey its scope to those skilled in the art.

I. DEFINITIONS

[0078] As used in this specification, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to a "polymer" includes a single polymer as well as two or more of the same or different polymers, reference to an "excipient" includes a single excipient as well as two or more of the same or different excipients, and the like.

[0079] Where a range of values is provided, it is intended that each intervening value between the upper and lower limit of that range and any other stated or intervening value in that stated range is encompassed within the disclosure. For example, if a range of 1 μm to 8 μm is stated, it is intended that 2 μm, 3 μm, 4 μm, 5 μm, 6 μm, and 7 μm are also explicitly disclosed, as well as the range of values greater than or equal to 1 μm and the range of values less than or equal to 8 μm. As used herein, the term “about” means ±5%, ±10%, or ±20% of the value being modified.

[0080] The term “emulsion” or “emulsion formulation” means a colloidal dispersion of two immiscible liquids in the form of droplets, whose diameter, in general, is between 10 nanometers and 100 microns. An emulsion is denoted by the symbol O/W (oil-in-water) if the continuous phase is an aqueous solution and by W/O (water-in-oil) if the continuous phase is an oil. Other examples of emulsions such as O/W/O (oil-in-water-oil) include oil droplets contained within aqueous droplets dispersed in a continuous oil phase.

[0081] “Physically stable” emulsions will meet the criteria under USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm

(PFAT5) not exceeding 0.05%, at 5 ºC or room temperature for a designated storage time period. In addition, physically stable emulsions will have no visible NK-1 receptor antagonist crystals upon storage at 5 °C or room temperature for a designated time period. Crystals are considered visible when viewed at magnification of 4X to 10X. An emulsion is physically stable if it meets the criteria under USP <729> and NK-1 receptor antagonist crystals are not visible upon storage at 5 °C or room temperature for a time period equal to or at least 1 week, 2 weeks, 4 weeks, 1 month, 2 months, 6 months, 1 year or 2 years.

[0082] "Chemically stable" emulsions of the disclosure are ones in which the concentration of the active component (i.e., the drug being delivered) does not change by more than about 20% under appropriate storage conditions for at least 1 month. In certain embodiments, the concentration the NK-1 receptor antagonist in an emulsion of the present disclosure does not change by more than about 5%, 10%, 15% or 20% under appropriate storage conditions for at least 1, 2, 3, 4, 5, 6, 9, 12, 15, 18, or 24 months.

[0083] In one example, the stable emulsion compositions of the disclosure are stable over a wide range of temperatures, e.g., −20 °C to 40 °C. The compositions of the disclosure may be stored at about 5 °C to about 25 °C.

[0084] "Oil phase" in a water-in-oil emulsion refers to all components in the formulation that individually exceed their solubility limit in the water phase; these are materials that generally have solubilities of less than 1% in distilled water, however, water phase components such as salts may decrease the solubility of certain oils resulting in their partitioning into the oil phase. The oil phase refers to the non-aqueous portion of a water-in-oil emulsion.

[0085] "Aqueous phase" or "water phase" in a water-in-oil emulsion refers to the water present and any components that are water soluble, i.e., have not exceeded their solubility limit in water. "Aqueous phase", as used herein, includes a water-containing liquid which can contain pharmaceutically acceptable additives such as acidifying, alkalizing, buffering, chelating, complexing and solubilizing agents, antioxidants and antimicrobial preservatives, humectants, suspending and/or viscosity modifying agents, tonicity and wetting or other biocompatible materials. The aqueous phase refers to the non-oil portion of a water-in-oil emulsion.

[0086] An "emulsifier" refers to a compound that deters the separation of the injectable emulsion into individual oil and aqueous phases. Emulsifiers useful in the present disclosure generally are (1) compatible with the other ingredients of the stable emulsions of the present disclosure, (2) do not

interfere with the stability or efficacy of the drugs contained in the emulsions, (3) are stable and do not deteriorate in the preparation, and (4) are non-toxic.

[0087] Suitable emulsifiers include, but are not limited to, propylene glycol mono- and di-fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, polyoxyethylene-polyoxypropylene co-polymers and block co-polymers, salts of fatty alcohol sulphates, sorbitan fatty acid esters, esters of polyethylene-glycol glycerol ethers, oil and wax based emulsifiers, glycerol monostearate, glycerine sorbitan fatty acid esters and phospholipids.

[0088] A "phospholipid" refers to a triester of glycerol in which the secondary alcohol and one of the primary alcohols has been esterified with fatty acids and the other primary alcohol has been esterified with a phosphate group. Exemplary phospholipids useful in the present invention include, but are not limited to, phosphatidyl chlorine, lecithin (a mixture of choline ester of phosphorylated diacylglyceride), phosphatidylethanolamine, phosphatidylglycerol, phosphatidic acid with about 4 to about 22 carbon atoms, and more generally from about 10 to about 18 carbon atoms and varying degrees of saturation. The phospholipids can have any combination of fatty acid as its fatty acyl side chain, for example, the phospholipids can have a saturated fatty acid such as a decanoic acid, lauric acid, myristic acid, palmitic acid, stearic acid, icosanoic acid, (a C20 saturated fatty acid); sodium behenic acid, or an unsaturated fatty acid such as myristoleic acid, palmitoleic acid, oleic acid, sodium linoleic acid, alpha linolenic acid, sodium arachidonic acid, eicosapentanoic acid, and the like. The two fatty acyl residues on the phospholipids may be the same or they may be different fatty acids. The phospholipid component of the drug delivery composition can be either a single phospholipid or a mixture of several phospholipids. The phospholipids should be acceptable for the chosen route of administration.

[0089] In one aspect, the phospholipids used as emulsifiers in the present invention are naturally occurring phospholipids from a natural origin. For example, naturally occurring lecithin is a mixture of the diglycerides of stearic, palmitic, and oleic acids, linked to the choline ester of phosphoric acid, commonly called phosphatidylcholine, and can be obtained from a variety of sources such as eggs and soya beans. Soy lecithin and egg lecithin (including hydrogenated versions of these compounds) have been characterized in various compositions and are generally recognized to be safe, have combined emulsification and solubilization properties, and tend to be broken down into innocuous substances more rapidly than most synthetic surfactants.

[0090] The term "lecithin" includes a complex mixture of acetone-insoluble phosphatides, of which phosphatidylcholine is a significant component. The term lecithin is also used as a synonym for

phosphatidylcholine. Useful lecithins include, but are not limited to, egg yolk-, egg-, soybean-, and corn-derived lecithin. In one embodiment, the emulsifier is lecithin, such as egg yolk-derived lecithin. The terms egg lecithin and egg yolk derived lecithin are used interchangeably throughout. The compositions described herein preferably comprise lecithin as an emulsifier.

[0091] The amount of phospholipids, by weight, in the emulsions of the present disclosure may be within a range of about 10 wt/wt% to about 20 wt/wt%, 11 wt/wt% to 19 wt/wt%, 11 wt/wt% to 15 wt/wt%, 12 wt/wt% to 13 wt/wt%, 13 wt/wt% to 14 wt/wt%, 13 wt/wt% to 20 wt/wt%, or 12 wt/wt% to 18 wt/wt%. In certain embodiments, the phospholipids in the emulsions are at a concentration, by weight, about 11 wt/wt%, 12 wt/wt%, 12.5 wt/wt%, 13 wt/wt%, 13.5 wt/wt%, 14 wt/wt%, 14.5 wt/wt%, or 15 wt/wt%.

[0092] "Oil" refers to an organic liquid of mineral, vegetable, animal, essential or synthetic origin, including, for example, aliphatic or wax-based hydrocarbons, aromatic hydrocarbons or mixed aliphatic and aromatic hydrocarbons.

[0093] The term "buffer" or "buffered" as used herein means a solution containing both a weak acid and its conjugate base, whose pH changes only slightly upon addition of acid or base. As used herein, the phrase "buffering agent" means a species whose inclusion in a solution provides a buffered solution. Buffers are well-known in the art and readily available. Buffers for use according to the methods and compositions described herein include but are not limited to phosphate, citrate, Tris, carbonate, succinate, maleate, borate, MES, Bis-Tris, ADA, aces,PIPES, MOPSO, Bis-Tri Propane, BES, MOPS, TES, HEPES, DIPSO, MOBS, TAPSO, Trizma, HEPPSO, POPSO, TEA, EPPS, Tricine, Gly-Gly, Bicine, GEPBS, TAPS, AMPD, TABS, AMPSO, CHES, CAPSO, AMP, CAPS, and CABS.

[0094] The term "therapeutic agent" describes any natural or synthetic compound which has a biological activity. A "therapeutically effective amount" means the amount that, when administered to an animal or subject for treating or preventing a disorder, condition, or disease, is sufficient to effect treatment for that disorder, condition, or disease.

[0095] As used herein, the term "emesis" includes nausea and vomiting.

[0096] The term "substantially" in reference to a certain feature or entity means to a significant degree or nearly completely (i.e. to a degree of 85% or greater) in reference to the feature or entity.

II. NK-1 RECEPTION ANTAGONIST EMULSION AND METHODS OF MAKING

[0097] The present disclosure is directed to stable pharmaceutical compositions including an NK-1 receptor antagonist, a surfactant or mixtures of surfactants, a co-surfactant, an oil, with an aqueous

phase. The composition can be an injectable emulsion and is in the form of an oil-in-water emulsion which remains stable over an extended period of time and which is suitable for dilution and intravenous administration.

[0098] The NK-1 receptor antagonist compound is present in the oil phase with an emulsifier, a co-surfactant and an oil. The oil phase is then combined with an aqueous phase comprising water and a tonicity agent as described below to generate the stable emulsion. Prior to combining the oil phase with the aqueous phase, the oil phase will have an oil:antagonist compound ratio of about 11:1 to 30:1, 11:1 to 15:1, or about 13:11. For example, in formulating an oil phase comprising aprepitant, use of an oil:aprepitant ratio of about 13:1 was surprisingly found to produce, when mixed with the water phase, an emulsion which is more stable as compared to an emulsion in which the oil phase contains an oil:aprepitant ratio of less than about 12:1 or 11:1, and/or greater than about 15:1, 20:1, or 30:1. Accordingly, in some embodiments the stable emulsion comprising an NK-1 receptor antagonist and to be administered to the subject can have an oil:antagonist compound ratio of about 11:1 to 30:, 11:1 to 15:1, or about 13:11. Also contemplated, however, are emulsions in which the oil:antagonist compound ratio is about 5:1 to 20:1, 5:1 to 15:1 or 5:1 to 10:1.

[0099] Moreover, the present compositions also possess favorable stability properties when the amount of emulsifier in the oil phase is greater than the amount of oil. For example, the oil phase contains an emulsifier:oil ratio of about 5:1 to 1:1, 3:1 to 1:1 or a ratio of about 1.5:1. Such ratios of emulsifier:oil have surprisingly been found to impart greater stability on a final emulsion which is suitable for injection into a patient. For example, an aprepitant emulsion having a phospholipid:oil ratio within the oil phase of about 1.5:1 was found to have greater stability than a similar aprepitant emulsion, wherein the oil phase comprises a phospholipid:oil ratio of about 0.01:1, 0.1:1, 0.5:1 or 0.9:1.

[0100] Suitable NK-1 receptor antagonists for use in the presently described pharmaceutical emulsions include RP 67580 ((3aR,7aR)-Octahydro-2-[1-imino-2-(2-methoxyphenyl)ethyl]-7,7-diphenyl-4H-isoindol)), WIN 51078 (17-β-Hydroxy-17-α-ethynyl-5-α-androstano[3,2-b]pyrimido[1,2-a]benzimidazole), l-733,060, (((2S,3S)-3-[[3,5-bis(Trifluoromethyl) phenyl]methoxy]-2-phenylpiperidine hydrochloride), l-703,606 (cis-2-(Diphenylmethel)-N- ([2-iodophenyl]methyl)-1-azabicyclo(2.2.2)octan-3-amine) MDL 105,212 (R)-1-[2-[3-(3,4-dichlorophenyl)-1-(3,4,5-trimethoxybenzoyl)-pyrrolidin-3-yl]-ethyl]-4-phenylpiperidine-4-carboxamide hydrochloride), serlopitant, maropitant, Antagonist D, aprepitant, fosaprepitant, R116301, CGP49823, CP-96345, CP-99994, GR-203040, MDL-103392, l-760735, SDZ-NKT-343,

nolpitanitium (SR-140333), AV608, rolapitant, SCH 900978, AV608, GSK424887 (GlaxoSmithKline), GSK206136 (GlaxoSmithKline), GR-205171, CP-99994, TAK 637 ((S)-7-(3,5-Bis-trifluoromethyl-benzyl)-9-methyl-5-p-tolyl-8,9,10,11-tetrahydro-7H-1,7,11a-triaza-cycloocta[b]naphthalene-6,12-dione), LY303870 ([(R)-1-[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4- (piperidin-1-yl)piperidin-1-yl)acetyl)amino]propane]), LY686017 ((2-chloro-phenyl)-{2-[5-pyridin-4-yl-1-(3,5-bistrifluoromethyl-benzyl)-1H-[1,2,3]triazol-4-yl]-pyridin-3-yl}-methanone), E-6006, casopitant/GW679769 ((2R,4S)-4-(4-acetylpiperazin-1-yl)-N-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl)ethyl]-2-(4-fluoro-2-methylphenyl)-N-methylpiperidine-1-carboxamide), vestipitant, orvepitant and orvepitant maleate, befetupitant, netupitant, ezlopitant, CP-122721, MPC-4505 (Myriad Genetics, Inc.), CP-122721 (Pfizer, Inc.), CJ-1 2,255 (Pfizer, Inc.), SRR 240600 (Sanofi-Aventis), or TA-5538 (Tanabe Seiyaku Co.) including all pharmaceutically acceptable salts thereof.

1. Oil Phase

[0101] The oil (hydrophobic) phase comprises an oil. Triglycerides are exemplary oils for use in the compositions described herein. In certain embodiments the oil is or comprises a vegetable oil. "Vegetable oil" refers to oil derived from plant seeds or nuts. Vegetable oils are typically "long-chain triglycerides" (LCTs), formed when three fatty acids (usually 14 to 22 carbons in length, with unsaturated bonds in varying numbers and locations, depending on the source of the oil) form ester bonds with the three hydroxyl groups on glycerol. In certain embodiments, vegetable oils of highly purified grade (also called "super refined") are used to ensure safety and stability of the oil-in-water emulsions. In certain embodiments hydrogenated vegetable oils, which are produced by controlled hydrogenation of the vegetable oil, may be used. Exemplary vegetable oils include but are not limited to almond oil, babassu oil, black currant seed oil, borage oil, canola oil, castor oil, coconut oil, corn oil, cottonseed oil, olive oil, peanut oil, palm oil, palm kernel oil, rapeseed oil, safflower oil, soybean oil, sunflower oil and sesame oil. Hydrogenated and/or or partially hydrogenated forms of these oils may also be used. In specific embodiments, the oil is or comprises safflower oil, sesame oil, corn oil, olive oil and/or soybean oil. In more specific embodiments, the oil is or comprises safflower oil, and/or soybean oil. The oil is present in the emulsion at about 9 wt/wt%, though this may vary between about 5 wt/wt% to 12 wt/wt% or 9 wt/wt% to 10 wt/wt%.

[0102] To generate the oil phase, the NK-1 receptor antagonist is first mixed with an emulsifier such as a phospholipid emulsifier. Examples 1-6 and 11-19 are examples in which NK-1 receptor antagonist emulsions made using an egg lecithin. A phospholipid emulsifier is added to a

concentration of greater than 10 wt/wt%, 11 wt/wt%, 12 wt/wt% or 13 wt/wt% of the emulsion but less than 15 wt/wt%, 17 wt/wt% or 20 wt/wt% of the emulsion.

[0103] The mixture of antagonist and emulsifier is dissolved in a co-surfactant such as a short chain alcohol (1 to 6 carbons). Examples 1-6 and 11-19 below are some examples in which the co-surfactant is ethanol. The mixture is mixed at an elevated temperature, such as at about 60 °C or 70 °C or at an elevated temperature within the range of about 50 °C or 70 °C, until the NK-1 receptor antagonist and emulsifier are dissolved. This mixture is then combined with the oil, such as soybean oil, by mixing again at an elevated temperature such as at about 60 °C to produce the oil phase containing the NK-1 receptor antagonist. Excess co-surfactant can be removed by standard evaporation methods including heating, or pressure reduction, or a combination thereof such employed in a rotary evaporator. In this process, about 10% to 100%, 20% to 95%, 80% to 100%, 90% to 100%, or 95% to 100% of the ethanol evaporates depending on preparation scale, any pressure reduction, and heating time.

[0104] In one embodiment, the NK-1 receptor antagonist and the emulsifier are dissolved in a co-surfactant and an oil. Examples 1-6 and 11-19 below are some examples in which the co-surfactant is ethanol and the oil is soybean oil, however, the methods can be used with any one or more of the co-surfactants and oils described herein. The mixture is mixed at an elevated temperature, such as at about 60 °C or 70 °C or at an elevated temperature within the range of about 50 °C or 70 °C, at least until the NK-1 receptor antagonist and emulsifier are dissolved to produce the oil phase containing the NK-1 receptor antagonist. The mixture of NK-1 receptor antagonist, emulsifier, co-surfactant and oil are mixed at the elevated temperature for about 15 min to 120 min, about 15 min to 45 min, about 30 min to 90 min, or for about 15 min, 30 min or 50 min.

[0105] Excess co-surfactant can be removed by standard evaporation methods including heating, or pressure reduction, or a combination thereof in a rotary evaporator. During this process, about 10% to 100%, 20% to 95%, 80% to 100%, 90% to 100%, or 95% to 100% of the ethanol evaporates depending on preparation scale, any pressure reduction, and heating time.

[0106] In one embodiment, dexamethasone is added to the oil phase comprising the NK-1 receptor antagonist, emulsifier and oil to generate an oil phase comprising both the NK-1 receptor antagonist and dexamethasone prior to mixing with the aqueous phase to generate the pharmaceutical emulsion for injection. Dexamethasone is added to the oil phase to provide a dose of about 12 mg dexamethasone.

2. Aqueous Phase

[0107] The aqueous phase of the NK-1 receptor antagonist emulsion can be a mixture of water and a tonicity agent, including those such as but not limited to sucrose, mannitol, glycerin or dextrose or a mixture thereof. Also included in the aqueous phase is a pH-modifying agent (pH modifier). Sodium oleate is used in Examples 1-3, 5, 6, and 11-15, and 17-19 below to adjust the pH of the emulsion to about 6 to 9, depending on the desired emulsion formulation. However, it is understood that the pH modifier can be other oleic acids or salts thereof including but not limited to sodium oleate, potassium oleate and ammonium oleate. The oleic acid can comprise about 0.1 wt/wt% to 1.0 wt/wt% or about 0.4 wt/wt% or 0.5 wt/wt% of the stable injectable emulsions as provided herein. The aqueous phase is produced by mixing water with the tonicity agent and pH modifier (e.g., sodium oleate). Additional pH modifiers that may be used include but are not limited to sodium hydroxide, potassium hydroxide, magnesium hydroxide, Tris, sodium carbonate and sodium linoleate. In some embodiments, the pH modifier comprises more than one pH modifier. For example, the aqueous phase may comprise both an oleate and a buffer such as a Tris buffer. The pH modifier used is effective for adjusting the pH of the emulsion to a preferred pH of about 6 to 9, 7 to 8, or about 6, 7, 8 or 9. The aqueous phase can readily form by mixing at room temperature.

[0108] The aqueous phase of the emulsion may further contain a buffering agent to promote stability of the emulsion formulation. The drug substance may degrade; for example, lipophilic drugs will partition into the oil phase, which will confer some degree of protection, but hydrolytic degradation may still occur at the oil-water interface. Possible chemical degradation within parenteral fat emulsions includes oxidation of unsaturated fatty acid residues present in triglyceride and lecithin, and hydrolysis of phospholipids leading to the formation of free fatty acids (FFA) and lysophospholipids. Such degradants lower pH, which may then promote further degradation. Thus, pH should be controlled during manufacture and emulsion formulations may include a buffering agent to provide additional control. Any decrease in pH over the assigned shelf-life may be indicative of chemical degradation. Suitable buffers are well known to the person skilled in the art and include but are not limited to a phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer or borate buffer. Tris buffer is used in Examples 11 and 19 below to adjust the pH of the emulsion to about 8 to 9. As shown in Examples 11 and 19, in some embodiments a buffer such as Tris buffer can be used in addition to another pH modifier (e.g., oleate or sodium oleate) to adjust or modify the pH of the emulsion. In some embodiments, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer. In a particular

embodiment, the aqueous phase comprises a buffer, that when mixed with the oil phase will provide a substantially isotonic oil in water emulsion.

[0109] Buffering agents useful for the presently described compositions include, but are not limited to, a phosphate buffer, citrate buffer, Tris buffer, carbonate buffer, succinate buffer, maleate buffer or borate buffer. In a particular embodiment, the buffer is selected from the group, phosphate buffered saline (PBS), modified PBS (PBS-mod) and citrate buffer. In a particular embodiment, the aqueous phase comprises a buffer, that when mixed with the oil phase will provide a substantially isotonic oil in water emulsion. In some embodiments, when the aqueous phase contains a buffering agent, the aqueous phase does not include a tonicity agent. Also, when a buffer is added to the aqueous phase, a pH-adjusting agent may not be added to the aqueous phase. It is understood that a buffer can be added to the aqueous phase or the buffer can be added to the emulsion.

[0110] In some embodiments, the aqueous phase of the emulsion contains a tonicity agent such as sucrose. The tonicity agent is added to an aqueous phase having about 0% to 30%, 0% to 25% or about 20% of the tonicity agent (wt/wt). It was surprisingly found that a composition containing about 20% sucrose wt/wt in the aqueous phase produced an emulsion that was particularly stable as determined by freeze-thaw testing. Accordingly, preferred embodiments include an emulsion in which the aqueous phase comprises a tonicity agent which imparts greater chemical and/or physical stability as compared to an emulsion wherein the aqueous phase contains less than about 10%, 15% or 20% wt/wt tonicity agent or more than about 30%, 40% or 50% wt/wt tonicity agent.

[0111] In one embodiment, the aqueous phase further comprises dexamethasone sodium phosphate (also referred to as “dexamethasone phosphate”). Dexamethasone sodium phosphate is a corticosteroid which is freely soluble in water. Daily dosages for dexamethasone sodium phosphate range from about 0.5 mg to 20 mg, more preferably from about 14 mg to 18 mg or 16 mg, depending on the severity of the disease or disorder. Accordingly, an NK-1 receptor antagonist emulsion further comprising dexamethasone may contain dexamethasone sodium phosphate in the aqueous phase. Accordingly, the aqueous phase of an emulsion suitable for intravenous administration may contain about 0.5 mg to 20 mg, 14 mg to 18 mg or about 16 mg dexamethasone sodium phosphate.

[0112] In another embodiment, a solution of dexamethasone sodium phosphate can be mixed into the fine emulsion prior to sterile filtration to prepare an emulsion containing dexamethasone sodium phosphate in the aqueous phase,

3. Pharmaceutical Emulsion Formulations

[0113] The pharmaceutical compositions comprising NK-1 receptor antagonists as disclosed herein are sterile oil-in-water emulsions comprising the aqueous and oil phases described above. Also encompassed by the disclosure are methods for preparing stable emulsions comprising the receptor antagonist which are suitable for intravenous administration and which can be prepared according to the conventional manufacturing procedures using aseptic techniques.

[0114] The aqueous phase is combined with the oil phase, under high-speed homogenization to produce a coarse emulsion. Examples 1-6 and 12-19 provide examples of NK-1 receptor antagonist emulsions which are produced using compositions and methods disclosed herein. As described in these examples, the combined aqueous and oil phases is homogenized using an IKA Ultra-Turrax T25 dispersing instrument at a speed of 20,000 rpm for 1 min. The speed used in this first homogenization step may vary, for example, from 2000 rpm to 25,000 rpm, or from 15,000 rpm to 22,000 rpm. The time of the homogenization step can also vary, for example, from 0.5 min to 1 hour, or from 1 min to 45 min. This crude emulsion is then homogenized into a fine emulsion by a high-pressure homogenizer, which may be a microfluidizer. The interaction chamber and the cooling coil portions of the microfluidizer are cooled by water, such as by an ice bath. The temperature of the ice bath may be between 0 to 10 ºC, or 2 to 6 ºC. The temperature of the emulsion coming out of the high-pressure homogenization may be between 0 to 60 ºC, 15 ºC, to 60 ºC, 20 ºC to 40 ºC, or at about 25 ºC. The microfluidizer is first primed with water and then the crude emulsion is introduced. The output from the homogenizer is initially run to waste to remove priming water, and priming water and emulsion mixtures, and then collected in a clean vessel when the stream becomes consistent in appearance. The high-pressure homogenizer cycle may be repeated to sufficiently reduce oil droplet size. The pressure used for the homogenization may vary. The pressures may be between 5000 and 30,000 psi. The number of passes through the microfluidizer may vary in order to achieve the desired droplet size. The number of passes may be from about 2 to 20, 2 to 15, 4 to 15, 4 to 12 or 7 to 8.

[0115] The pharmaceutical formulation may then be passed through a filter system at room temperature, and/or autoclaved, to achieve sterilization. The filters used to achieve sterilization may be chosen by the skilled artisan and may have a nominal pore size of 0.2 μm. The filter material used may vary. In one embodiment, the filter is nylon. In another embodiment, the filter is a Posidyne® filter (covalent charge-modified Nylon 6,6 membrane which exhibits a net positively-charged zeta potential in aqueous solutions). For large scale production the method above may need to be

modified. A skilled practitioner could combine these materials in a different order and using different processing equipment to achieve the desired end result.

[0116] In one embodiment of the disclosure, the homogenization can be done in repeated cycles to achieve an emulsion in which the oil particle/globule size is less than 2 microns (μm) with intermediate cooling of the homogenized product to a temperature less than about 25 °C.

[0117] The final emulsion comprises an oil portion (oil phase) dispersed in an aqueous portion (aqueous phase). The ratio of components to the NK-1 receptor antagonist within the oil phase is an important characteristic of the emulsion which may affect stability of the formulation prepared for injection and each of these ratios within the final pharmaceutical emulsion are presented in more detail below. As described above, the oil phase comprises the NK-1 receptor antagonist, an oil and an emulsifier, examples of which are provided herein.

[0118] The final emulsion contains about 0.7 wt/wt% of the NK-1 receptor antagonist, but may range from about 0.2 wt/wt% to 1.5 wt/wt%, 0.4 wt/wt% to 1.0 wt/wt%, 0.6 wt/wt% to 0.7 wt/wt%, or 0.7 wt/wt% to 0.8 wt/wt%. The emulsion is prepared which can contain about 130 mg of the NK-1 receptor antagonist, however, preparations may also be prepared according to the present disclosure which contain about 100 mg to 1000 mg, 100 mg to 500 mg, 250 mg to 750 mg or 100 mg to 200 mg NK-1 receptor antagonist.

[0119] In one embodiment, the ratio of oil:NK-1 receptor antagonist (wt%:wt%) within the oil phase of the final emulsion is about 13:1 to 14:1, but can range from about 11:1 to 15:1, 12:1 to 14:1, 13:1 to 13.5:1, or 12:1 to 15:1. In another embodiment, the ratio of oil:NK-1 receptor antagonist is about 11:1, 11.5:1, 12:1, 12.5:1, 13:1, 13.5:1, 14:1, 14.5:1 or 15:1.

[0120] The ratio of emulsifier to NK-1 receptor antagonist in the final emulsion can be about 20:1 but may also vary. For example, the ratio of emulsifier:NK-1 receptor antagonist (wt%:wt%) within the oil portion ranges from about 15:1 to 30:1, 20:1 to 25:1, 18:1 to 22:1, 19:1 to 20:1, or 10:1 to 30:1. In one embodiment, the emulsifier:NK-1 receptor antagonist (wt%:wt%) is about 15:1, 18:1, 19:1, 20:1, 21:1, 22:1 or 23:1.

[0121] The ratio of components within the oil phase of the final emulsion may alternatively be expressed in the ratio of (emulsifier plus oil):NK-1 receptor antagonist (wt%:wt%). The ratio of (emulsifier plus oil):NK-1 receptor antagonist can be about 33:1, but the ratios for the present emulsion can range from about 20:1 to 40:1, 25:1 to 35:1, 30:1 to 35:1 or 33:1 to 37:1, or may be, for example, about 30:1, 32:1, 33:1, 34:1, 35:1, 36:1, 37:1, 38:1 or 40:1.

[0122] The composition of the present disclosure has a significant advantage in terms of reduced toxicity as compared to injectable formulations which may contain less desirable excipients such as detergents, e.g., Tween-20 or Tween-80. The present formulations take advantage of the ability to solubilize therapeutically effective amounts of a NK-1 receptor antagonist in an oil phase which can then be used to generate an emulsion suitable for injection. Accordingly, described herein are pharmaceutical emulsion compositions containing a NK-1 receptor antagonist and optionally dexamethasone or dexamethasone sodium phosphate, wherein the emulsion does not comprise a detergent.

[0123] The composition of the present disclosure gives a product suitable for parenteral use because of low particle size. The composition of the present disclosure is easy to use as the product can be diluted with an agent such as an aqueous solution of sucrose, an aqueous solution of maltose or dextrose 5% injection or normal saline to achieve the required concentration for parenteral administration. The composition of the present disclosure also has a prolonged shelf life and hence is suitable for a readily marketable product.

[0124] The compositions of the disclosure are both chemically and physically stable. A physically stable emulsion of the invention is one which can be stored under appropriate conditions for at least 1, 2, 3, 4, 5, 6, 9, 12, 15, 18, 24 or 36 months, without an increase in average droplet size above that allowed as stated in USP <729>. As well, the population of large-diameter fat globules should be within the limits stated in USP <729>.

[0125] Droplet size limits defined in USP <729> apply throughout the assigned shelf life, which for a commercial pharmaceutical formulation may extend to 2-3 years or longer. All true emulsions are thermodynamically unstable and may over time undergo a range of processes which tend to increase the droplet size. These include direct droplet coalescence, when two droplets collide and form a single new droplet, and aggregation, in which droplets adhere together to form larger masses. Aggregation may in some cases be a precursor of further coalescence into larger droplets. These processes may result in large aggregates rising to the surface of the container, a phenomenon known as 'creaming', and ultimately to free oil being visible on the emulsion surface, known as ‘cracking’.

[0126] Droplet size limits are typified by USP33-NF28 General Chapter <729> for Globule Size Distribution in Lipid Injectable Emulsions, hereinafter referred to as USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm (PFAT5) not exceeding 0.05%, irrespective of the final lipid concentration.

[0127] Droplet size measurements such as those defined in USP<729> can measure the initial increases in size, and hence are predictive of emulsion physical stability, at early times, long before the formulation shows macroscopic visible changes. Accordingly, the emulsions as described herein are stable compositions having an intensity-weighted mean droplet diameter less than about 500 nm, 400 nm, 300 nm, 200 nm or 100 nm.

[0128] The oil or particle droplet size, i.e. diameter, according to the present disclosure is measured using a dynamic light scattering (DLS) instrument, such as the Malvern Zetasizer 4000, Malvern Zetasize Nano S90 or preferably the Malvern Zetasizer Nano ZS. Intensity-weighted particles sizes were recorded, since they do not require the knowledge of the refractive index of the particle. In Malvern Zetasizer instruments, there are two fits for determining the intensity-weighted diameter of the oil droplet size. The first is a cumulant fit that is used to determine the Z-average diameter; this fit can additionally give the polydispersity index (PDI). This cumulant fit is recommended for monodisperse samples possessing a PDI of lower than 0.2. The second is a non-negative least squares (NNLS) fit. This gives the Peak 1 diameter, Peak 2 diameter and Peak 3 diameter. This is more suitable for polydisperse samples having a PDI of greater than 0.2.

[0129] The emulsion preparations as described herein may further comprise a preservative in quantities that preserve the composition. Suitable preservatives used in some of the embodiments of present disclosure include, but are not limited to, disodium edetate, tocopherol, benzalkonium chloride, methyl, ethyl, propyl or butylparaben, benzyl alcohol, phenylethyl alcohol, benzethonium, chlorobutanol, potassium sorbate or combination thereof.

III. MEDICAL USE

[0130] The pharmaceutical compositions of the present disclosure can be used for the prevention or treatment of emesis and provide a non-oral option for patients undergoing highly or moderately emetogenic chemotherapy such as chemotherapy used in cancer patients. The disclosure thus encompasses a method of treatment comprising intravenously administering an emulsion comprising a NK-1 receptor antagonist as described herein to a subject undergoing highly or moderately emetogenic chemotherapy whether the chemotherapy is an initial treatment or repeat courses of the chemotherapy. The pharmaceutical emulsions described herein can be used, for example, in preventing or treating acute and delayed nausea and vomiting associated with the chemotherapy or radiotherapy.

[0131] Another embodiment relates to the use of the pharmaceutical formulations of the disclosure in the manufacture of a medicament for use preventing or treating emesis in a subject in need thereof.

[0132] The amount of the NK-1 receptor antagonist and optionally dexamethasone required for use in the methods of the disclosure may vary with the method of administration and condition of the patient, and the degree of therapy required, and will be ultimately at the discretion of the attendant physician or clinician.

IV. EXAMPLES

The following examples are illustrative in nature and are in no way intended to be limiting.

Example 1: Preparing Aprepitant Emulsions for Intravenous Injection

[0133] To prepare the aprepitant emulsion, an oil phase was first prepared by combining 750 mg of aprepitant and 15.0 g of egg lecithin (LIPOID E 80) with 12.0 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added in 10.0 g of soybean oil. Heating at 60 ºC and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 5.60 g of sucrose and 0.500 g of sodium oleate in 70.0 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 1 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using non-negative least squares (NNLS) fit gave a Peak 1 diameter of 99 nm. The intensity-weighted mean particle size determined using cumulant fit provided a Z-average diameter of 87 nm. The zeta potential was measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.74. This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 1

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.750	0.679	1
Lipoid E 80	15.0	13.6	20
Soybean Oil	10.0	9.05	13.3
Ethanol[1]	8.59	7.78	11.5
Sucrose	5.60	5.07	7.5
Sodium Oleate	0.500	0.453	0.667
Water for Injection	70.0	63.4	93.3
Total	110	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 2: Preparing Aprepitant Emulsions for Intravenous Injection

[0134] To prepare the aprepitant emulsion, an oil phase was first prepared by combining 450 mg of aprepitant and 9.00 g of egg lecithin (LIPOID E 80) with 4.0 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added 6.00 g of soybean oil. Heating at 60 ºC and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 3.36 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 2 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using NNLS fit gave a Peak 1 diameter of 127 nm. The intensity-weighted mean particle sized determined using cumulant fit provided a Z-average diameter of 101 nm. The zeta potential was measured to be -47 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.77. This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 2

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.450	0.714	1
Lipoid E 80	9.00	14.3	20
Soybean Oil	6.00	9.52	13.3
Ethanol[1]	1.89	3.00	4.20
Sucrose	3.36	5.33	7.47
Sodium Oleate	0.300	0.476	0.667
Water for Injection	42.0	66.7	93.3
Total	63.0	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 3: Preparing Aprepitant Emulsions for Intravenous Injection

[0135] To prepare the aprepitant emulsion, an oil phase was first prepared by combining 450 mg of aprepitant and 9.00 g of egg lecithin (LIPOID E 80) with 6.0 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added in 6.00 g of soybean oil. Heating at 60ºC and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 15.62 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 3 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using NNLS fit gave a Peak 1 diameter of 88 nm. The intensity-weighted mean particle sized determined using cumulant fit provided a Z-average diameter of 68 nm. The zeta potential was measured to be -42 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.80. This aprepitant-containing emulsion is to be diluted with water for injection by 4-fold prior to injection.

Table 3

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.450	0.587	1
Lipoid E 80	9.00	11.7	20
Soybean Oil	6.00	7.83	13.3
Ethanol[1]	3.27	4.26	7.26
Sucrose	15.6	20.4	34.7
Sodium Oleate	0.300	0.391	0.667
Water for Injection	42.0	54.8	93.3
Total	76.6	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 4: Preparing an Alternate Aprepitant Emulsion Formulation for Intravenous Injection

[0136] An aprepitant emulsion was prepared which has less than 10% wt/wt of the phospholipid emulsifier and which was adjusted to a pH of less than 8.0. To prepare the aprepitant emulsion, an oil phase was first prepared by combining 450 mg of aprepitant and 6.67 g of egg lecithin (LIPOID E 80) with 7.2 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm. Heating and stirring was carried out until the ethanol was evaporated and a thick residue was observed. To the resultant solution was added in 6.00 g of soybean oil and an appropriate amount of ethanol to obtain a clear oil phase upon heating at 60ºC. The aqueous phase was prepared by dissolving 3.36 g of sucrose in 50.5 ml of water for injection at 60ºC. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. The pH of this crude emulsion was adjusted to 7.0 and then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 4 below. Within 4 days post preparation at room temperature, crystals were observed in the product by microscopy.

Table 4

Component	Amount (g)	Concentration (w/w%)	Ratio to Aprepitant
Aprepitant	0.450	0.672	1
Lipoid E 80	6.67	9.95	14.8
Soybean Oil	6.00	8.96	13.3
Sucrose	3.36	5.02	7.47
Water for Injection	50.5	75.4	112
Total	67.0	100	-

Example 5: Preparing Aprepitant Emulsions for Intravenous Injection

[0137] An aprepitant emulsion was prepared which contains oleic acid. To prepare the aprepitant emulsion, an oil phase was first prepared by combining 250 mg of aprepitant, 2.50 g of egg lecithin (LIPOID E 80), 15.0 g of soybean oil and 125 mg of oleic acid. Ten ml of ethanol was added to dissolve the mixture at 70 ºC. The ethanol was removed by pressure reduction in a 70 ºC water bath to yield a clear oil phase. A preheated aqueous phase containing 82.1 ml of water for injection at 70 ºC was added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion was sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 5 below. Within 4 days post-preparation at room temperature, crystals were observed in the product by microscopy.

Table 5

Component	Amount (g)	Concentration (w/w%)	Ratio to aprepitant
Aprepitant	0.250	0.250	1
Lipoid E 80	2.50	2.50	10
Soybean Oil	15.0	15.0	60
Oleic Acid	0.125	0.125	0.5
Water for Injection	82.1	82.1	328
Total	100	100	-

Example 6: Preparing Emulsions Containing Aprepitant and Dexamethasone Sodium Phosphate for Intravenous Injection

[0138] To prepare an injectable emulsion containing aprepitant and dexamethasone sodium phosphate, an oil phase was first prepared by combining 773 mg of aprepitant and 15.5 g of egg lecithin (LIPOID E 80) with 10.3 ml of ethanol. This mixture was dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution was added in 10.3 g of soybean oil. Heating at 60 ºC and stirring at 200 rpm was continued for another 15 min. The aqueous phase was prepared by dissolving 5.77 g of sucrose and 0.515 g of sodium oleate in 71.1 ml of water for injection. This mixture was stirred at 300 rpm at room temperature for 30 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. Dexamethasone sodium phosphate (93.5 mg) dissolved in 1 ml of water for injection was mixed into the fine emulsion. This resultant fine emulsion containing both aprepitant and dexamethasone sodium phosphate was sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 6 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using NNLS fit gave a Peak 1 diameter of 95 nm. The intensity-weighted mean particle size determined using cumulant fit provided a Z-average diameter of 70 nm. The zeta potential was measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion was 8.92. This aprepitant and dexamethasone sodium phosphate containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 6

Component	Amount (g)	Concentration (w/w%)	Ratio to aprepitant
Aprepitant	0.773	0.688	1
Dexamethasone Sodium Phosphate	0.0935	0.0832	0.121
Lipoid E 80	15.5	13.8	20
Soybean Oil	10.3	9.17	13.3
Ethanol[1]	7.31	6.51	9.47
Sucrose	5.77	5.14	7.47
Sodium Oleate	0.515	0.459	0.667
Water for Injection	72.1	64.2	93.3
Total	112	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Example 7: Stability of the Aprepitant Emulsion at Room Temperature and 5 °C

[0139] Stability of the aprepitant emulsions prepared as described in Examples 1, 2 3 and 6 was measured by incubating each emulsion preparation at room temperature (about 25 °C) or at 5 °C. Mean particle size and percentage of fat globules above 5 μm were measured using DLS and light obscuration respectively to determine if they satisfy USP <729>. The emulsions were also inspected by microscopy for aprepitant crystals. Example 1 was stable at room temperature for 2 months, that is, the mean particle size and percentage of fat globules above 5 μm satisfied USP <729>. Additionally, no aprepitant crystals were visible by microscopy. After 2 months storage at room temperature, creaming was observed in Examples 1 and 6. This corresponded with the observation of aprepitant crystals. Examples 2 and 3 were stable at room temperature for 3 and 2 months respectively. After these time points, aprepitant crystals were observed in these formulations. Storage at 5 ºC resulted in longer emulsion stability for Examples 1, 2, 3 and 6. Table 7 shows the characterizations of Examples 1, 2, 3 and 6 and their respective stabilities at room temperature and at 5 ºC.

Table 7

Sample	PDI	Particle Size as Peak 1 Diameter (nm)	Particle Size as Z-Average Diameter (nm)	Zeta Potential (mV)	pH	Stability at 25 °C per USP <729> (months)	Stability at 5 °C per USP <729>
Example 1	0.122	99	87	-43	8.74	2	>10 months
Example 2	0.200	127	101	-47	8.77	3	>10 months
Example 3	0.219	88	68	-42	8.80	2	>10 months
Example 6	0.244	95	70	-43	8.92	2	>10 months

Example 8: Stability of the Aprepitant Emulsion to Freeze-Thaw Cycle

[0140] The aprepitant emulsions prepared according to Examples 1, 2, 3 and 6 were tested for stability upon exposure to a freeze-thaw cycle. Samples from the Examples 1, 2, 3 and 6 were stored at -20 °C overnight. They were thawed to room temperature the next day and visualized by microscopy. Prior to freezing, all samples did not present any visible particles under the microscope. FIG. 1 shows microscope images, at 10X, of emulsions after the freeze-thaw cycle (Examples 1, 2, 3 and 6 are shown as FIG. 1 A, B, C, and D, respectively). Emulsions prepared as described in examples 1, 2 and 6 showed visible particles after exposure to freezing. Only Example 3 was stable after freezing. As FIG. 1C shows, no visible particles were observed for the formulation of Example 3. This enhanced stability was conferred by the presence of a large concentration of sucrose (20 w/w% in Example 3 compared to 5 w/wt% in Examples 1, 2 and 6).

Example 9: Pharmacokinetics of an Aprepitant Emulsion

[0141] The pharmacokinetics of an aprepitant emulsion prepared according to Example 1 was determined. Two groups of six male Sprague-Dawley rats each were injected intravenously with, respectively, fosaprepitant in solution or aprepitant emulsion prepared according to Example 1. All drugs were administered at an effective concentration equivalent to 14 mg/kg aprepitant. Blood from all rats was collected at the appropriate time intervals and processed to plasma by centrifugation. Plasma samples were analyzed by LC-MS/MS for aprepitant and fosaprepitant, as appropriate. A plasma concentration versus time curve of aprepitant for the emulsion described in Example 1 and for fosaprepitant is presented in FIG. 2 (fosaprepitant in solution, ●; aprepitant emulsion, ▲). The

curves indicate the initial aprepitant level reached immediately after injection of the aprepitant emulsion was almost 3 times higher than the initial aprepitant level reached immediately after injection of the fosaprepitant solution. Plasma levels of aprepitant resulting from each injection, however, were essentially the same by the 3-hour time point indicating the formulations were bioequivalent except for a delay in the conversion of fosaprepitant to aprepitant.

Example 10: Pharmacokinetics of an Aprepitant and Dexamethasone Emulsion

[0142] The pharmacokinetics of an aprepitant and dexamethasone sodium phosphate combination emulsion prepared according to Example 6 was determined. Male Sprague-Dawley rats each were injected intravenously with fosaprepitant solution (group 1), dexamethasone sodium phosphate solution (group 2), or an emulsion containing aprepitant and dexamethasone sodium phosphate prepared according to Example 6 (group 3). Groups 1 and 2 consisted of six rats each; for group 3, twelve rats were injected with the aprepitant and dexamethasone sodium phosphate combination emulsion to allow for the collection of sufficient samples for the measurement of both active ingredients.

[0143] In groups 1 and 3, a dose was administered at an effective drug concentration equivalent to 2 mg/kg aprepitant. In groups 2 and 3, a dose was administered at an effective drug concentration equivalent to 0.24 mg/kg dexamethasone sodium phosphate. Blood from all rats was collected at the appropriate time intervals and processed to plasma by centrifugation. Plasma samples were analyzed by LC-MS/MS for dexamethasone, aprepitant, and fosaprepitant, as appropriate.

[0144] FIGS. 3 and 4 present the plasma concentration versus time curve of aprepitant and dexamethasone, respectively. FIG. 3 compares the aprepitant plasma concentration versus time curve resulting from injection of the emulsion described in Example 6 (FIG. 3, ●) vs. injection of a solution of fosaprepitant (FIG. 3, ▲). FIG. 4 compares the dexamethasone plasma concentration versus time curve resulting from injection of a dexamethasone sodium phosphate solution (FIG. 4, ●) vs. injection of the emulsion described in Example 6. The curves indicate that the aprepitant in the emulsion is released approximately simultaneously with the dexamethasone sodium phosphate. The presence of dexamethasone sodium phosphate in the emulsion does not affect the pharmacokinetics of aprepitant.

Example 11: Preparing Aprepitant Emulsions for Intravenous Injection

[0145] To prepare the aprepitant emulsion comprising a buffering agent, an oil phase is first prepared by combining 750 mg of aprepitant, 15.0 g of egg lecithin (LIPOID E 80), 10.0 g of soybean oil and 3.75 ml of ethanol. This mixture is dissolved by heating and stirring at 70 °C and 200 rpm for

30 min. The aqueous phase is prepared by dissolving 2.17 g of sucrose and 0.500 g of sodium oleate in a mixture of 4.1 ml of 1M Tris buffer (pH 8.4) and 65.9 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). Dynamic light scattering is used to determine the intensity-weighted particle size using NNLS fit to give the Peak 1 diameter, the intensity-weighted mean particle sized is determined using cumulant fit to provide the Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Example 12: Preparing Rolapitant Emulsions for Intravenous Injection

[0146] To prepare the rolapitant emulsion, an oil phase was first prepared by combining 1.080 g of rolapitant and 21.6 g of egg lecithin (LIPOID E 80) with 14.4 g of soybean oil and 5.40 ml of ethanol in a glass jar. This mixture was allowed to incubate at room temperature for 30 min followed by heating and stirring at 70°C and 200 rpm for another 30 min. The aqueous phase was prepared by dissolving 8.06 g of sucrose and 0.720 g of sodium oleate in 100.8 ml of water for injection by heating and stirring at 35°C and 300 rpm for 15 min. The aqueous phase was then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion was passed 8 times through a high-pressure microfluidizer (Microfluidizer® M-110P, F12Y interaction chamber) at a pressure of 20,000 psi. The outlet fine emulsion temperature was kept at approximately 25°C using cooling water. The resultant fine emulsion was sterilized by passing through a 0.2 μm nylon filter (Nalgene). Details of the emulsion composition are provided in Table 8 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size analyzed using non-negative least squares (NNLS) fit gave a Peak 1 diameter of 127 nm (Table 9). The intensity-weighted mean particle size determined using cumulant fit provided a Z-average diameter of 100 nm. The pH and osmolality of the injectable emulsion were 8.51 and 318 mmol/kg respectively. This rolapitant-containing emulsion can be injected as is, or diluted for infusion with 0.9% saline or 5% dextrose.

Table 8

Component	Amount (g)	Concentration (w/w%)	Ratio to Rolapitant
Rolapitant	1.080	0.728	1
Lipoid E 80	21.6	14.55	20
Soybean Oil	14.4	9.70	13.3
Ethanol[1]	1.78	1.20	1.65
Sucrose	8.06	5.43	7.47
Sodium Oleate	0.720	0.485	0.667
Water for Injection	100.8	67.9	93.3
Total	148	100	-

[1]Final amount after taking into account the ethanol that was evaporated during processing.

Table 9

Sample	PDI	Particle Size as Peak 1 Diameter (nm)	Particle Size as Z-Average Diameter (nm)	pH	Osmolality (mmol/kg)	Stability at 25°C per USP <729>	Stability at 5°C per USP <729>
Example 1	0.213	127	100	8.51	318	>1 months	>1 months

Example 13: Preparing Netupitant Emulsions for Intravenous Injection

[0147] To prepare the emulsion containing a therapeutically effective amount of netupitant, an oil phase is first prepared by combining about 750 mg of netupitant and 15.0 g of egg lecithin (LIPOID E 80) with 12.0 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added in 10.0 g of soybean oil. Heating at 60 °C and stirring at 200 rpm is continued for another 15 min. The aqueous phase is prepared by dissolving 5.60 g of sucrose and 0.500 g of sodium oleate in 70.0 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 10 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using non-negative least squares (NNLS) fit to obtain a Peak 1 diameter of the particle. The

intensity-weighted mean particle size is also determined using cumulant fit and provides a Z-average diameter. The zeta potential is measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion is also measured and is preferably about pH 7.8 to 8.8. This NK-1 receptor antagonist-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 10

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.750	0.679	1
Lipoid E 80	15.0	13.6	20
Soybean Oil	10.0	9.05	13.3
Ethanol[1]	8.59	7.78	11.5
Sucrose	5.60	5.07	7.5
Sodium Oleate	0.500	0.453	0.667
Water for Injection	70.0	63.4	93.3
Total	110	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 14: Preparing Netupitant Emulsions for Intravenous Injection

[0148] To prepare the netupitant emulsion, an oil phase is first prepared by combining about 450 mg of netupitant and 9.00 g of egg lecithin (LIPOID E 80) with 4.0 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added 6.00 g of soybean oil. Heating at 60 ºC and stirring at 200 rpm is continued for about another 15 min. The aqueous phase is prepared by dissolving 3.36 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 11 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using NNLS fit to give a Peak 1 diameter. The intensity-weighted mean particle size is determined using cumulant fit provides a Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis

(Malvern® Zetasizer Nano ZS). The pH of the injectable emulsion is also measured and is preferably about pH 7.8 to 8.8. This netupitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 11

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.450	0.714	1
Lipoid E 80	9.00	14.3	20
Soybean Oil	6.00	9.52	13.3
Ethanol[1]	1.89	3.00	4.20
Sucrose	3.36	5.33	7.47
Sodium Oleate	0.300	0.476	0.667
Water for Injection	42.0	66.7	93.3
Total	63.0	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 15: Preparing Netupitant Emulsions for Intravenous Injection

[0149] To prepare the netupitant emulsion, an oil phase is first prepared by combining 450 mg of netupitant and 9.00 g of egg lecithin (LIPOID E 80) with 6.0 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added in 6.00 g of soybean oil. Heating at 60°C and stirring at 200 rpm is continued for another 15 min. The aqueous phase is prepared by dissolving 15.62 g of sucrose and 0.300 g of sodium oleate in 42.0 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 12 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using NNLS fit gave a Peak 1 diameter. The intensity-weighted mean particle size is determined using cumulant fit provided a Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano

ZS). The pH of the injectable emulsion is also measured and is preferably about pH 7.8 to 8.8. This netupitant-containing emulsion is to be diluted with water for injection by 4-fold prior to injection.

Table 12

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.450	0.587	1
Lipoid E 80	9.00	11.7	20
Soybean Oil	6.00	7.83	13.3
Ethanol[1]	3.27	4.26	7.26
Sucrose	15.6	20.4	34.7
Sodium Oleate	0.300	0.391	0.667
Water for Injection	42.0	54.8	93.3
Total	76.6	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 16: Alternate Netupitant Emulsion Formulations for Intravenous Injection

[0150] A netupitant emulsion is prepared which has less than 10% wt/wt of the phospholipid emulsifier and which is adjusted to a pH of less than 8.0. To prepare the netupitant emulsion, an oil phase is first prepared by combining 450 mg of netupitant and 6.67 g of egg lecithin (LIPOID E 80) with 7.2 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm. Heating and stirring is carried out until the ethanol is evaporated and a thick residue is observed. To the resultant solution is added in 6.00 g of soybean oil and an appropriate amount of ethanol to obtain a clear oil phase upon heating at 60ºC. The aqueous phase is prepared by dissolving 3.36 g of sucrose in 50.5 ml of water for injection at 60ºC. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. The pH of this crude emulsion is adjusted to 7.0 and then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 µm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 13 below. Within 4 days post preparation at room temperature, the emulsion product is analyzed for the presence of crystals by microscopy.

Table 13

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.450	0.672	1
Lipoid E 80	6.67	9.95	14.8
Soybean Oil	6.00	8.96	13.3
Sucrose	3.36	5.02	7.47
Water for Injection	50.5	75.4	112
Total	67.0	100	-

Example 17: Alternate Netupitant Emulsion Formulations for Intravenous Injection

[0151] A netupitant emulsion is prepared which contains oleic acid. To prepare the netupitant emulsion, an oil phase is first prepared by combining 250 mg of netupitant, 2.50 g of egg lecithin (LIPOID E 80), 15.0 g of soybean oil and 125 mg of oleic acid. Ten ml of ethanol is added to dissolve the mixture at 70 ºC. The ethanol is removed by pressure reduction in a 70 ºC water bath to yield a clear oil phase. A preheated aqueous phase containing 82.1 ml of water for injection at 70 ºC is added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 14 below. Within 4 days post preparation at room temperature, the emulsion product is analyzed for the presence of crystals by microscopy.

Table 14

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.250	0.250	1
Lipoid E 80	2.50	2.50	10
Soybean Oil	15.0	15.0	60
Oleic Acid	0.125	0.125	0.5
Water for Injection	82.1	82.1	328
Total	100	100	-

Example 18: Preparing Emulsions Containing Netupitant and Dexamethasone Sodium Phosphate for Intravenous Injection

[0152] To prepare an injectable emulsion containing netupitant and dexamethasone sodium phosphate, an oil phase are first prepared by combining 773 mg of netupitant and 15.5 g of egg lecithin (LIPOID E 80) with 10.3 ml of ethanol. This mixture is dissolved by heating and stirring at 60 °C and 200 rpm for 15 min. To the resultant solution is added in 10.3 g of soybean oil. Heating at 60 °C and stirring at 200 rpm is continued for another 15 min. The aqueous phase is prepared by dissolving 5.77 g of sucrose and 0.515 g of sodium oleate in 71.1 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. Dexamethasone sodium phosphate (93.5 mg) dissolved in 1 ml of water for injection is mixed into the fine emulsion. This resultant fine emulsion containing both netupitant and dexamethasone sodium phosphate is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). The details of the emulsion composition are provided in Table 15 below. By dynamic light scattering (Malvern® Zetasizer Nano ZS), the intensity-weighted particle size is analyzed using NNLS fit to determine a Peak 1 diameter. The intensity-weighted mean particle size is determined using cumulant fit to determine a Z-average diameter. The zeta potential is measured to be -43 mV by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). The preferred pH of the injectable emulsion is between about 8.5 and 9.5. This netupitant and dexamethasone sodium phosphate containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Table 15

Component	Amount (g)	Concentration (w/w%)	Ratio to Netupitant
Netupitant	0.773	0.688	1
Dexamethasone Sodium Phosphate	0.0935	0.0832	0.121
Lipoid E 80	15.5	13.8	20
Soybean Oil	10.3	9.17	13.3
Ethanol[1]	7.31	6.51	9.47
Sucrose	5.77	5.14	7.47
Sodium Oleate	0.515	0.459	0.667
Water for Injection	72.1	64.2	93.3
Total	112	100	-

[1]Final amount after taking into account the ethanol that is evaporated during processing.

Example 19: Preparing NK-1 Receptor Antagonist Emulsions for Intravenous Injection

[0153] To prepare an NK-1 receptor antagonist emulsion comprising a buffering agent, an oil phase is first prepared by combining 750 mg of aprepitant, 15.0 g of egg lecithin (LIPOID E 80), 10.0 g of soybean oil and 3.75 ml of ethanol. This mixture is dissolved by heating and stirring at 70 °C and 200 rpm for 30 min. The aqueous phase is prepared by dissolving 2.17 g of sucrose and 0.500 g of sodium oleate in a mixture of 4.1 ml of 1M Tris buffer (pH 8.4) and 65.9 ml of water for injection. This mixture is stirred at 300 rpm at room temperature for 30 min. The aqueous phase is then added to the oil phase and subsequently subjected to high-speed homogenization (Ultra-Turrax® IKA T25) at a speed of 20,000 rpm for 1 min to produce the crude emulsion. This crude emulsion is then passed 8 times through an ice-cooled high-pressure microfluidizer (Microfluidizer® M-110L, F12Y interaction chamber) at a pressure of 18,000 psi. The resultant fine emulsion is sterilized by passing it through a 0.2 μm nylon syringe filter (Corning). Dynamic light scattering is used to determine the intensity-weighted particle size using NNLS fit to give the Peak 1 diameter, the intensity-weighted mean particle sized is determined using cumulant fit to provide the Z-average diameter. The zeta potential is measured by laser Doppler micro-electrophoresis (Malvern® Zetasizer Nano ZS). This aprepitant-containing emulsion can be injected as is, or diluted for infusion with 5% dextrose or 0.9% saline.

Example 20: Stability of the Rolapitant Emulsion at Room Temperature and 5 °C

[0154] Stability of the rolapitant emulsion prepared as described in Example 12 was measured by incubating the emulsion preparation at room temperature (about 25 °C) or at 5 °C. Mean particle size and percentage of fat globules above 5 μm were measured using DLS and light obscuration respectively and demonstrated to satisfy USP <729> after 2 months of storage. The emulsions were also inspected by microscopy for rolapitant crystals and visually for the presence of emulsion creaming. The absence of crystals or emulsion creaming further indicated product stability.

Example 21: Stability of the Netupitant Emulsion at Room Temperature and 5 °C

[0155] Stability of the netupitant emulsions prepared as described in Examples 13-17 can be measured by incubating each emulsion preparation at room temperature (about 25 °C) or at 5 °C. Mean particle size and percentage of fat globules above 5 μm are measured using DLS and light obscuration respectively to determine if they satisfy USP <729>. The emulsions are also inspected by microscopy for netupitant crystals and/or visually for the presence of emulsion creaming. The absence of crystals or emulsion creaming indicates product stability.

Example 22: Stability of the Netupitant Emulsion to Freeze-Thaw Cycle

[0156] The netupitant emulsions prepared according to Examples 13-17 can be tested for stability upon exposure to a freeze-thaw cycle. Samples from the Examples 13-17 are stored at -20 ºC overnight. The absence of visible particles when the samples are viewed under a microscope indicates product stability.

[0157] While a number of exemplary aspects and embodiments have been discussed above, those of skill in the art will recognize certain modifications, permutations, additions and sub-combinations thereof. It is therefore intended that the following appended claims and claims hereafter introduced are interpreted to include all such modifications, permutations, additions and sub-combinations as are within their true spirit and scope.

WHAT IS CLAIMED IS:

1. An injectable emulsion, comprising:
0.7-0.8 wt% aprepitant;
13 wt/wt% to 20 wt/wt% of an emulsifier;
an oil;
a co-emulsifier which is an alcohol;
a tonicity modifier;
a pH modifier; and
water;
wherein the pH of the emulsion ranges from about 7.5 to 9.0.

2. The emulsion of claim 1, wherein the emulsifier is a phospholipid.

3. The emulsion of claim 2, wherein the phospholipid is present in the emulsion at about 17 wt/wt%.

4. The emulsion of claim 2, wherein the phospholipid is present in the emulsion at about 18 wt/wt%.

5. The emulsion of claim 1, wherein the emulsifier is an egg lecithin.

6. The emulsion of claim 5, wherein the egg lecithin is present in the emulsion at about 17 wt/wt%.

7. The emulsion of claim 5, wherein the egg lecithin is present in the emulsion at about 18 wt/wt%.

8. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is between about 20:1 to 25:1.

9. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 23:1.

10. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 24:1.

11. The emulsion of claim 5, wherein the ratio of egg lecithin to aprepitant is about 25:1.

12. The emulsion of claim 1, wherein the oil in the emulsion is soybean oil.

13. The emulsion of claim 11, wherein the soybean oil is present at a concentration of about 9 wt/wt % to 10 wt/wt %.

14. The emulsion of claim 1, wherein the alcohol in the emulsion is ethanol.

15. The emulsion of claim 13, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

16. The emulsion of claim 13, wherein the ethanol is present in the emulsion at a concentration of about 2 wt/wt % to 3 wt/wt %.

17. The emulsion of claim 1, wherein the tonicity modifier in the emulsion is sucrose.

18. The emulsion of claim 16, wherein the sucrose is present at a concentration of about 3 wt/wt % to 8 wt/wt %.

19. The emulsion of claim 16, wherein the sucrose is present at a concentration of about 5 wt/wt %.

20. The emulsion of claim 1, wherein the pH modifier in the emulsion is sodium oleate.

21. The emulsion of claim 19, wherein the sodium oleate is present at a concentration of about 0.4 wt/wt % to 0.5 wt/wt %.

22. The emulsion of claim 1, wherein the aprepitant is present in the emulsion at about 0.7 wt/wt%.

23. The emulsion of claim 21, wherein the phospholipid is an egg lecithin.

24. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is between about 20:1 to 25:1.

25. The emulsion of claim 21, wherein the phospholipid is present at a concentration of about 17 wt/wt %.

26. The emulsion of claim 21, wherein the phospholipid is present at a concentration of about 18 wt/wt %.

27. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 23:1.

28. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 24:1.

29. The emulsion of claim 21, wherein the ratio of phospholipid to aprepitant is about 25:1.

30. An injectable pharmaceutical emulsion, comprising:
about 0.7-0.8 wt% aprepitant;
an egg phospholipid emulsifier;
an oil;
a co-surfactant;
water; and
a pH modifier,
wherein the ratio of the emulsifier to aprepitant is about 20:1 to 25:1 (wt/wt%).

ABSTRACT OF THE DISCLOSURE

Disclosed herein are novel pharmaceutical formulations of a neurokinin-1 (NK-1) receptor antagonist suitable for parenteral administration including intravenous administration. Also included are formulations including both the NK-1 receptor antagonist and dexamethasone sodium phosphate. The pharmaceutical formulations are stable oil-in-water emulsions for non-oral treatment of emesis and are particularly useful for treatment of subjects undergoing highly emetogenic cancer chemotherapy.