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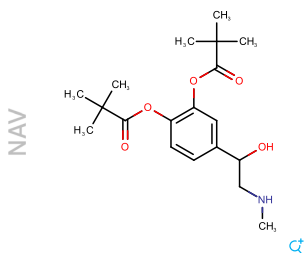
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Dipivefrin

Star

3

Structure



Description

A medication found in eye drops that is used to decrease pressure in the eye.

DrugBank ID

DB00449

US Approved

YES

[Patents](#)

0

Modality

Small Molecule

Other Approved

YES

[Indicated Conditions](#)

1

Clinical Trials

Phase 0

0

Phase 3

0

Phase 1

0

Phase 4

0

Phase 2

0

Therapeutic Categories

Adrenergic Agonists [✕](#)

Mydriatics [✕](#)

Mechanism of Action

[Alpha-1A adrenergic receptor](#) **Agonist**

[Alpha-2A adrenergic receptor](#) **Agonist**

[Beta-2 adrenergic receptor](#) **Agonist**

[+ 1 more target](#)

IDENTIFICATION

Summary

Dipivefrin is a prodrug of epinephrine used in ophthalmic solutions to reduce intraocular pressure in chronic open-angle glaucoma.

Generic Name

Dipivefrin

DrugBank Accession Number

DB00449

Background

Dipivefrin is a prodrug of adrenaline, which is used to treat glaucoma. It is available as ophthalmic solution (eye drops).

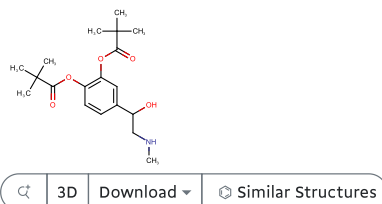
Modality

Small Molecule

Groups

Approved, Withdrawn

Structure



Weight

Average: 351.4373
Monoisotopic: 351.204573043

Chemical Formula

C₁₉H₂₉NO₅

IPR2025-00874

Aquestive Therapeutics, Inc. v. Iono Pharma, LLC

Ionon's Exhibit 2033

EX2033, Page 1

Synonyms
[Show All Synonyms](#)

Dipivalyl epinephrine Dipivefrin Dipivefrina Dipivéfrine Dipivefrine
Dipivefrinum

External IDs ⓘ
[View As Table](#)

DPE K 30081

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PHARMACOLOGY

Indication Dipivefrin is a prodrug which is used as initial therapy for the control of intraocular pressure in chronic open-angle glaucoma.

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Associated Conditions

Show entries

INDICATION TYPE	INDICATION	COMBINED PRODUCT DETAILS	APPROVAL LEVEL	AGE GROUP	PATIENT CHARACTERISTICS	
Management of	Intraocular pressure					

Create Account

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≤ 1 ≥

Contraindications & Blackbox Warnings

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Pharmacodynamics

Dipivefrin is a member of a class of drugs known as prodrugs. Prodrugs are usually not active in themselves and require biotransformation to the parent compound before therapeutic activity is seen. These modifications are undertaken to enhance absorption, decrease side effects and enhance stability and comfort, thus making the parent compound a more useful drug. Enhanced absorption makes the prodrug a more efficient delivery system for the parent drug because less drug will be needed to produce the desired therapeutic response. Dipivefrin is a prodrug of epinephrine formed by the diesterification of epinephrine and pivalic acid. The addition of pivaloyl groups to the epinephrine molecule enhances its lipophilic character and, as a consequence, its penetration into the anterior chamber.

Mechanism of action

Dipivefrin is a prodrug with little or no pharmacologically activity until it is hydrolyzed into epinephrine inside the human eye. The liberated epinephrine, an adrenergic agonist, appears to exert its action by stimulating α - and/or β_2 -adrenergic receptors, leading to a decrease in aqueous production and an enhancement of outflow facility. The dipivefrin prodrug delivery system is a more efficient way of delivering the therapeutic effects of epinephrine, with fewer side effects than are associated with conventional epinephrine therapy.

A Alpha-1A adrenergic receptor
agonist
Humans
A Alpha-2A adrenergic receptor
agonist
Humans
A Beta-2 adrenergic receptor
agonist
Humans
A Cholinesterase
substrate
Humans
U Beta-1 adrenergic receptor
antagonist
Humans
U Acetylcholinesterase
inhibitor
Humans

Absorption	Well absorbed following ocular administration.
Volume of distribution	Not Available
Protein binding	Not Available
Metabolism	Dipivefrin is converted to epinephrine inside the human eye by enzyme hydrolysis.
Route of elimination	Not Available
Half-life	Not Available
Clearance	Not Available
Adverse Effects	Improve decision support & research outcomes with our structured adverse effects data. SEE A DATA SAMPLE
Toxicity	Oral LD ₅₀ in rat is 183 mg/kg.
Pathways	Not Available
Pharmacogenomic Effects/ADRs ⓘ	Not Available

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INTERACTIONS

Drug Interactions ⓘ

This information should not be interpreted without the help of a healthcare provider. If you believe you are experiencing an interaction, contact a healthcare

provider immediately. The absence of an interaction does not necessarily mean no interactions exist.

APPROVED [VET APPROVED](#) [NUTRACEUTICAL](#) [ILLICIT](#) [WITHDRAWN](#)



[INVESTIGATIONAL](#) [EXPERIMENTAL](#) [ALL DRUGS](#)

Show entries

DRUG	INTERACTION
INTEGRATE DRUG-DRUG INTERACTIONS IN YOUR SOFTWARE	
Aminophylline	The risk or severity of hypokalemia can be increased when Aminophylline is combined with Dipivefrin.
Bendroflumethiazide	The risk or severity of hypokalemia can be increased when Dipivefrin is combined with Bendroflumethiazide.
Benzthiazide	The risk or severity of hypokalemia can be increased when Dipivefrin is combined with Benzthiazide.
Bromotheophylline	The risk or severity of hypokalemia can be increased when Bromotheophylline is combined with Dipivefrin.
Caffeine	The risk or severity of hypokalemia can be increased when Caffeine is combined with Dipivefrin.

Showing 1 to 5 of 24 entries

[1](#) [2](#) [3](#) [4](#) [5](#) [6](#)

Food Interactions

No interactions found.

PRODUCTS

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Product Ingredients

[Dipivefrin hydrochloride](#)

64019-93-8

International/Other Brands

AKPro (Akorn) / D Epifrin (Allergan) / Diopine (Allergan) / Pivalephrine (Santen Pharmaceutical) / Pro-Epinephrine / Thilodrin (Alcon)

Brand Name Prescription Products

Show entries

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END
Dipivefrin-liq Oph 0.1%	Liquid	.1 %	Ophthalmic	Alcon, Inc.	1995-12-31	1996-08-16
Dpe Ophthalmic Solution - 0.1%	Solution / drops	.1 %	Ophthalmic; Topical	Alcon, Inc.	1995-12-31	1999-12-23
Propine	Solution / drops	1 mg/1mL	Ophthalmic	Allergan, Inc.	2001-09-04	2010-01-04
Propine Liq 0.1%	Liquid	1 mg / mL	Ophthalmic	Allergan, Inc.	1981-12-31	2011-08-04

Showing 1 to 4 of 4 entries

≤ 1 ≥

Generic Prescription Products

Show entries

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKET END
Apo-dipivefrin	Liquid	0.1 %	Ophthalmic	Apotex Corporation	2000-07-17	2022-03-
Dipivefrin Hydrochloride	Solution	1 mg/1mL	Ophthalmic	Sandoz S.P.A.	1994-06-30	2004-12-
Dipivefrin Hydrochloride	Solution / drops	1 mg/1mL	Ophthalmic	Bauch & Lomb Incorporated	1995-05-19	2007-12-
PMS-dipivefrin	Solution / drops	0.1 %	Ophthalmic	Pharmascience Inc	1998-08-31	2016-10-
Ratio-dipivefrin	Solution	0.1 %	Ophthalmic	Ratiopharm Inc Division Of Teva Canada Limited	1995-12-31	2006-08-

Showing 1 to 5 of 5 entries

≤ 1 ≥

Mixture Products

Show entries

NAME	INGREDIENTS	DOSAGE	ROUTE	LABELLER	MARKETING START	MARKETING END
Probeta - Liq Oph	Dipivefrin hydrochloride (0.1 %) + Levobunolol hydrochloride (0.5 %)	Liquid	Ophthalmic	Allergan, Inc.	1996-08-30	2012-07-16

Showing 1 to 1 of 1 entries

≤ 1 ≥

CATEGORIES

ATC Codes

[S01EA02 — Dipivefrine](#)

- [S01EA — Sympathomimetics in glaucoma therapy](#)
- [S01E — ANTIGLAUCOMA PREPARATIONS AND MIOTICS](#)
- [S01 — OPHTHALMOLOGICALS](#)
- [S — SENSORY ORGANS](#)

Drug Categories

[Adrenergic Agents](#)

[Adrenergic Agonists](#)

[Adrenergic alpha-1 Receptor Agonists](#)

[Adrenergic alpha-2 Receptor Agonists](#)

[Adrenergic alpha-Agonists](#)

[Adrenergic beta-1 Receptor Agonists](#)

[Adrenergic beta-2 Receptor Agonists](#)

[Adrenergic beta-3 Receptor Agonists](#)

[Adrenergic beta-Agonists](#)

[Alcohols](#)
[Amines](#)
[Amino Alcohols](#)
[Antiglaucoma Preparations and Miotics](#)
[Benzene Derivatives](#)
[Biogenic Amines](#)
[Biogenic Monoamines](#)
[Catecholamines](#)
[Catechols](#)
[Cholinesterase substrates](#)
[Ethanolamines](#)
[Mydriatics](#)
[Neurotransmitter Agents](#)
[Ophthalmics](#)
[Ophthalmologicals](#)
[Phenols](#)
[Sensory Organs](#)
[Sympathomimetics in Glaucoma Therapy](#)

Chemical Taxonomy

Provided by [Classyfire](#)

Description	This compound belongs to the class of organic compounds known as phenol esters. These are aromatic compounds containing a benzene ring substituted by a hydroxyl group and an ester group.
Kingdom	Organic compounds
Super Class	Benzenoids
Class	Phenol esters
Sub Class	Not Available
Direct Parent	Phenol esters
Alternative Parents	Phenoxy compounds / Aralkylamines / Dicarboxylic acids and derivatives / Secondary alcohols / Carboxylic acid esters / Amino acids and derivatives / 1,2-aminoalcohols / Dialkylamines / Organopnictogen compounds / Organic oxides ↗ show 3 more
Substituents	1,2-aminoalcohol / Alcohol / Amine / Amino acid or derivatives / Aralkylamine / Aromatic alcohol / Aromatic homomonocyclic compound / Carbonyl group / Carboxylic acid derivative / Carboxylic acid ester ↗ show 14 more
Molecular Framework	Aromatic homomonocyclic compounds
External Descriptors	ethanolamines, pivalate ester (CHEBI:4646)

Affected organisms

Humans and other mammals

CHEMICAL IDENTIFIERS

UNII

[8Q1PVL543G](#)

CAS number

52365-63-6

InChI Key	OCUJLLGVOUDECM-UHFFFAOYSA-N
InChI	InChI=1S/C19H29NO5/c1-18(2,3)16(22)24-14-9-8-12(13(21)11-20-7)10-15(14)25-17(23)19(4,5)6/h8-10,13,20-21H,11H 2,1-7H3
IUPAC Name	2-[[2,2-dimethylpropanoyl]oxy]-5-[1-hydroxy-2-(methylamino)ethyl]phenyl 2,2-dimethylpropanoate
SMILES	CNCC(O)C1=CC(OC(=O)C(C)(C)C)=C(OC(=O)C(C)(C)C)C=C1
REFERENCES	
Synthesis Reference	Hussain, A. and Truelove, J.E.; U.S. Patents 3,809,714; May 7,1974; and 3,839,584; October 1, 1974; both assigned to Inter Rx Research Corp. Henschler, D., Wagner, J. and Hampel, H.; US. Patent 4,085,270; April 18,1978; assigned to Chemisch-Pharmazeutische Fabrik Adolf Klinge & Co. (W. Germany).
General References	1. FDA Approved Drug Products: PROPINE (dipivefrin hydrochloride) solution [Link]
External Links	Human Metabolome Database HMDB0014592 KEGG Drug D02349 KEGG Compound C06963 PubChem Compound 3105 PubChem Substance 46504716 ChemSpider 2994 RxNav 23410 ChEBI 4646 ChEMBL ChEMBL1201262 Therapeutic Targets Database DAP000593 PharmGKB PA449364 RxList RxList Drug Page Drugs.com Drugs.com Drug Page PDRhealth PDRhealth Drug Page Wikipedia Dipivefrine
FDA label	Download (60.3 KB)
MSDS	Download (50.2 KB)
CLINICAL TRIALS	

Clinical Trials

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entries

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT	START DATE	WHY STOPPED	100+ ADDITIO COLUMN
Unlock 175K+ rows when you subscribe. View sample data No data available in table							

Showing 0 to 0 of 0 entries

PHARMACOECONOMICS

Manufacturers

Akorn inc
Bausch and lomb pharmaceuticals inc
Falcon pharmaceuticals ltd
Allergan pharmaceutical

Packagers

Allergan Inc.
Dispensing Solutions
Pacific Pharma Lp
Pharmedix
Physicians Total Care Inc.
Taylor Pharmaceuticals

Dosage Forms

Show 10 entries

Search

FORM	ROUTE	STRENGTH
Liquid	Ophthalmic	0.1 %
Solution	Ophthalmic	1 mg/1mL
Solution / drops	Ophthalmic	1 mg/1mL
Liquid	Ophthalmic	.1 %
Solution / drops	Ophthalmic; Topical	.1 %
Solution / drops	Ophthalmic	0.1 %
Liquid	Ophthalmic	
Solution / drops	Ophthalmic	
Liquid	Ophthalmic	1 mg / mL
Solution	Ophthalmic	0.1 %

Showing 1 to 10 of 10 entries

Prices

Show 10 entries

Search

UNIT DESCRIPTION	COST	UNIT
Propine 0.1% eye drops	5.02USD	ml

Showing 1 to 1 of 1 entries

DrugBank does not sell nor buy drugs. Pricing information is supplied for informational purposes only.

Patents

Not Available

PROPERTIES

State

Solid

Experimental Properties

PROPERTY	VALUE	SOURCE
melting point (°C)	146-147	Hussain, A. and Truelove, J.E.; U.S. Patents 3,809,714; May 7,1974; and 3,839,584; October 1, 1974; both assigned to Inter Rx Research Corp. Henschler, D., Wagner, J. and Hampel, H.; US. Patent 4,085,270; April 18,1978; assigned to Chemisch-Pharmazeutische Fabrik Adolf Klinge & Co. (W. Germany).
water solubility	Freely soluble as HCl salt	Not Available
logP	1.7	Not Available

Predicted Properties

Water Solubility
0.0582 mg/mL
ALOGPS
logP
3.17
ALOGPS
logP
3.71
Chemaxon
logS
-3.8
ALOGPS
pKa (Strongest Acidic)
14
Chemaxon
pKa (Strongest Basic)
9.33
Chemaxon
Physiological Charge
1
Chemaxon
Hydrogen Acceptor Count
4
Chemaxon
Hydrogen Donor Count
2
Chemaxon
Polar Surface Area
84.86 Å²
Chemaxon
Rotatable Bond Count
9
Chemaxon
Refractivity
94.94 m³·mol⁻¹
Chemaxon

Polarizability
39.33 Å ³
Chemaxon
Number of Rings
1
Chemaxon
Bioavailability
1
Chemaxon
Rule of Five
Yes
Chemaxon
Ghose Filter
Yes
Chemaxon
Veber's Rule
No
Chemaxon
MDDR-like Rule
No
Chemaxon

Predicted ADMET Features

Human Intestinal Absorption
+
Blood Brain Barrier
-
Caco-2 permeable
-
P-glycoprotein substrate
Substrate
P-glycoprotein inhibitor I
Non-inhibitor
P-glycoprotein inhibitor II
Non-inhibitor
Renal organic cation transporter
Non-inhibitor
CYP450 2C9 substrate
Non-substrate
CYP450 2D6 substrate
Non-substrate
CYP450 3A4 substrate
Non-substrate
CYP450 1A2 substrate
Non-inhibitor
CYP450 2C9 inhibitor
Non-inhibitor

CYP450 2D6 inhibitor
Non-inhibitor
CYP450 2C19 inhibitor
Non-inhibitor
CYP450 3A4 inhibitor
Non-inhibitor
CYP450 inhibitory promiscuity
Low CYP Inhibitory Promiscuity
Ames test
Non AMES toxic
Carcinogenicity
Non-carcinogens
Biodegradation
Not ready biodegradable
Rat acute toxicity
2.2818 LD50, mol/kg
hERG inhibition (predictor I)
Weak inhibitor
hERG inhibition (predictor II)
Non-inhibitor

ADMET data is predicted using [admetSAR](#), a free tool for evaluating chemical ADMET properties. ([23092397](#))

SPECTRA

Mass Spec (NIST)

Not Available

Spectra

Predicted GC-MS Spectrum - GC-MS
Predicted MS/MS Spectrum - 10V, Positive (Annotated)
Predicted MS/MS Spectrum - 10V, Negative (Annotated)
Predicted MS/MS Spectrum - 20V, Positive (Annotated)
Predicted MS/MS Spectrum - 20V, Negative (Annotated)
Predicted MS/MS Spectrum - 40V, Positive (Annotated)
Predicted MS/MS Spectrum - 40V, Negative (Annotated)
Predicted 1H NMR Spectrum
Predicted 13C NMR Spectrum

Chromatographic Properties

Collision Cross Sections (CCS)

[M-H]-
203.3527354
predicted
DarkChem Lite v0.1.0
[M-H]-
188.77998
predicted
DeepCCS 1.0 (2019)

[M+H] ⁺
203.6900354
predicted
DarkChem Lite v0.1.0
[M+H] ⁺
191.3637
predicted
DeepCCS 1.0 (2019)
[M+Na] ⁺
203.8397354
predicted
DarkChem Lite v0.1.0
[M+Na] ⁺
198.85207
predicted
DeepCCS 1.0 (2019)

TARGETS

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1. Alpha-1A adrenergic receptor

Details

Kind	Protein
Organism	Humans
Pharmacological action	Yes
Actions	Agonist
General Function	This alpha-adrenergic receptor mediates its action by association with G proteins that activate a phosphatidylinositol-calcium second messenger system. Its effect is mediated by G(q) and G(11) proteins. Nuclear ADRA1A-ADRA1B heterooligomers regulate phenylephrine(PE)-stimulated ERK signaling in cardiac myocytes
Specific Function	alpha1-adrenergic receptor activity
Gene Name	ADRA1A
Uniprot ID	P35348
Uniprot Name	Alpha-1A adrenergic receptor
Molecular Weight	51486.005 Da

References

1. Sanbe A, Tanaka Y, Fujiwara Y, Tsumura H, Yamauchi J, Cotecchia S, Koike K, Tsujimoto G, Tanoue A: Alpha1-adrenoceptors are required for normal male sexual function. Br J Pharmacol. 2007 Oct;152(3):332-40. Epub 2007 Jul 2. [\[Article\]](#)

2. Tomiyama Y, Kobayashi K, Tadachi M, Kobayashi S, Inada Y, Kobayashi M, Yamazaki Y: Expressions and mechanical functions of alpha1-adrenoceptor subtypes in hamster ureter. Eur J Pharmacol. 2007 Nov 14;573(1-3):201-5. Epub 2007 Jul 6. [\[Article\]](#)

2. Alpha-2A adrenergic receptor

[Details](#)

Kind	Protein
Organism	Humans
Pharmacological action	Yes
Actions	Agonist
General Function	Alpha-2 adrenergic receptors mediate the catecholamine-induced inhibition of adenylate cyclase through the action of G proteins. The rank order of potency for agonists of this receptor is oxymetazoline > clonidine > epinephrine > norepinephrine > phenylephrine > dopamine > p-synephrine > p-tyramine > serotonin = p-octopamine. For antagonists, the rank order is yohimbine > phentolamine = mianserine > chlorpromazine = spiperone = prazosin > propranolol > alprenolol = pindolol
Specific Function	alpha-1B adrenergic receptor binding
Gene Name	ADRA2A
Uniprot ID	P08913
Uniprot Name	Alpha-2A adrenergic receptor
Molecular Weight	50646.17 Da

References

1. Arthur S, Cantor LB: Update on the role of alpha-agonists in glaucoma management. Exp Eye Res. 2011 Sep;93(3):271-83. doi: 10.1016/j.exer.2011.04.002. Epub 2011 Apr 20. [\[Article\]](#)

3. Beta-2 adrenergic receptor

[Details](#)

Kind	Protein
Organism	Humans
Pharmacological action	Yes
Actions	Agonist
General Function	Beta-adrenergic receptors mediate the catecholamine-induced activation of adenylate cyclase through the action of G proteins. The beta-2-adrenergic receptor binds epinephrine with an approximately 30-fold greater affinity than it does norepinephrine
Specific Function	adenylate cyclase binding
Gene Name	ADRB2
Uniprot ID	P07550
Uniprot Name	Beta-2 adrenergic receptor
Molecular Weight	46458.32 Da

References

1. Chen X, Ji ZL, Chen YZ: TTD: Therapeutic Target Database. Nucleic Acids Res. 2002 Jan 1;30(1):412-5. [\[Article\]](#)
2. Ozakca I, Arioglu E, Guner S, Altan VM, Ozelikay AT: Role of beta-3-adrenoceptor in catecholamine-induced relaxations in gastric fundus from control and diabetic rats. Pharmacology. 2007;80(4):227-38. Epub 2007 Jul 6. [\[Article\]](#)
3. Prenner L, Sieben A, Zeller K, Weiser D, Haberlein H: Reduction of high-affinity beta2-adrenergic receptor binding by hyperforin and hyperoside on rat C6 glioblastoma cells measured by fluorescence correlation spectroscopy. Biochemistry. 2007 May 1;46(17):5106-13. Epub 2007 Apr 7. [\[Article\]](#)

4. Lucin KM, Sanders VM, Jones TB, Malarkey WB, Popovich PG: Impaired antibody synthesis after spinal cord injury is level dependent and is due to sympathetic nervous system dysregulation. *Exp Neurol*. 2007 Sep;207(1):75-84. Epub 2007 Jun 2. [\[Article\]](#)

4. Cholinesterase

Details

Kind	Protein
Organism	Humans
Pharmacological action	Yes
Actions	Substrate
General Function	Esterase with broad substrate specificity. Contributes to the inactivation of the neurotransmitter acetylcholine. Can degrade neurotoxic organophosphate esters
Specific Function	acetylcholinesterase activity
Gene Name	BCHE
Uniprot ID	P06276
Uniprot Name	Cholinesterase
Molecular Weight	68417.575 Da

References

1. Nakamura M, Shirasawa E, Hikida M: Characterization of esterases involved in the hydrolysis of dipivefrin hydrochloride. *Ophthalmic Res*. 1993;25(1):46-51. [\[Article\]](#)

5. Beta-1 adrenergic receptor

Details

Kind	Protein
Organism	Humans
Pharmacological action	Unknown
Actions	Antagonist
General Function	Beta-adrenergic receptors mediate the catecholamine-induced activation of adenylate cyclase through the action of G proteins. This receptor binds epinephrine and norepinephrine with approximately equal affinity. Mediates Ras activation through G(s)-alpha- and cAMP-mediated signaling. Involved in the regulation of sleep/wake behaviors (PubMed:31473062)
Specific Function	alpha-2A adrenergic receptor binding
Gene Name	ADRB1
Uniprot ID	P08588
Uniprot Name	Beta-1 adrenergic receptor
Molecular Weight	51222.97 Da

References

1. Zhou Y, Zhang Y, Zhao D, Yu X, Shen X, Zhou Y, Wang S, Qiu Y, Chen Y, Zhu F: TTD: Therapeutic Target Database describing target druggability information. *Nucleic Acids Res*. 2024 Jan 5;52(D1):D1465-D1477. doi: 10.1093/nar/gkad751. [\[Article\]](#)

6. Acetylcholinesterase

[Details](#)

Kind	Protein
Organism	Humans
Pharmacological action	Unknown
Actions	Inhibitor
General Function	Hydrolyzes rapidly the acetylcholine neurotransmitter released into the synaptic cleft allowing to terminate the signal transduction at the neuromuscular junction. Role in neuronal apoptosis
Specific Function	acetylcholine binding
Gene Name	ACHE
Uniprot ID	P22303
Uniprot Name	Acetylcholinesterase
Molecular Weight	67795.525 Da

References

1. Nakamura M, Shirasawa E, Hikida M: Characterization of esterases involved in the hydrolysis of dipivefrin hydrochloride. Ophthalmic Res. 1993;25(1):46-51. [\[Article\]](#)

Drug created at June 13, 2005 13:24 / Updated at September 01, 2025 11:14

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