

AFFIDAVIT OF NATHANIEL E FRANK-WHITE

1. I am a Records Request Processor at the Internet Archive. I make this declaration of my own personal knowledge.

2. The Internet Archive is a website that provides access to a digital library of Internet sites and other cultural artifacts in digital form. Like a paper library, we provide free access to researchers, historians, scholars, and the general public. The Internet Archive has partnered with and receives support from various institutions, including the Library of Congress.

3. The Internet Archive has created a service known as the Wayback Machine. The Wayback Machine makes it possible to browse more than 450 billion pages stored in the Internet Archive's web archive. Visitors to the Wayback Machine can search archives by URL (i.e., a website address). If archived records for a URL are available, the visitor will be presented with a display of available dates. The visitor may select one of those dates, and begin browsing an archived version of the Web. Links on archived files in the Wayback Machine point to other archived files (whether HTML pages or other file types), if any are found for the URL indicated by a given link. For instance, the Wayback Machine is designed such that when a visitor clicks on a hyperlink on an archived page that points to another URL, the visitor will be served the archived file found for the hyperlink's URL with the closest available date to the initial file containing the hyperlink.

4. The archived data made viewable and browsable by the Wayback Machine is obtained by use of web archiving software that automatically stores copies of files available via the Internet, each file preserved as it existed at a particular point in time.

5. The Internet Archive assigns a URL on its site to the archived files in the format http://web.archive.org/web/[Year in yyyy][Month in mm][Day in dd][Time code in hh:mm:ss]/[Archived URL] aka an "extended URL". Thus, the extended URL http://web.archive.org/web/19970126045828/http://www.archive.org/ would be the URL for the record of the Internet Archive home page HTML file (http://www.archive.org/) archived on January 26, 1997 at 4:58 a.m. and 28 seconds (1997/01/26 at 04:58:28). The date indicated by an extended URL applies to a preserved instance of a file for a given URL, but not necessarily to any other files linked therein. Thus, in the case of a page constituted by a primary HTML file and other separate files (e.g., files with images, audio, multimedia, design elements, or other embedded content) linked within that primary HTML file, the primary HTML file and the other files will each have their own respective extended URLs and may not have been archived on the same dates.

6. Attached hereto as Exhibit A are true and accurate copies of screenshots of the Internet Archive's records of the archived files for the URLs and the dates specified in the attached coversheet of each printout.



7. Attached hereto as Exhibit B are true and accurate copies of the Internet Archive's records of the archived files for the URLs and the dates specified in the attached coversheet of each file.

8. I declare under penalty of perjury that the foregoing is true and correct.

DATE: 03/29/2023

Nathaniel Frank-White

Nathaniel E Frank-White

Please see attached
All Purpose
Jurat form
for additional
Notary Events

JURAT ATTACHMENT

A notary public or other officer completing this certificate verifies only the identity of the individual who signed the document to which this certificate is attached, and not the truthfulness, accuracy, or validity of that document.

STATE OF Tennessee }

COUNTY OF Cheatham }

The foregoing instrument was subscribed and sworn before me this date of 03/29/2023, by Nathaniel Frank-White

This notarial act ~~was an online notarization.~~

SAMANTHA B. DOMINGUEZ
STATE OF TENNESSEE
NOTARY PUBLIC
COUNTY OF CHEATHAM

ONLINE NOTARY PUBLIC
MY COMMISION EXPIRES: JULY 26 2025

(Notary Seal)

Notary's Signature

Registration No.: 0

Commission Expiration Date: July 26, 2025

EXHIBIT A

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9 captures 17 Jul 2014 - 4 Aug 2020

Now FDA approved

Indicated for adults with moderately to severely active:

- Ulcerative colitis
- Crohn's disease

Read press release

EntyvioCONNECT

Healthcare professionals and patients can get reimbursement assistance and more with *Entyvio Connect*

Sign up
Get more information about Entyvio

Adult Ulcerative Colitis (UC)

Entyvio is indicated in adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for inducing and maintaining clinical response, inducing and maintaining clinical remission, improving endoscopic appearance of the mucosa, and achieving corticosteroid-free remission.

Important Safety Information

Adult Crohn's Disease (CD)

Expand

Entyvio is indicated in adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for achieving clinical response, achieving clinical remission, and achieving corticosteroid-free remission.

Sign up to stay informed

Sign up below to receive ongoing communications and updates about Entyvio. Also, be the first to access helpful online tools as they become available.

All fields marked with an asterisk (*) are required.

Name

*Salutation:

Select

*First name:

Middle initial:

*Last name:

Suffix:

Select

Professional information

*Profession:

Select

*Primary specialty:

Select

Secondary specialty:

Select

Professional affiliation:

Select

Contact

*E-mail address:

*Confirm e-mail address:

*Primary office address:

Address 2:

Address 3:

*City:

*State:

Select

*ZIP code:

-

*Office phone:

- -

By clicking below, you agree to receive product and disease state information from Takeda Pharmaceuticals U.S.A., Inc., its affiliates, service providers, and co-promotion partners. To learn how Takeda will use and protect your personal information, click here to view our privacy policy.

Submit

Important Safety Information

- ENTYVIO is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.
- Infusion-related reactions and hypersensitivity reactions including anaphylaxis have occurred. If anaphylaxis or other serious allergic reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.
- Patients treated with ENTYVIO are at increased risk for developing infections. Serious infections have been reported in patients treated with ENTYVIO. ENTYVIO is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding ENTYVIO in patients who develop a severe infection while on treatment with ENTYVIO. Exercise caution in patients with a history of recurring severe infections.
- Although no cases of PML have been observed in ENTYVIO clinical trials, JC virus infection resulting in progressive multifocal leukoencephalopathy (PML) and death has occurred in patients treated with another integrin receptor

multifocal leukoencephalopathy (PML) and death has occurred in patients treated with another integrin receptor antagonist. A risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms. If PML is suspected, withhold dosing with ENTYVIO and refer to a neurologist; if confirmed, discontinue ENTYVIO dosing permanently.

- There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury.
- Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.
- Most common adverse reactions (incidence ≥3% and ≥1% higher than placebo): nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities.

Indications

Adult Ulcerative Colitis (UC)
ENTYVIO is indicated in adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for inducing and maintaining clinical response, inducing and maintaining clinical remission, improving endoscopic appearance of the mucosa, and achieving corticosteroid-free remission.

Adult Crohn's Disease (CD)
ENTYVIO is indicated in adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for achieving clinical response, achieving clinical remission, and achieving corticosteroid-free remission.

Please see full Prescribing Information including Medication Guide for Entyvio.

Sign up for Entyvio information

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FDA APPROVED FOR THE TREATMENT OF ADULT PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE

CHANGE YOUR CROHN'S DISEASE STORY

The Symptoms of Crohn's Disease Can Strike at Any Time

Has the unpredictability of Crohn's disease ambushed you for far too long?

I want to learn more about:

- Crohn's Disease Symptoms >
- My Treatment Options >
- Results With STELARA® >

IMPORTANT SAFETY INFORMATION

STELARA® (ustekinumab) is a prescription medicine that affects your immune system. STELARA® can increase your chance of having serious side effects including:

Serious Infections

STELARA® may lower your ability to fight infections and may increase your risk of infections. While taking STELARA®, some people have serious infections, which may require hospitalization, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses.

- Your doctor should check you for TB before starting STELARA® and watch you closely for signs and symptoms of TB during treatment with STELARA®.
- If your doctor feels that you are at risk for TB, you may be treated for TB before and during treatment with STELARA®.

You should not start taking STELARA® if you have any kind of infection unless your doctor says it is okay.

Before starting STELARA®, tell your doctor if you:

- think you have an infection or have symptoms of an infection such as:
  - fever, sweats, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in your phlegm
  - weight loss
  - warm, red, or painful skin or sores on your body
  - diarrhea or stomach pain
  - burning when you urinate or urinate more often than normal
  - feel very tired
- are being treated for an infection
- get a lot of infections or have infections that keep coming back
- have TB, or have been in close contact with someone who has TB

- Your doctor should check you for TB before starting STELARA® and watch you closely for signs and symptoms of TB during treatment with STELARA®.
- If your doctor feels that you are at risk for TB, you may be treated for TB before and during treatment with STELARA®.

You should not start taking STELARA® if you have any kind of infection unless your doctor says it is okay.

WHAT IS STELARA®?

STELARA® is a prescription medicine approved to treat adults 18 years and older with moderate or severe plaque psoriasis that involves large areas or many areas of their body, who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light alone or with pills).

STELARA® is a prescription medicine approved to treat adults 18 years and older with active psoriatic arthritis, either alone or with methotrexate.

STELARA® is a prescription medicine used to treat adults 18 years and older with moderately to severely active Crohn's disease who have already taken other medicine that did not work well enough or they could not tolerate it.

STELARA® is a prescription medicine approved to treat adults 18 years and older with active psoriatic arthritis, either alone or with methotrexate.

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  - fever, sweats, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in your phlegm
  - weight loss
  - warm, red, or painful skin or sores on your body
  - diarrhea or stomach pain
  - burning when you urinate or urinate more often than normal
  - feel very tired
- are being treated for an infection
- get a lot of infections or have infections that keep coming back
- have TB, or have been in close contact with someone who has TB

After starting STELARA®, call your doctor right away if you have any symptoms of an infection (see above).

STELARA® can make you more likely to get infections or make an infection that you have worse. People who have a genetic problem where the body does not make any of the proteins interleukin 12 (IL-12) and interleukin 23 (IL-23) are at a higher risk for certain serious infections that can spread throughout the body and cause death. People who take STELARA® may also be more likely to get these infections.

Cancers

STELARA® may decrease the activity of your immune system and increase your risk for certain types of cancer. Tell your doctor if you have ever had any type of cancer. Some people who had risk factors for skin cancer developed certain types of skin cancers while receiving STELARA®. Tell your doctor if you have any new skin growths.

Reversible posterior leukoencephalopathy syndrome (RPLS)

RPLS is a rare condition that affects the brain and can cause death. The cause of RPLS is not known. If RPLS is found early and treated, most people recover. Tell your doctor right away if you have any new or worsening medical problems including: headache, seizures, confusion, and vision problems.

Serious Allergic Reactions

Serious allergic reactions can occur. Stop using STELARA® and get medical help right away if you have any symptoms such as: feeling faint, swelling of your face, eyelids, tongue, or throat, chest tightness, or skin rash.

Before receiving STELARA®, tell your doctor if you:

- have any of the conditions or symptoms listed above for serious infections, cancers, or RPLS.
- ever had an allergic reaction to STELARA® or any of its ingredients. Ask your doctor if you are not sure.
- are allergic to latex. The needle cover on the prefilled syringe contains latex.
- have recently received or are scheduled to receive an immunization (vaccine). People who take STELARA® should not receive live vaccines. Tell your doctor if anyone in your house needs a vaccine. The viruses used in some types of vaccines can spread to people with a weakened immune system, and can cause serious problems. **You should not receive the BCG vaccine during the one year before taking STELARA® or one year after you stop taking STELARA®.**
- have any new or changing lesions within psoriasis areas or on normal skin.
- are receiving or have received allergy shots, especially for serious allergic reactions.
- receive or have received phototherapy for your psoriasis.
- have any other medical conditions.
- are pregnant or plan to become pregnant. It is not known if STELARA® will harm your unborn baby. You and your doctor should decide if you will take STELARA®.
- are breast-feeding or plan to breast-feed. It is thought that STELARA® passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take STELARA®.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

When prescribed STELARA®:

- Use STELARA® exactly as prescribed by your doctor.
- If your doctor decides that you or a caregiver may give your injections of STELARA® at home, you should receive training on the right way to prepare and inject STELARA®. Do not try to inject STELARA® yourself until you or your caregiver has been shown how to inject STELARA® by your doctor or nurse.

Common side effects of STELARA® include: upper respiratory infections, headache, and tiredness **in psoriasis** patients; joint pain and nausea **in psoriatic arthritis** patients; and upper respiratory infections, redness at the injection site, vaginal yeast infections, itching, urinary tract infections, and vomiting **in Crohn's disease** patients. These are not all of the possible side effects with STELARA®. Tell your doctor about any side effect that you experience. Ask your doctor or pharmacist for more information.

Please read the full Prescribing Information and Medication Guide for STELARA® and discuss any questions you have with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Requires Adobe® Reader®. Click here to download

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janssen Immunology

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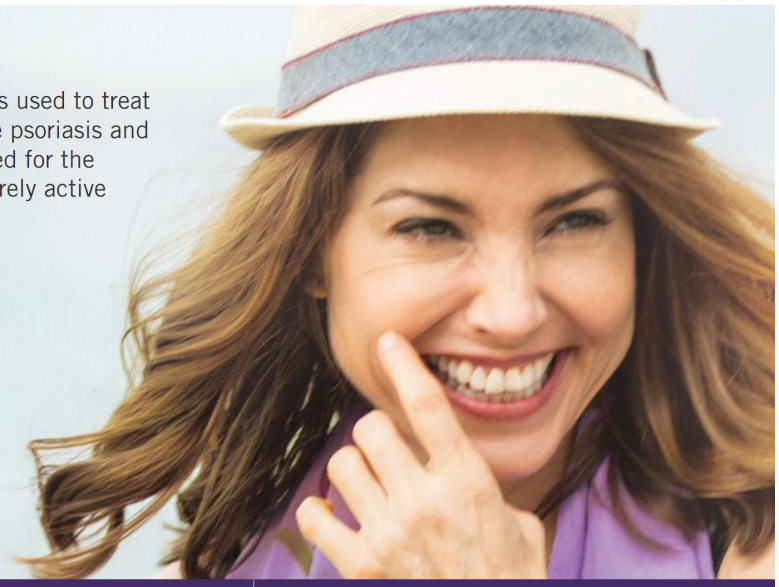
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486 captures 1 Oct 2009 - 26 Mar 2023

Welcome to STELARA®

STELARA® is a medication for adult patients that is used to treat two psoriatic conditions: moderate or severe plaque psoriasis and active psoriatic arthritis. STELARA® is also approved for the treatment of adult patients with moderately to severely active Crohn's disease.

TAKE ME TO:

- Moderate or Severe **PLAQUE PSORIASIS** ›
- Moderately or Severely Active **CROHN'S DISEASE** ›
- Active **PSORIATIC ARTHRITIS** ›



IMPORTANT SAFETY INFORMATION

STELARA® (ustekinumab) is a prescription medicine that affects your immune system. STELARA® can increase your chance of having serious side effects including:

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WHAT IS STELARA®?

STELARA® is a prescription medicine approved to treat adults 18 years and older with moderate or severe plaque psoriasis that involves large areas or many areas of their body, who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light alone or with pills).

janssen Immunology

Be The You Who Takes Control Of Your Symptoms With STELARA®.

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  - warm, red, or painful skin or sores on your body
  - diarrhea or stomach pain
  - burning when you urinate or urinate more often than normal
  - feel very tired
- are being treated for an infection
- get a lot of infections or have infections that keep coming back

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Before receiving STELARA®, tell your doctor if you:

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- ever had an allergic reaction to STELARA® or any of its ingredients. Ask your doctor if you are not sure.
- are allergic to latex. The needle cover on the prefilled syringe contains latex.
- have recently received or are scheduled to receive an immunization (vaccine). People who take STELARA® should not receive live vaccines. Tell your doctor if
- are breast-feeding or plan to breast-feed. It is thought that STELARA® passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take STELARA®.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

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- Use STELARA® exactly as prescribed by your doctor.
- If your doctor decides that you or a caregiver may give your injections of STELARA® at home, you should receive training on the right way to prepare and inject STELARA®. Do not try to inject STELARA® yourself until you or your caregiver has been shown how to inject STELARA® by your doctor or nurse.

Common side effects of STELARA® include: upper respiratory infections, headache, and tiredness **in psoriasis** patients; joint pain and nausea **in psoriatic arthritis** patients; and upper respiratory infections, redness at the injection site, vaginal yeast infections, itching, urinary tract infections, and vomiting **in Crohn's disease** patients. These are not all of the possible side effects with STELARA®. Tell your doctor about any side effect that you experience. Ask your doctor or pharmacist for more information.

Please read the full Prescribing Information and Medication Guide for STELARA® and discuss any questions you have with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Requires Adobe® Reader®. Click here to download

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janssen Immunology

janssen CarePath

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7 Oct 2015 - 14 Mar 2023 2014 2015 2019 About this capture

A Study to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Participants With Moderately to Severely Active Ulcerative Colitis (UNIFI)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified September 2015 by Janssen Research & Development, LLC

Sponsor:
Janssen Research & Development, LLC

Information provided by (Responsible Party):
Janssen Research & Development, LLC

ClinicalTrials.gov Identifier:
NCT02407236

First received: March 30, 2015
Last updated: September 23, 2015
Last verified: September 2015
History of Changes

Purpose

The purpose of this study is to evaluate the efficacy and safety of ustekinumab as intravenous (IV: into the vein) infusion in induction study in participants with moderately to severely active Ulcerative Colitis (UC) and as subcutaneous (SC) administration in maintenance study in participants with moderately to severely active Ulcerative Colitis (UC) who have demonstrated a clinical response to Induction treatment with IV ustekinumab.

Condition	Intervention	Phase
Colitis, Ulcerative Inflammatory Bowel Diseases	Drug: Placebo IV Drug: Placebo SC Drug: Ustekinumab IV Drug: Ustekinumab SC	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)

Official Title: A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Protocol to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Subjects With Moderately to Severely Active Ulcerative Colitis

Resource links provided by NLM:

Genetics Home Reference related topics: ulcerative colitis

MedlinePlus related topics: Ulcerative Colitis

Drug Information available for: Ustekinumab

U.S. FDA Resources

Further study details as provided by Janssen Research & Development, LLC:

Primary Outcome Measures:

- Induction Study - Number of Participants With Clinical Remission [Time Frame: Week 8] [Designated as safety issue: No]

  The global definition of Clinical remission is defined as Mayo score less than or equal to (<=) 2 points, with no individual subscore greater than (>) 1, for countries outside the United States (US). For the US, Clinical remission is defined as absolute stool number <=3, a rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1. The Mayo score is a tool designed to measure disease activity for ulcerative colitis. The Mayo score ranges from 0 to 12 points and consists of 4 subscores (stool frequency, rectal bleeding, findings on flexible sigmoidoscopy and physician's global assessment), each subscore is graded from 0 to 3 with the higher score indicating more severe disease activity.

- Maintenance Study - Number of Participants with Clinical Remission Among Participants in Clinical Response to IV Ustekinumab Induction Treatment [Time Frame: Week 44] [Designated as safety issue: No]

  The global definition of Clinical remission is defined as Mayo score less than or equal to (<=) 2 points, with no individual subscore greater than (>) 1, for countries outside the United States (US). For the US Clinical remission is defined as absolute stool number <=3, a rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1. The Mayo score is a tool designed to measure disease activity for ulcerative colitis. The Mayo score ranges from 0 to 12 points and consists of 4

subscores (stool frequency, rectal bleeding, findings on flexible sigmoidoscopy and physician's global assessment), each subscore is graded from 0 to 3 with the higher score indicating more severe disease activity.

Secondary Outcome Measures:

- Induction Study - Number of Participants with Clinical Response [Time Frame: Week 8] [Designated as safety issue: No]

  Clinical response is defined as a decreased from Induction baseline in the Mayo score by greater than or equal to (>=) 30 percent (%) and >=3 points, with either a decrease from induction baseline in the rectal bleeding subscore >=1 or rectal bleeding subscore = 0 or 1.

- Induction Study - Number of Participants With Endoscopic Healing [Time Frame: Week 8] [Designated as safety issue: No]

  Endoscopic healing is improvement in the endoscopic appearance of the mucosa. It will be defined as Mayo endoscopic subscore = 0 or 1.

- Induction Study - Mean Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Score [Time Frame: Week 8] [Designated as safety issue: No]

  The IBDQ is a 32-item questionnaire for participants with Inflammatory Bowel Disease (IBD) that will be used to evaluate the disease-specific health-related quality of life across 4 dimensional scores: bowel (loose stools, abdominal pain), systemic (fatigue, altered sleep pattern), social (work attendance, need to cancel social events), and emotional (anger, depression, irritability). The total score ranges from 32 to 224 with higher scores indicating better quality of life.

- Maintenance Study - Number of Participants with Clinical Response Among Participants in Clinical Response to IV Ustekinumab Induction Treatment [Time Frame: Through Week 44] [Designated as safety issue: No]

  Clinical response is defined as a decreased from Induction baseline in the Mayo score by greater than or equal to (>=) 30 percent (%) and >=3 points, with either a decrease from Induction baseline in the rectal bleeding subscore >=1 or rectal bleeding subscore = 0 or 1.

- Maintenance Study - Number of Participants with Endoscopic Healing Among Participants in Clinical Response to IV Ustekinumab Induction Treatment [Time Frame: Week 44] [Designated as safety issue: No]

  Endoscopic healing is improvement in the endoscopic appearance of the mucosa. It will be defined as Mayo endoscopic subscore = 0 or 1.

- Maintenance Study - Number of Participants with Clinical Remission Among those who Achieved Clinical Remission at Maintenance Study Baseline [Time Frame: Through Week 44] [Designated as safety issue: No]

  The global definition of Clinical remission is defined as Mayo score less than or equal to (<=) 2 points, with no individual subscore greater than (>) 1, for countries outside the United States (US). For the US Clinical remission is defined as absolute stool number <=3, a rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1. The Mayo score is a tool designed to measure disease activity for ulcerative colitis.

- Maintenance Study - Number of Participants with Clinical Remission and not Receiving Concomitant Corticosteroids Among those Receiving Concomitant Corticosteroids at Maintenance Baseline [Time Frame: Week 44] [Designated as safety issue: No]

  The global definition of Clinical remission is defined as Mayo score less than or equal to (<=) 2 points, with no individual subscore greater than (>) 1, for countries outside the United States (US). For the US Clinical remission is defined as absolute stool number <=3, a rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1. The Mayo score is a tool designed to measure disease activity for ulcerative colitis.

Estimated Enrollment:	951
Study Start Date:	July 2015
Estimated Study Completion Date:	July 2021
Estimated Primary Completion Date:	April 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Placebo Comparator: Induction Study - Placebo Intravenous (IV) Participants will be randomized to receive single dose of placebo as Intravenous (IV: into the vein) infusion at Week 0. Participants with clinical response at Week 8 will be eligible to enter the Maintenance study, but will not be randomized.	Drug: Placebo IV Placebo will be administered as intravenous infusion.
Experimental: Induction Study - Ustekinumab 130 milligram (mg) IV Participants will be randomized to receive single dose of ustekinumab 130 mg as IV infusion at Week 0. Participants with clinical response at Week 8 will be eligible to enter the Maintenance study and will be randomized.	Drug: Ustekinumab IV Ustekinumab will be administered as intravenous infusion at Week 0 or Week 8 in Induction Study.
Experimental: Induction Study - Ustekinumab 6 mg/kg IV Participants will be randomized to receive ustekinumab approximating 6 mg/kg of body weight, as intravenous infusion at Week 0. Participants with clinical response at Week 8 will be eligible to enter the Maintenance study and will be randomized.	Drug: Ustekinumab IV Ustekinumab will be administered as intravenous infusion at Week 0 or Week 8 in Induction Study.
Induction Study- Placebo- Nonresponsders at Week 8 Participants without clinical response to placebo at Week 8 will receive a single IV infusion of ustekinumab approximating 6mg/kg along with matching subcutaneous (SC) placebo (to maintain the blind). Participants in clinical response at Week 16 will be eligible to enter Maintenance study and will be randomized.	Drug: Ustekinumab IV Ustekinumab will be administered as intravenous infusion at Week 0 or Week 8 in Induction Study.
Induction study-Ustekinumab Nonresponders at Week 8 Participants without clinical response to ustekinumab (130 mg or 6 mg/kg [IV]) at Week 8 will receive a single dose of ustekinumab 90 mg subcutaneously along with matching placebo intravenously (to maintain the blind). Participants in clinical response at Week 16 (that is, delayed responders) will be eligible to enter Maintenance study, but will not be randomized.	Drug: Ustekinumab SC Ustekinumab will be administered as subcutaneously.
Placebo Comparator: Maintenance Study - Placebo Subcutaneous (SC)	Drug: Placebo SC

Participants in clinical response (at Week 8 or Week 16) to Induction treatment with single IV infusion of Ustekinumab will be randomized to receive placebo subcutaneously, beginning Week 0 of Maintenance study through Week 44.	Placebo will be administered Subcutaneously.
Experimental: Maintenance Study - Ustekinumab 90mg SC every 12 weeks Participants in clinical response (at Week 8 or Week 16) to Induction treatment with single IV infusion of Ustekinumab will be randomized to receive ustekinumab 90 mg subcutaneously every 12 weeks, beginning Week 0 of Maintenance study through Week 44.	Drug: Ustekinumab SC Ustekinumab will be administered as subcutaneously.
Experimental: Maintenance Study - Ustekinumab 90mg SC every 8 weeks (q8w) Participants in clinical response (at Week 8 or Week 16) to Induction treatment with single IV infusion of Ustekinumab will be randomized to receive ustekinumab 90 mg subcutaneously every 8 weeks, beginning Week 0 of Maintenance study through Week 44.	Drug: Ustekinumab SC Ustekinumab will be administered as subcutaneously.
Maintenance Study - Placebo IV - Responder - Placebo SC Participants in clinical response to Induction treatment with IV Placebo will receive placebo subcutaneously, beginning Week 0 of Maintenance study through Week 44. Participants are not randomized.	Drug: Placebo SC Placebo will be administered Subcutaneously.
Maintenance Study-Delayed Responder-Ustekinumab 90mg SC q8w Participants without clinical response to induction treatment ustekinumab (130 mg or 6 mg/kg [IV]) at Week 8 but in clinical response at Week 16 after receiving Induction Ustekinumab at week 8 (delayed responders) will receive ustekinumab 90 mg subcutaneously every 8 weeks, beginning Week 0 of Maintenance study through Week 44. Participants are not randomized.	Drug: Ustekinumab SC Ustekinumab will be administered as subcutaneously.

Detailed Description:

This is a Phase 3, randomized (assignment of study drug by chance), double-blind (neither the participant or study staff will know the identity of study drugs), placebo-controlled (placebo is an inactive substance that is compared with a drug to test whether the drug has a real effect in a clinical trial), parallel-group (a medical research study comparing the response in 2 or more groups of participants receiving different interventions), multi-center (more than one clinical site will work on a medical research study), protocol of ustekinumab. The protocol will consist of 2 studies: an Induction study and a Maintenance study with unique endpoints. Screening period will be up to 8 Weeks. Induction study will be at least 8 weeks duration for each participant. Participant with clinical response in the Induction study will be eligible for the Maintenance study. The Maintenance study will be 44 weeks duration. After completion of the maintenance study, a long term extension will follow eligible participants for an additional 3 years. Clinical remission will be evaluated at Week 8 in the Induction study. Clinical remission among ustekinumab Induction responders will be evaluated at week 44 in the Maintenance study. Participants' safety will be monitored throughout.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Has a clinical diagnosis of Ulcerative Colitis (UC) at least 3 months before Screening
- Has moderately to severely active UC, defined as a Baseline (Week 0) Mayo score of 6 to 12, including a Screening endoscopy subscore of the Mayo score greater than or equal to (>=) 2 as determined by a central reading of the video endoscopy
- Have failed biologic therapy, that is, have received treatment with 1 or more tumour necrosis factor (TNF) antagonists or vedolizumab at a dose approved for the treatment of UC, and have a documented history of failure to respond to or tolerate such treatment; OR Be naïve to biologic therapy (TNF antagonists or vedolizumab) or have received biologic therapy but have not demonstrated a history of failure to respond to, or tolerate, a biologic therapy and have a prior or current UC medication history that includes at least 1 of the following: a. Inadequate response to or failure to tolerate current treatment with oral corticosteroids or immunomodulators (6-mercaptopurine [6-MP] or azathioprine [AZA]) OR b. History of failure to respond to, or tolerate, at least 1 of the following therapies: oral or IV corticosteroids or immunomodulators (6-MP or AZA) OR c. History of corticosteroid dependence (that is, an inability to successfully taper corticosteroids without a return of the symptoms of UC)
- Before the first administration of study agent, the following conditions must be met: vedolizumab must have been discontinued for at least 4 months and anti-tumor necrosis factors (TNFs) for at least 8 weeks

Exclusion Criteria:

- Has severe extensive colitis and is at imminent risk of colectomy
- Has UC limited to the rectum only or to < 20 centimeters (cm) of the colon
- Presence of a stoma or history of a fistula
- Participants with history of extensive colonic resection (for example, less than 30 cm of colon remaining) that would prevent adequate evaluation of the effect of study agent on clinical disease activity
- Participants with history of colonic mucosal dysplasia. Participants will not be excluded from the study because of a pathology finding of "indefinite dysplasia with reactive atypia"

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02407236

Contacts

Contact: Use link at the bottom of the page to see if you qualify for an enrolling site (see list). If you still have questions: JNJ.CT@sylogent.com

Show 146 Study Locations

Sponsors and Collaborators

Janssen Research & Development, LLC

Investigators

Study Director: Janssen Research & Development, LLC Clinical Trial Janssen Research & Development, LLC

More Information

Additional Information:

To learn how to participate in this trial please click here.

No publications provided

Responsible Party:	Janssen Research & Development, LLC
ClinicalTrials.gov Identifier:	NCT02407236 History of Changes
Other Study ID Numbers:	CR106920, 2014-005606-38, CNTO1275UCO3001
Study First Received:	March 30, 2015
Last Updated:	September 23, 2015
Health Authority:	United States: Food and Drug Administration Canada: Health Canada Israel: Israeli Health Ministry Pharmaceutical Administration Russia: Ministry of Health of the Russian Federation Serbia: Medicines and Medical Devices Agency South Africa: Medicines Control Council Australia: Department of Health and Ageing Therapeutic Goods Administration South Korea: Ministry of Food and Drug Safety New Zealand: New Zealand Medicines and Medical Devices Safety Authority United Kingdom: Medicines and Healthcare Products Regulatory Agency Poland: Urząd Rejestracji Produktów Leczniczych, Wyrobów Medycznych i Produktów Biobójczychul Hungary: National Institute of Pharmacy Germany: Paul-Ehrlich-Institut France: Agence Nationale de Sécurité du Médicament et des produits de santé Denmark: Danish Health and Medicines Authority Bulgaria: Bulgarian Drug Agency Austria: Bundesamt für Sicherheit im Gesundheitswesen Belgium: Agence Fédérale des Médicaments et Produits de Santé Czech Republic: Statni Ustav pro kontrolu leciv Italy: Agenzia Italiana del Farmaco Netherlands: Centrale Commissie Mensgebonden Onderzoek Romania: Agentia Nationala a Medicamentului si a Dispozitivelor Medicale Slovak Republic: Štátny ústav pre kontrolu liečiv

Keywords provided by Janssen Research & Development, LLC:
Ustekinumab
Inflammatory Bowel Diseases (IBD)
Colitis, Ulcerative

Additional relevant MeSH terms:

Colitis	Colonic Diseases
Colitis, Ulcerative	Digestive System Diseases
Inflammatory Bowel Diseases	Gastroenteritis
Intestinal Diseases	Gastrointestinal Diseases
Ulcer	Pathologic Processes

ClinicalTrials.gov processed this record on October 07, 2015

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