Archived Drug Label

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use STELARA® safely and effectively. See full prescribing information for STELARA®.

STELARA® (ustekinumab) injection, for subcutaneous or intravenous use
Initial U.S. Approval: 2009

RECENT MAJOR CHANGES

Indications and Usage, Crohn's Disease (1.3)	09/2016
Dosage and Administration (2.3)	09/2016
Dosage and Administration (2.6)	09/2016

INDICATIONS AND USAGE

STELARA® is a human interleukin-12 and -23 antagonist indicated for the treatment of adult patients with:

- *moderate to severe plaque psoriasis (Ps)* who are candidates for phototherapy or systemic therapy. (1.1)
- *active psoriatic arthritis (PsA)*, alone or in combination with methotrexate. (1.2)
- *moderately to severely active Crohn's disease (CD)* who have
  - failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker or
  - failed or were intolerant to treatment with one or more TNF blockers. (1.3)

DOSAGE AND ADMINISTRATION

Psoriasis Recommended Adult Subcutaneous Dosage (2.1):

Weight Range (kilogram)	Dosage Regimen
less than or equal to 100 kg	45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks
greater than 100 kg	90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks

Psoriatic Arthritis Recommended Adult Subcutaneous Dosage (2.2):

- The recommended dosage is 45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks.
- For patients with co-existent moderate-to-severe plaque psoriasis weighing greater than 100 kg, the recommended dosage is 90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks.

Crohn's Disease Recommended Initial Adult Intravenous Dosage (2.3):
A single intravenous infusion using weight-based dosing:

Crohn's Disease Recommended Maintenance Adult Subcutaneous Dosage (2.3):
A subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.

DOSAGE FORMS AND STRENGTHS

Subcutaneous Injection

- Injection: 45 mg/0.5 mL or 90 mg/mL in a single-dose prefilled syringe (3)
- Injection: 45 mg/0.5 mL in a single-dose vial (3)

Intravenous Infusion

- Injection: 130 mg/26 mL (5 mg/mL) solution in a single-dose vial (3)

CONTRAINDICATIONS

Clinically significant hypersensitivity to ustekinumab or to any of the excipients. (4)

WARNINGS AND PRECAUTIONS

- Infections: Serious infections have occurred. Do not start STELARA® during any clinically important active infection. If a serious infection or clinically significant infection develops, consider discontinuing STELARA® until the infection resolves. (5.1)
- Theoretical Risk for Particular Infections: Serious infections from mycobacteria, salmonella and Bacillus Calmette-Guerin (BCG) vaccinations have been reported in patients genetically deficient in IL-12/IL-23. Diagnostic tests for these infections should be considered as dictated by clinical circumstances. (5.2)
- Tuberculosis (TB): Evaluate patients for TB prior to initiating treatment with STELARA®. Initiate treatment of latent TB before administering STELARA®. (5.3)
- Malignancies: STELARA® may increase risk of malignancy. The safety of STELARA® in patients with a history of or a known malignancy has not been evaluated. (5.4)
- Hypersensitivity Reactions: Anaphylaxis or other clinically significant hypersensitivity reactions may occur. (5.5)
- Reversible Posterior Leukoencephalopathy Syndrome (RPLS): One case was reported. If suspected, treat promptly and discontinue STELARA®. (5.6)

ADVERSE REACTIONS

Most common adverse reactions are:

- Psoriasis (≥3%): nasopharyngitis, upper respiratory tract infection, headache, and fatigue. (6.1)
- Crohn's Disease, induction (≥3%): vomiting. (6.1)
- Crohn's Disease, maintenance (≥3%): nasopharyngitis, injection site erythema, vulvovaginal candidiasis/mycotic infection, bronchitis, pruritus, urinary tract infection, and sinusitis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Biotech, Inc. at 1-800-JANSSEN (1-800-526-7736) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

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Weight Range (kilogram)	Recommended Dosage
Up to 55 kg	260 mg (2 vials)
Greater than 55 kg to 85 kg	390 mg (3 vials)
Greater than 85 kg	520 mg (4 vials)

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Psoriasis (Ps)

STELARA® is indicated for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

1.2 Psoriatic Arthritis (PsA)

STELARA® is indicated for the treatment of adult patients with active psoriatic arthritis. STELARA® can be used alone or in combination with methotrexate (MTX).

1.3 Crohn's Disease

STELARA® is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have:

- failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed treatment with a tumor necrosis factor (TNF) blocker or
- failed or were intolerant to treatment with one or more TNF blockers.

2 DOSAGE AND ADMINISTRATION

2.1 Psoriasis

Subcutaneous Adult Dosage Regimen

- For patients weighing 100 kg or less, the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
- For patients weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.

In subjects weighing more than 100 kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these subjects *[see Clinical Studies (14)]*.

2.2 Psoriatic Arthritis

Subcutaneous Adult Dosage Regimen

- The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
- For patients with co-existent moderate-to-severe plaque psoriasis weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.

2.3 Crohn's Disease

Intravenous Induction Adult Dosage Regimen

A single intravenous infusion dose of STELARA® using the weight-based dosage regimen specified in Table 1 *[see Instructions for dilution of STELARA® 130 mg vial for intravenous infusion (2.6)]*.

Table 1: Initial Intravenous Dosage of STELARA®

Body Weight of Patient at the time of dosing	Dose	Number of 130 mg/26 mL (5 mg/mL) STELARA® vials
55 kg or less	260 mg	2
more than 55 kg to 85 kg	390 mg	3
more than 85 kg	520 mg	4

Subcutaneous Maintenance Adult Dosage Regimen

The recommended maintenance dosage is a subcutaneous 90 mg dose administered 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.

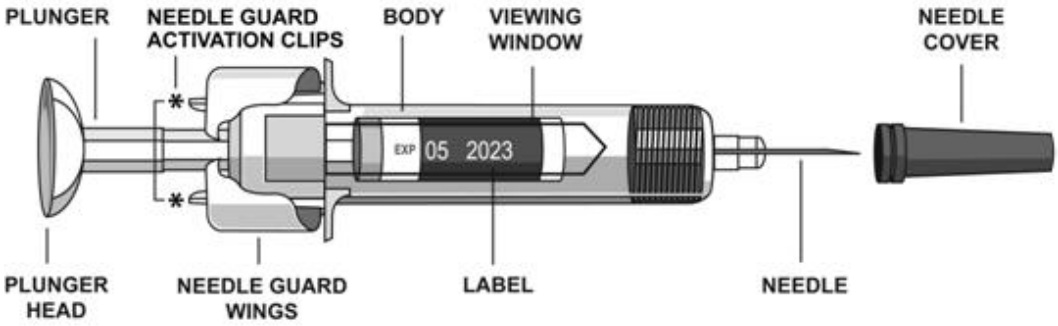
2.4 General Considerations for Administration

- After proper training in subcutaneous injection technique, a patient may self-inject with STELARA® if a physician determines that it is appropriate. Patients should be instructed to follow the directions provided in the Medication Guide *[see Medication Guide]*.
- The needle cover on the prefilled syringe contains dry natural rubber (a derivative of latex). The needle cover should not be handled by persons sensitive to latex.
- It is recommended that each injection be administered at a different anatomic location (such as upper arms, gluteal regions, thighs, or any quadrant of abdomen) than the previous injection, and not into areas where the skin is tender, bruised, erythematous, or indurated. When using the single-dose vial, a 27 gauge, ½ inch needle is recommended.
- STELARA® is intended for use under the guidance and supervision of a physician. STELARA® should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.
- Prior to administration, visually inspect STELARA® for particulate matter and discoloration. STELARA® is clear, colorless to light yellow and may contain a few small translucent or white particles. Do not use STELARA® if it is discolored or cloudy, or if other particulate matter is present. STELARA® does not contain preservatives; therefore, discard any unused product remaining in the vial and/or syringe.

2.5 Instructions for Administration of STELARA® Prefilled Syringes Equipped with Needle Safety Guard

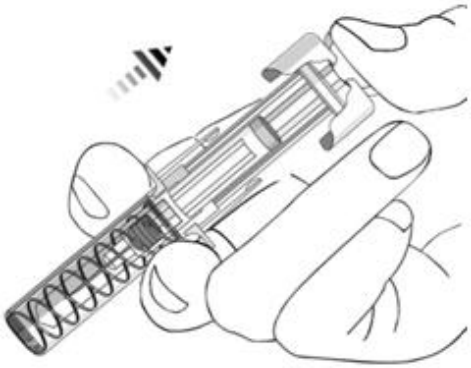
Refer to the diagram below for the provided instructions.

To prevent premature activation of the needle safety guard, do not touch the NEEDLE GUARD ACTIVATION CLIPS at any time during use.



- Hold the BODY and remove the NEEDLE COVER. **Do not hold the PLUNGER or PLUNGER HEAD while removing the NEEDLE COVER or the PLUNGER may move. Do not use the prefilled syringe if it is dropped without the NEEDLE COVER in place**.
- Inject STELARA® subcutaneously as recommended *[see Dosage and Administration (2.1, 2.2, 2.3)]*.
- Inject all of the medication by pushing in the PLUNGER until the PLUNGER HEAD is completely between the needle guard wings. **Injection of the entire prefilled syringe contents is necessary to activate the needle guard**.

- After injection, maintain the pressure on the PLUNGER HEAD and remove the needle from the skin. Slowly take your thumb off the PLUNGER HEAD to allow the empty syringe to move up until the entire needle is covered by the needle guard, as shown by the illustration below:



- Used syringes should be placed in a puncture-resistant container.

2.6 Preparation and Administration of STELARA® 130 mg/26 mL (5 mg/mL) Vial for Intravenous Infusion (Crohn's Disease)

STELARA® solution for intravenous infusion must be diluted, prepared and infused by a healthcare professional using aseptic technique.

1. Calculate the dose and the number of STELARA® vials needed based on patient weight (Table 1). Each 26 mL vial of STELARA® contains 130 mg of ustekinumab.
2. Withdraw, and then discard a volume of the 0.9% Sodium Chloride Injection, USP from the 250 mL infusion bag equal to the volume of STELARA® to be added (discard 26 mL sodium chloride for each vial of STELARA® needed, for 2 vials- discard 52 mL, for 3 vials- discard 78 mL, 4 vials- discard 104 mL).
3. Withdraw 26 mL of STELARA® from each vial needed and add it to the 250 mL infusion bag. The final volume in the infusion bag should be 250 mL. Gently mix.
4. Visually inspect the diluted solution before infusion. Do not use if visibly opaque particles, discoloration or foreign particles are observed.
5. Infuse the diluted solution over a period of at least one hour. Once diluted, the infusion solution may be stored for up to four hours prior to infusion.
6. Use only an infusion set with an in-line, sterile, non-pyrogenic, low protein-binding filter (pore size 0.2 micrometer).
7. Do not infuse STELARA® concomitantly in the same intravenous line with other agents.
8. STELARA® does not contain preservatives. Each vial is for single use only. Discard any remaining solution. Dispose any unused medicinal product in accordance with local requirements.

Storage

If necessary, the diluted infusion solution may be stored for up to 4 hours at room temperature up to 25°C (77°F). Do not freeze. Discard any unused portion of the infusion solution.

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3 DOSAGE FORMS AND STRENGTHS

STELARA® (ustekinumab) is colorless to slightly yellow solution.

Subcutaneous Injection

- Injection: 45 mg/0.5 mL or 90 mg/mL solution in a single-dose prefilled syringe
- Injection: 45 mg/0.5 mL in a single-dose vial

Intravenous Infusion

- Injection: 130 mg/26 mL (5 mg/mL) solution in a single-dose vial

4 CONTRAINDICATIONS

STELARA® is contraindicated in patients with clinically significant hypersensitivity to ustekinumab or to any of the excipients *[see Warnings and Precautions (5.5)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Infections

STELARA® may increase the risk of infections and reactivation of latent infections. Serious bacterial, fungal, and viral infections were observed in subjects receiving STELARA® *[see Adverse Reactions (6.1)]*.

Serious infections requiring hospitalization occurred in patients with psoriasis, psoriatic arthritis and Crohn's disease in clinical studies. In patients with psoriasis, serious infections included diverticulitis, cellulitis, pneumonia, appendicitis, cholecystitis, sepsis, osteomyelitis, viral infections, gastroenteritis and urinary tract infections. In patients with psoriatic arthritis, serious infections included cholecystitis. In patients with Crohn's disease, serious or other clinically significant infections included anal abscess, gastroenteritis, ophthalmic herpes, pneumonia, and listeria meningitis.

Treatment with STELARA® should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. Consider the risks and benefits of treatment prior to initiating use of STELARA® in patients with a chronic infection or a history of recurrent infection.

Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur while on treatment with STELARA® and consider discontinuing STELARA® for serious or clinically significant infections until the infection resolves or is adequately treated.

5.2 Theoretical Risk for Vulnerability to Particular Infections

Individuals genetically deficient in IL-12/IL-23 are particularly vulnerable to disseminated infections from mycobacteria (including nontuberculous, environmental mycobacteria), salmonella (including nontyphi strains), and Bacillus Calmette-Guerin (BCG) vaccinations. Serious infections and fatal outcomes have been reported in such patients.

It is not known whether patients with pharmacologic blockade of IL-12/IL-23 from treatment with STELARA® may be susceptible to these types of infections. Appropriate diagnostic testing should be considered, e.g., tissue culture, stool culture, as dictated by clinical circumstances.

5.3 Pre-treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis infection prior to initiating treatment with STELARA®.

Do not administer STELARA® to patients with active tuberculosis infection. Initiate treatment of latent tuberculosis prior to administering STELARA®. Consider anti-tuberculosis therapy prior to initiation of STELARA® in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed. Closely monitor patients receiving STELARA® for signs and symptoms of active tuberculosis during and after treatment.

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5.4 Malignancies

STELARA® is an immunosuppressant and may increase the risk of malignancy. Malignancies were reported among subjects who received STELARA® in clinical studies *[see Adverse Reactions (6.1)]*. In rodent models, inhibition of IL-12/IL-23p40 increased the risk of malignancy *[see Nonclinical Toxicology (13)]*.

The safety of STELARA® has not been evaluated in patients who have a history of malignancy or who have a known malignancy.

There have been post marketing reports of the rapid appearance of multiple cutaneous squamous cell carcinomas in patients receiving STELARA® who had pre-existing risk factors for developing non-melanoma skin cancer. All patients receiving STELARA® should be monitored for the appearance of non-melanoma skin cancer. Patients greater than 60 years of age, those with a medical history of prolonged immunosuppressant therapy and those with a history of PUVA treatment should be followed closely *[see Adverse Reactions (6.1)]*.

5.5 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with STELARA® *[see Adverse Reactions (6.1, 6.3)]*. If an anaphylactic or other clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue STELARA®.

5.6 Reversible Posterior Leukoencephalopathy Syndrome

One case of reversible posterior leukoencephalopathy syndrome (RPLS) was observed in clinical studies of psoriasis and psoriatic arthritis. The subject, who had received 12 doses of STELARA® over approximately two years, presented with headache, seizures and confusion. No additional STELARA® injections were administered and the subject fully recovered with appropriate treatment. No cases of RPLS were observed in clinical studies of Crohn's disease.

RPLS is a neurological disorder, which is not caused by demyelination or a known infectious agent. RPLS can present with headache, seizures, confusion and visual disturbances. Conditions with which it has been associated include preeclampsia, eclampsia, acute hypertension, cytotoxic agents and immunosuppressive therapy. Fatal outcomes have been reported.

If RPLS is suspected, administer appropriate treatment and discontinue STELARA®.

5.7 Immunizations

Prior to initiating therapy with STELARA®, patients should receive all age-appropriate immunizations as recommended by current immunization guidelines. Patients being treated with STELARA® should not receive live vaccines. BCG vaccines should not be given during treatment with STELARA® or for one year prior to initiating treatment or one year following discontinuation of treatment. Caution is advised when administering live vaccines to household contacts of patients receiving STELARA® because of the potential risk for shedding from the household contact and transmission to patient.

Non-live vaccinations received during a course of STELARA® may not elicit an immune response sufficient to prevent disease.

5.8 Concomitant Therapies

In clinical studies of psoriasis the safety of STELARA® in combination with other immunosuppressive agents or phototherapy was not evaluated. Ultraviolet-induced skin cancers developed earlier and more frequently in mice genetically manipulated to be deficient in both IL-12 and IL-23 or IL-12 alone *[see Nonclinical Toxicology (13.1)]*.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the label:

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- Infections *[see Warnings and Precautions (5.1)]*
- Malignancies *[see Warnings and Precautions (5.4)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.5)]*
- Reversible Posterior Leukoencephalopathy Syndrome *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Psoriasis

The safety data reflect exposure to STELARA® in 3117 psoriasis subjects, including 2414 exposed for at least 6 months, 1855 exposed for at least one year, 1653 exposed for at least two years, 1569 exposed for at least three years, 1482 exposed for at least four years and 838 exposed for at least five years.

Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the STELARA® groups than the placebo group during the placebo-controlled period of Ps STUDY 1 and Ps STUDY 2 *[see Clinical Studies (14)]*.

Table 2: Adverse reactions reported by ≥1% of subjects through Week 12 in Ps STUDY 1 and Ps STUDY 2

		STELARA®	
	Placebo	**45 mg**	**90 mg**
Subjects treated	**665**	**664**	**666**
Nasopharyngitis	51 (8%)	56 (8%)	49 (7%)
Upper respiratory tract infection	30 (5%)	36 (5%)	28 (4%)
Headache	23 (3%)	33 (5%)	32 (5%)
Fatigue	14 (2%)	18 (3%)	17 (3%)
Diarrhea	12 (2%)	13 (2%)	13 (2%)
Back pain	8 (1%)	9 (1%)	14 (2%)
Dizziness	8 (1%)	8 (1%)	14 (2%)
Pharyngolaryngeal pain	7 (1%)	9 (1%)	12 (2%)
Pruritus	9 (1%)	10 (2%)	9 (1%)
Injection site erythema	3 (<1%)	6 (1%)	13 (2%)
Myalgia	4 (1%)	7 (1%)	8 (1%)
Depression	3 (<1%)	8 (1%)	4 (1%)

Adverse reactions that occurred at rates less than 1% in the controlled period of Ps STUDIES 1 and 2 through week 12 included: cellulitis, herpes zoster, diverticulitis and certain injection site reactions (pain, swelling, pruritus, induration, hemorrhage, bruising, and irritation).

One case of RPLS occurred during clinical studies *[see Warnings and Precautions (5.6)]*.

Infections

In the placebo-controlled period of clinical studies of psoriasis subjects (average follow-up of 12.6 weeks for placebo-treated subjects and 13.4 weeks for STELARA®-treated subjects), 27% of STELARA®-treated subjects reported infections (1.39 per subject-year of follow-up) compared with 24% of placebo-treated subjects (1.21 per subject-year of follow-up). Serious infections occurred in 0.3% of STELARA®-treated

subjects (0.01 per subject-year of follow-up) and in 0.4% of placebo-treated subjects (0.02 per subject-year of follow-up) *[see Warnings and Precautions (5.1)]*.

In the controlled and non-controlled portions of psoriasis clinical studies (median follow-up of 3.2 years), representing 8998 subject-years of exposure, 72.3% of STELARA®-treated subjects reported infections (0.87 per subject-years of follow-up). Serious infections were reported in 2.8% of subjects (0.01 per subject-years of follow-up).

Malignancies

In the controlled and non-controlled portions of psoriasis clinical studies (median follow-up of 3.2 years, representing 8998 subject-years of exposure), 1.7% of STELARA®-treated subjects reported malignancies excluding non-melanoma skin cancers (0.60 per hundred subject-years of follow-up). Non-melanoma skin cancer was reported in 1.5% of STELARA®-treated subjects (0.52 per hundred subject-years of follow-up) *[see Warnings and Precautions (5.4)]*. The most frequently observed malignancies other than non-melanoma skin cancer during the clinical studies were: prostate, melanoma, colorectal and breast. Malignancies other than non-melanoma skin cancer in STELARA®-treated patients during the controlled and uncontrolled portions of studies were similar in type and number to what would be expected in the general U.S. population according to the SEER database (adjusted for age, gender and race).[1]

Psoriatic Arthritis

The safety of STELARA® was assessed in 927 patients in two randomized, double-blind, placebo-controlled studies in adult patients with active psoriatic arthritis (PsA). The overall safety profile of STELARA® in patients with PsA was consistent with the safety profile seen in psoriasis clinical studies. A higher incidence of arthralgia, nausea, and dental infections was observed in STELARA®-treated patients when compared with placebo-treated patients (3% vs. 1% for arthralgia and 3% vs. 1% for nausea; 1% vs. 0.6% for dental infections) in the placebo-controlled portions of the PsA clinical studies.

Crohn's Disease

The safety of STELARA® was assessed in 1407 patients with moderately to severely active Crohn's disease (Crohn's Disease Activity Index [CDAI] greater than or equal to 220 and less than or equal to 450) in three randomized, double-blind, placebo-controlled, parallel-group, multicenter studies. These 1407 patients included 40 patients who received a prior investigational intravenous ustekinumab formulation but were not included in the efficacy analyses. In Studies CD-1 and CD-2 there were 470 patients who received STELARA® 6 mg/kg as a weight-based single intravenous induction dose and 466 who received placebo *[see Dosage and Administration (2.3)]*. Patients who were responders in either Study CD-1 or CD-2 were randomized to receive a subcutaneous maintenance regimen of either 90 mg STELARA® every 8 weeks, or placebo for 44 weeks in Study CD-3. Patients in these 3 studies may have received other concomitant therapies including aminosalicylates, immunomodulatory agents [azathioprine (AZA), 6-mercaptopurine (6-MP), methotrexate (MTX)], oral corticosteroids (prednisone or budesonide), and/or antibiotics for their Crohn's Disease *[see Clinical Studies (14.3)]*.

The overall safety profile of STELARA® was consistent with the safety profile seen in the psoriasis and psoriatic arthritis clinical studies. Common adverse reactions in Studies CD-1 and CD-2 and in Study CD-3 are listed in Tables 3 and 4, respectively.

Table 3: Common adverse reactions through Week 8 in Studies CD-1 and CD-2 occurring in ≥3% of STELARA®-treated patients and higher than placebo

	Placebo **N=466**	**STELARA® 6 mg/kg single intravenous induction dose** **N=470**

	Placebo N=466	STELARA® 6 mg/kg single intravenous induction dose N=470
Vomiting	3%	4%

Other less common adverse reactions reported in patients in Studies CD-1 and CD-2 included asthenia (1% vs 0.4%), acne (1% vs 0.4%), and pruritus (2% vs 0.4%).

Table 4: Common adverse reactions through Week 44 in Study CD-3 occurring in ≥3% of STELARA®-treated patients and higher than placebo

	Placebo N=133	STELARA® 90 mg subcutaneous maintenance dose every 8 weeks N=131
Nasopharyngitis	8%	11%
Injection site erythema	0	5%
Vulvovaginal candidiasis/mycotic infection	1%	5%
Bronchitis	3%	5%
Pruritus	2%	4%
Urinary tract infection	2%	4%
Sinusitis	2%	3%

Infections

In patients with Crohn's disease, serious or other clinically significant infections included anal abscess, gastroenteritis, and pneumonia. In addition, listeria meningitis and ophthalmic herpes were reported in one patient each.

Malignancies

With up to one year of treatment in the Crohn's disease clinical studies, 0.2% of STELARA®-treated patients (0.36 events per hundred patient-years) and 0.2% of placebo-treated patients (0.58 events per hundred patient-years) developed non-melanoma skin cancer. Malignancies other than non-melanoma skin cancers occurred in 0.2% of STELARA®-treated patients (0.27 events per hundred patient-years) and in none of the placebo-treated patients.

Hypersensitivity Reactions Including Anaphylaxis

In CD studies, two patients reported hypersensitivity reactions following STELARA® administration. One patient experienced signs and symptoms consistent with anaphylaxis (tightness of the throat, shortness of breath, and flushing) after a single subcutaneous administration (0.1% of patients receiving subcutaneous STELARA®). In addition, one patient experienced signs and symptoms consistent with or related to a hypersensitivity reaction (chest discomfort, flushing, urticaria, and increased body temperature) after the initial intravenous STELARA® dose (0.08% of patients receiving intravenous STELARA®). These patients were treated with oral antihistamines or corticosteroids and in both cases symptoms resolved within an hour.

6.2 Immunogenicity

Approximately 6% of patients treated with STELARA® in psoriasis and psoriatic arthritis clinical studies developed antibodies to ustekinumab, which were generally low-titer. In Crohn's disease clinical studies, less than 3% of patients treated with STELARA® developed antibodies to ustekinumab. No apparent association between the development of antibodies to ustekinumab and the development of injection site reactions was seen. No ustekinumab-related serious hypersensitivity reactions were observed in psoriasis, psoriatic arthritis and Crohn's disease clinical studies. In psoriasis studies, the majority of patients who were positive for antibodies to ustekinumab had neutralizing antibodies.

The data above reflect the percentage of subjects whose test results were positive for antibodies to ustekinumab and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including sample handling, timing of sample collection, concomitant medications and underlying disease. For these reasons, comparison of the incidence of antibodies to ustekinumab with the incidence of antibodies to other products may be misleading.

6.3 Postmarketing Experience

The following adverse reactions have been reported during post-approval of STELARA®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to STELARA® exposure.

Immune system disorders: Serious hypersensitivity reactions (including anaphylaxis and angioedema), other hypersensitivity reactions (including rash and urticaria) *[see Warnings and Precautions (5.5)]*.

Skin reactions: Pustular psoriasis, erythrodermic psoriasis.

7 DRUG INTERACTIONS

7.1 Live Vaccines

Avoid use of live vaccines with STELARA® *[see Warnings and Precautions (5.7)]*.

7.2 Concomitant Therapies

In psoriasis studies the safety of STELARA® in combination with immunosuppressive agents or phototherapy has not been evaluated *[see Warnings and Precautions (5.8)]*. In psoriatic arthritis studies, concomitant methotrexate use did not appear to influence the safety or efficacy of STELARA®. In Crohn's disease studies, immunomodulators (6-mercaptopurine, azathioprine, methotrexate) were used concomitantly in approximately 30% of patients and corticosteroids were used concomitantly in approximately 40% of patients. Use of these concomitant therapies did not appear to influence the overall safety or efficacy of STELARA®.

7.3 CYP450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Thus, STELARA®, an antagonist of IL-12 and IL-23, could normalize the formation of CYP450 enzymes. Upon initiation of STELARA® in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, monitoring for therapeutic effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) should be considered and the individual dose of the drug adjusted as needed *[see Clinical Pharmacology (12.3)]*.

7.4 Allergen Immunotherapy

STELARA® has not been evaluated in patients who have undergone allergy immunotherapy. STELARA® may decrease the protective effect of allergen immunotherapy (decrease tolerance) which may increase the

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risk of an allergic reaction to a dose of allergen immunotherapy. Therefore, caution should be exercised in patients receiving or who have received allergen immunotherapy, particularly for anaphylaxis.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy registry that monitors pregnancy outcomes in women exposed to STELARA® during pregnancy. Patients should be encouraged to enroll by calling 1-877-311-8972.

Risk Summary

Limited data on the use of STELARA® in pregnant women are insufficient to inform a drug associated risk *[see Data]*. In animal reproductive and developmental toxicity studies, no adverse developmental effects were observed after administration of ustekinumab to pregnant monkeys at exposures greater than 100 times the human exposure at the maximum recommended human subcutaneous dose (MRHD).

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The estimated background risk of major birth defects and miscarriage for the indicated population(s) are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage of clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human Data

Limited data on use of STELARA® in pregnant women from observational studies, published case reports, and postmarketing surveillance are insufficient to inform a drug associated risk.

Animal Data

Ustekinumab was tested in two embryo-fetal development toxicity studies in cynomolgus monkeys. No teratogenic or other adverse developmental effects were observed in fetuses from pregnant monkeys that were administered ustekinumab subcutaneously twice weekly or intravenously weekly during the period of organogenesis. Serum concentrations of ustekinumab in pregnant monkeys were greater than 100 times the serum concentration in patients treated subcutaneously with 90 mg of ustekinumab weekly for 4 weeks.

In a combined embryo-fetal development and pre- and post-natal development toxicity study, pregnant cynomolgus monkeys were administered subcutaneous doses of ustekinumab twice weekly at exposures greater than 100 times the human subcutaneous exposure from the beginning of organogenesis to Day 33 after delivery. Neonatal deaths occurred in the offspring of one monkey administered ustekinumab at 22.5 mg/kg and one monkey dosed at 45 mg/kg. No ustekinumab-related effects on functional, morphological, or immunological development were observed in the neonates from birth through six months of age.

8.2 Lactation

Risk Summary

There are no data on the presence of ustekinumab in human milk, the effects on the breastfed infant, or the effects on milk production. Ustekinumab was present in the milk of lactating monkeys administered ustekinumab. Due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk. Maternal IgG is known to be present in human milk. Published data suggest that the systemic exposure to a breastfed infant is expected to be low because ustekinumab is a large molecule and is degraded in the gastrointestinal tract. However, if ustekinumab is transferred into human milk the effects of local exposure in the gastrointestinal tract are unknown.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for STELARA® and any potential adverse effects on the breastfed child from STELARA® or from the

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underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of STELARA® in pediatric patients have not been established.

8.5 Geriatric Use

Of the 5884 subjects exposed to STELARA®, a total of 306 were 65 years or older (183 patients with psoriasis, 65 patients with psoriatic arthritis and 58 with Crohn's disease), and 34 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 and over is not sufficient to determine whether they respond differently from younger subjects.

10 OVERDOSAGE

Single doses up to 6 mg/kg intravenously have been administered in clinical studies without dose-limiting toxicity. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment be instituted immediately.

11 DESCRIPTION

Ustekinumab is a human IgG1κ monoclonal antibody against the p40 subunit of the IL-12 and IL-23 cytokines. Using DNA recombinant technology, ustekinumab is produced in a well characterized recombinant cell line and is purified using standard bio-processing technology. The manufacturing process contains steps for the clearance of viruses. Ustekinumab is comprised of 1326 amino acids and has an estimated molecular mass that ranges from 148,079 to 149,690 Daltons.

STELARA® (ustekinumab) Injection is a sterile, preservative-free, colorless to slightly yellow solution that may contain a few small translucent or white particles with pH of 5.7– 6.3.

STELARA® for Subcutaneous Use

Available as 45 mg of ustekinumab in 0.5 mL and 90 mg of ustekinumab in 1 mL, supplied as a sterile solution in a single-dose prefilled syringe with a 27 gauge fixed ½ inch needle and as 45 mg of ustekinumab in 0.5 mL in a single-dose 2 mL Type I glass vial with a coated stopper. The syringe is fitted with a passive needle guard and a needle cover that contains dry natural rubber (a derivative of latex).

Each 0.5 mL prefilled syringe or vial delivers 45 mg ustekinumab, L-histidine and L-histidine monohydrochloride monohydrate (0.5 mg), Polysorbate 80 (0.02 mg), and sucrose (38 mg).

Each 1 mL prefilled syringe delivers 90 mg ustekinumab, L-histidine and L-histidine monohydrochloride monohydrate (1 mg), Polysorbate 80 (0.04 mg), and sucrose (76 mg).

STELARA® for Intravenous Infusion

Available as 130 mg of ustekinumab in 26 mL, supplied as a single-dose 30 mL Type I glass vial with a coated stopper.

Each 26 mL vial delivers 130 mg ustekinumab, EDTA disodium salt dihydrate (0.52 mg), L-histidine (20 mg), L-histidine hydrochloride monohydrate (27 mg), L-methionine (10.4 mg), Polysorbate 80 (10.4 mg) and sucrose (2210 mg).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ustekinumab is a human IgG1κ monoclonal antibody that binds with specificity to the p40 protein subunit used by both the IL-12 and IL-23 cytokines. IL-12 and IL-23 are naturally occurring cytokines that are

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involved in inflammatory and immune responses, such as natural killer cell activation and CD4+ T-cell differentiation and activation. In *in vitro* models, ustekinumab was shown to disrupt IL-12 and IL-23 mediated signaling and cytokine cascades by disrupting the interaction of these cytokines with a shared cell-surface receptor chain, IL-12Rβ1. The cytokines IL-12 and IL-23 have been implicated as important contributors to the chronic inflammation that is a hallmark of Crohn's Disease. In animal models of colitis, genetic absence or antibody blockade of the p40 subunit of IL-12 and IL-23, the target of ustekinumab, was shown to be protective.

12.2 Pharmacodynamics

In a small exploratory study, a decrease was observed in the expression of mRNA of its molecular targets IL-12 and IL-23 in lesional skin biopsies measured at baseline and up to two weeks post-treatment in subjects with psoriasis.

12.3 Pharmacokinetics

Absorption

In subjects with psoriasis, the median time to reach the maximum serum concentration (T_{max}) was 13.5 days and 7 days, respectively, after a single subcutaneous administration of 45 mg (N=22) and 90 mg (N=24) of ustekinumab. In healthy subjects (N=30), the median T_{max} value (8.5 days) following a single subcutaneous administration of 90 mg of ustekinumab was comparable to that observed in subjects with psoriasis.

Following multiple subcutaneous doses of STELARA® in patients with psoriasis, the steady-state serum concentrations of ustekinumab were achieved by Week 28. There was no apparent accumulation in serum ustekinumab concentration over time when given subcutaneously every 12 weeks.

In patients with Crohn's disease, following the recommended intravenous induction dose, mean peak serum ustekinumab concentration was 125.2 ± 33.6 mcg/mL. Starting at Week 8, the recommended subcutaneous maintenance dosing of 90 mg ustekinumab was administered every 8 weeks. Steady state ustekinumab concentration was achieved by the start of the second maintenance dose. There was no apparent accumulation in ustekinumab concentration over time when given subcutaneously every 8 weeks. Mean steady-state trough concentration was 2.51 ± 2.06 mcg/mL for 90 mg ustekinumab administered every 8 weeks.

Distribution

In a population pharmacokinetic analysis of ustekinumab, the volume of distribution of the central compartment was 2.74 L (95% CI: 2.69, 2.78), and the total volume of distribution at steady-state was 4.62 L in patients with Crohn's disease.

Elimination

The mean (±SD) half-life ranged from 14.9 ± 4.6 to 45.6 ± 80.2 days across all psoriasis studies following subcutaneous administration. In a population pharmacokinetic analysis of ustekinumab, the clearance was 0.19 L/day (95% CI: 0.185, 0.197) with an estimated median terminal half-life of approximately 19 days in patients with Crohn's disease.

Metabolism

The metabolic pathway of ustekinumab has not been characterized. As a human IgG1κ monoclonal antibody ustekinumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Specific Populations

Weight

When given the same dose, subjects with psoriasis or psoriatic arthritis weighing more than 100 kg had lower median serum ustekinumab concentrations compared with those subjects weighing 100 kg or less. The

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median trough serum concentrations of ustekinumab in subjects of higher weight (greater than 100 kg) in the 90 mg group were comparable to those in subjects of lower weight (100 kg or less) in the 45 mg group.

Age: Geriatric Population

A population pharmacokinetic analysis (N=106/1937 patients with psoriasis greater than or equal to 65 years old) was performed to evaluate the effect of age on the pharmacokinetics of ustekinumab. There were no apparent changes in pharmacokinetic parameters (clearance and volume of distribution) in subjects older than 65 years old.

Drug Interaction Studies

The effects of IL-12 or IL-23 on the regulation of CYP450 enzymes were evaluated in an *in vitro* study using human hepatocytes, which showed that IL-12 and/or IL-23 at levels of 10 ng/mL did not alter human CYP450 enzyme activities (CYP1A2, 2B6, 2C9, 2C19, 2D6, or 3A4). However, the clinical relevance of *in vitro* data has not been established *[see Drug Interactions (7.3)]*.

No *in vivo* drug interaction studies have been conducted with STELARA®.

Population pharmacokinetic data analyses indicated that the clearance of ustekinumab was not impacted by concomitant MTX, NSAIDs, and oral corticosteroids, or prior exposure to a TNF blocker in patients with psoriatic arthritis.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of STELARA®. Published literature showed that administration of murine IL-12 caused an anti-tumor effect in mice that contained transplanted tumors and IL-12/IL-23p40 knockout mice or mice treated with anti-IL-12/IL-23p40 antibody had decreased host defense to tumors. Mice genetically manipulated to be deficient in both IL-12 and IL-23 or IL-12 alone developed UV-induced skin cancers earlier and more frequently compared to wild-type mice. The relevance of these experimental findings in mouse models for malignancy risk in humans is unknown.

No effects on fertility were observed in male cynomolgus monkeys that were administered ustekinumab at subcutaneous doses up to 45 mg/kg twice weekly (45 times the MRHD on a mg/kg basis) prior to and during the mating period. However, fertility and pregnancy outcomes were not evaluated in mated females.

No effects on fertility were observed in female mice that were administered an analogous IL-12/IL-23p40 antibody by subcutaneous administration at doses up to 50 mg/kg, twice weekly, prior to and during early pregnancy.

13.2 Animal Toxicology and/or Pharmacology

In a 26-week toxicology study, one out of 10 monkeys subcutaneously administered 45 mg/kg ustekinumab twice weekly for 26 weeks had a bacterial infection.

14 CLINICAL STUDIES

14.1 Psoriasis

Two multicenter, randomized, double-blind, placebo-controlled studies (Ps STUDY 1 and Ps STUDY 2) enrolled a total of 1996 subjects 18 years of age and older with plaque psoriasis who had a minimum body surface area involvement of 10%, and Psoriasis Area and Severity Index (PASI) score ≥12, and who were candidates for phototherapy or systemic therapy. Subjects with guttate, erythrodermic, or pustular psoriasis were excluded from the studies.

Ps STUDY 1 enrolled 766 subjects and Ps STUDY 2 enrolled 1230 subjects. The studies had the same design through Week 28. In both studies, subjects were randomized in equal proportion to placebo, 45 mg or 90 mg of STELARA®. Subjects randomized to STELARA® received 45 mg or 90 mg doses, regardless of weight, at Weeks 0, 4, and 16. Subjects randomized to receive placebo at Weeks 0 and 4 crossed over to receive STELARA® (either 45 mg or 90 mg) at Weeks 12 and 16.

In both studies, the endpoints were the proportion of subjects who achieved at least a 75% reduction in PASI score (PASI 75) from baseline to Week 12 and treatment success (cleared or minimal) on the Physician's Global Assessment (PGA). The PGA is a 6-category scale ranging from 0 (cleared) to 5 (severe) that indicates the physician's overall assessment of psoriasis focusing on plaque thickness/induration, erythema, and scaling.

In both studies, subjects in all treatment groups had a median baseline PASI score ranging from approximately 17 to 18. Baseline PGA score was marked or severe in 44% of subjects in Ps STUDY 1 and 40% of subjects in Ps STUDY 2. Approximately two-thirds of all subjects had received prior phototherapy, 69% had received either prior conventional systemic or biologic therapy for the treatment of psoriasis, with 56% receiving prior conventional systemic therapy and 43% receiving prior biologic therapy. A total of 28% of subjects had a history of psoriatic arthritis.

Clinical Response

The results of Ps STUDY 1 and Ps STUDY 2 are presented in Table 5 below.

Table 5: Clinical Outcomes Ps STUDY 1 and Ps STUDY 2

Week 12	**Ps STUDY 1**			**Ps STUDY 2**		
		STELARA®			**STELARA®**	
	Placebo	**45 mg**	**90 mg**	**Placebo**	**45 mg**	**90 mg**
Subjects randomized	255	255	256	410	409	411
PASI 75 response	8 (3%)	171 (67%)	170 (66%)	15 (4%)	273 (67%)	311 (76%)
PGA of Cleared or Minimal	10 (4%)	151 (59%)	156 (61%)	18 (4%)	277 (68%)	300 (73%)

Examination of age, gender, and race subgroups did not identify differences in response to STELARA® among these subgroups.

In subjects who weighed 100 kg or less, response rates were similar with both the 45 mg and 90 mg doses; however, in subjects who weighed greater than 100 kg, higher response rates were seen with 90 mg dosing compared with 45 mg dosing (Table 6 below).

Table 6: Clinical Outcomes by Weight Ps STUDY 1 and Ps STUDY 2

	Ps STUDY 1			**Ps STUDY 2**		
		STELARA®			**STELARA®**	
	Placebo	**45 mg**	**90 mg**	**Placebo**	**45 mg**	**90 mg**
Subjects randomized	**255**	**255**	**256**	**410**	**409**	**411**
PASI 75 response at Week 12*						
≤100 kg	4%	74%	65%	4%	73%	78%
	6/166	124/168	107/164	12/290	218/297	225/289
>100 kg	2%	54%	68%	3%	49%	71%
	2/89	47/87	63/92	3/120	55/112	86/121
PGA of Cleared or Minimal at Week 12*						

* Patients were dosed with study medication at Weeks 0 and 4.

	Ps STUDY 1			Ps STUDY 2		
		STELARA®			STELARA®	
	Placebo	45 mg	90 mg	Placebo	45 mg	90 mg
≤100 kg	4%	64%	63%	5%	74%	75%
	7/166	108/168	103/164	14/290	220/297	216/289
>100 kg	3%	49%	58%	3%	51%	69%
	3/89	43/87	53/92	4/120	57/112	84/121

* Patients were dosed with study medication at Weeks 0 and 4.

Subjects in Ps STUDY 1 who were PASI 75 responders at both Weeks 28 and 40 were re-randomized at Week 40 to either continued dosing of STELARA® (STELARA® at Week 40) or to withdrawal of therapy (placebo at Week 40). At Week 52, 89% (144/162) of subjects re-randomized to STELARA® treatment were PASI 75 responders compared with 63% (100/159) of subjects re-randomized to placebo (treatment withdrawal after Week 28 dose). The median time to loss of PASI 75 response among the subjects randomized to treatment withdrawal was 16 weeks.

14.2 Psoriatic Arthritis

The safety and efficacy of STELARA® was assessed in 927 patients (PsA STUDY 1, n=615; PsA STUDY 2, n=312), in two randomized, double-blind, placebo-controlled studies in adult patients 18 years of age and older with active PsA (≥5 swollen joints and ≥5 tender joints) despite non-steroidal anti-inflammatory (NSAID) or disease modifying antirheumatic (DMARD) therapy. Patients in these studies had a diagnosis of PsA for at least 6 months. Patients with each subtype of PsA were enrolled, including polyarticular arthritis with the absence of rheumatoid nodules (39%), spondylitis with peripheral arthritis (28%), asymmetric peripheral arthritis (21%), distal interphalangeal involvement (12%) and arthritis mutilans (0.5%). Over 70% and 40% of the patients, respectively, had enthesitis and dactylitis at baseline.

Patients were randomized to receive treatment with STELARA® 45 mg, 90 mg, or placebo subcutaneously at Weeks 0 and 4 followed by every 12 weeks (q12w) dosing. Approximately 50% of patients continued on stable doses of MTX (≤25 mg/week). The primary endpoint was the percentage of patients achieving ACR 20 response at Week 24.

In PsA STUDY 1 and PsA STUDY 2, 80% and 86% of the patients, respectively, had been previously treated with DMARDs. In PsA STUDY 1, previous treatment with anti-tumor necrosis factor (TNF)-α agent was not allowed. In PsA STUDY 2, 58% (n=180) of the patients had been previously treated with TNF blocker, of whom over 70% had discontinued their TNF blocker treatment for lack of efficacy or intolerance at any time.

Clinical Response

In both studies, a greater proportion of patients achieved ACR 20, ACR 50 and PASI 75 response in the STELARA® 45 mg and 90 mg groups compared to placebo at Week 24 (see Table 7). ACR 70 responses were also higher in the STELARA® 45 mg and 90 mg groups, although the difference was only numerical (p=NS) in STUDY 2. Responses were similar in patients regardless of prior TNFα exposure.

Table 7: ACR 20, ACR 50, ACR 70 and PASI 75 responses in PsA STUDY 1 and PsA STUDY 2 at Week 24

	PsA STUDY 1			PsA STUDY 2		
		STELARA®			STELARA®	
	Placebo	45 mg	90 mg	Placebo	45 mg	90 mg
Number of patients	**206**	**205**	**204**	**104**	**103**	**105**

* Number of patients with ≥ 3% BSA psoriasis skin involvement at baseline

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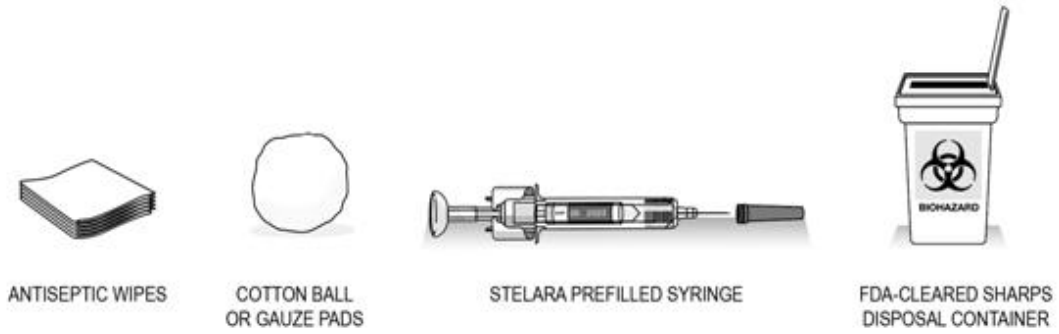
	PsA STUDY 1			PsA STUDY 2		
		STELARA®			STELARA®	
	Placebo	45 mg	90 mg	Placebo	45 mg	90 mg
randomized						
ACR 20 response, N (%)	47 (23%)	87 (42%)	101 (50%)	21 (20%)	45 (44%)	46 (44%)
ACR 50 response, N (%)	18 (9%)	51 (25%)	57 (28%)	7 (7%)	18 (17%)	24 (23%)
ACR 70 response, N (%)	5 (2%)	25 (12%)	29 (14%)	3 (3%)	7 (7%)	9 (9%)
*Number of patients with ≥ 3% BSA**	146	145	149	80	80	81
PASI 75 response, N (%)	16 (11%)	83 (57%)	93 (62%)	4 (5%)	41 (51%)	45 (56%)

* Number of patients with ≥ 3% BSA psoriasis skin involvement at baseline

The percent of patients achieving ACR 20 responses by visit is shown in Figure 1.

Figure 1: Percent of patients achieving ACR 20 response through Week 24

PsA STUDY 1



The results of the components of the ACR response criteria are shown in Table 8.

Table 8: Mean change from baseline in ACR components at Week 24

	PsA STUDY 1		
		STELARA®	
	Placebo (N=206)	45 mg (N= 205)	90 mg (N= 204)
Number of swollen joints*			
Baseline	15	12	13
Mean Change at Week 24	-3	-5	-6

* Number of swollen joints counted (0–66)

† Number of tender joints counted (0–68)

‡ Visual analogue scale; 0= best, 10=worst.

§ Disability Index of the Health Assessment Questionnaire; 0 = best, 3 = worst, measures the patient's ability to perform the following: dress/groom, arise, eat, walk, reach, grip, maintain hygiene, and maintain daily activity.

¶ CRP: (Normal Range 0.0–1.0 mg/dL)

	PsA STUDY 1		
		STELARA®	
	Placebo (N=206)	45 mg (N= 205)	90 mg (N= 204)
Number of tender joints †			
Baseline	25	22	23
Mean Change at Week 24	-4	-8	-9
Patient's assessment of pain‡			
Baseline	6.1	6.2	6.6
Mean Change at Week 24	-0.5	-2.0	-2.6
Patient global assessment‡			
Baseline	6.1	6.3	6.4
Mean Change at Week 24	-0.5	-2.0	-2.5
Physician global assessment‡			
Baseline	5.8	5.7	6.1
Mean Change at Week 24	-1.4	-2.6	-3.1
Disability index (HAQ)§			
Baseline	1.2	1.2	1.2
Mean Change at Week 24	-0.1	-0.3	-0.4
CRP (mg/dL)¶			
Baseline	1.6	1.7	1.8
Mean Change at Week 24	0.01	-0.5	-0.8

* Number of swollen joints counted (0–66)

† Number of tender joints counted (0–68)

‡ Visual analogue scale; 0= best, 10=worst.

§ Disability Index of the Health Assessment Questionnaire; 0 = best, 3 = worst, measures the patient's ability to perform the following: dress/groom, arise, eat, walk, reach, grip, maintain hygiene, and maintain daily activity.

¶ CRP: (Normal Range 0.0–1.0 mg/dL)

An improvement in enthesitis and dactylitis scores was observed in each STELARA® group compared with placebo at Week 24.

Physical Function

STELARA® treated patients showed improvement in physical function compared to patients treated with placebo as assessed by HAQ-DI at Week 24. In both studies, the proportion of HAQ-DI responders (≥0.3 improvement in HAQ-DI score) was greater in the STELARA® 45 mg and 90 mg groups compared to placebo at Week 24.

14.3 Crohn's Disease

STELARA® was evaluated in three randomized, double-blind, placebo-controlled clinical studies in adult patients with moderately to severely active Crohn's disease (Crohn's Disease Activity Index [CDAI] score of 220 to 450). There were two 8-week intravenous induction studies (CD-1 and CD-2) followed by a 44-week subcutaneous randomized withdrawal maintenance study (CD-3) representing 52 weeks of therapy.

Studies CD-1 and CD-2

In studies CD-1 and CD-2, 1409 patients were randomized, of whom 1368 (CD-1, n=741; CD-2, n=627) were included in the final efficacy analysis. Induction of clinical response (defined as a reduction in CDAI

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score of greater than or equal to 100 points or CDAI score of less than 150) at Week 6 and clinical remission (defined as a CDAI score of less than 150) at Week 8 were evaluated. In both studies, patients were randomized to receive a single intravenous administration of STELARA® at either approximately 6 mg/kg, placebo (see Table 1), or 130 mg (a lower dose than recommended).

In Study CD-1, patients had failed or were intolerant to prior treatment with a TNF blocker: 29% patients had an inadequate initial response (primary non-responders), 69% responded but subsequently lost response (secondary non-responders) and 36% were intolerant to a TNF blocker. Of these patients, 48% failed or were intolerant to one TNF blocker and 52% had failed 2 or 3 prior TNF blockers. At baseline and throughout the study, approximately 46% of the patients were receiving corticosteroids and 31% of the patients were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The median baseline CDAI score was 319 in the STELARA® approximately 6 mg/kg group and 313 in the placebo group.

In Study CD-2, patients had failed or were intolerant to prior treatment with corticosteroids (81% of patients), at least one immunomodulator (6-mercaptopurine, azathioprine, methotrexate; 68% of patients), or both (49% of patients). Additionally, 69% never received a TNF blocker and 31% previously received but had not failed a TNF blocker. At baseline, and throughout the study, approximately 39% of the patients were receiving corticosteroids and 35% of the patients were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The median baseline CDAI score was 286 in the STELARA® and 290 in the placebo group.

In these induction studies, a greater proportion of patients treated with STELARA® achieved clinical response at Week 6 and clinical remission at Week 8 compared to placebo (see Table 9 for clinical response and remission rates). Clinical response and remission were significant as early as Week 3 in STELARA® treated patients and continued to improve through Week 8.

Table 9: Induction of Clinical Response and Remission in CD-1* and CD-2†

	CD-1 n=741			CD-2 n=627		
	Placebo N=247	**STELARA®‡ N=249**	**Treatment difference and 95% CI**	**Placebo N=209**	**STELARA®‡ N=209**	**Treatment difference and 95% CI**
Clinical Response (100 point), Week 6	53 (21%)	84 (34%)§	12% (4%, 20%)	60 (29%)	116 (56%)¶	27% (18%, 36%)
Clinical Remission, Week 8	18 (7%)	52 (21%)¶	14% (8%, 20%)	41 (20%)	84 (40%)¶	21% (12%, 29%)
Clinical Response (100 point), Week 8	50 (20%)	94 (38%)¶	18% (10%, 25%)	67 (32%)	121 (58%)¶	26% (17%, 35%)

Clinical remission is defined as CDAI score < 150; Clinical response is defined as reduction in CDAI score by at least 100 points or being in clinical remission:

70 point response is defined as reduction in CDAI score by at least 70 points

* Patient population consisted of patients who failed or were intolerant to TNF blocker therapy

† Patient population consisted of patients who failed or were intolerant to corticosteroids or immunomodulators (e.g., 6-mercaptopurine, azathioprine, methotrexate) and previously received but not failed a TNF blocker or were never treated with a TNF blocker.

‡ Infusion dose of STELARA® using the weight-based dosage regimen specified in Table 1.

§ $0.001 \leq p < 0.01$

¶ $p < 0.001$

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	CD-1 n=741			CD-2 n=627		
	Placebo N=247	STELARA®‡ N=249	Treatment difference and 95% CI	Placebo N=209	STELARA®‡ N=209	Treatment difference and 95% CI
70 Point Response, Week 6	75 (30%)	109 (44%)§	13% (5%, 22%)	81 (39%)	135 (65%)¶	26% (17%, 35%)
70 Point Response, Week 3	67 (27%)	101 (41%)§	13% (5%, 22%)	66 (32%)	106 (51%)¶	19% (10%, 28%)

Clinical remission is defined as CDAI score < 150; Clinical response is defined as reduction in CDAI score by at least 100 points or being in clinical remission:

70 point response is defined as reduction in CDAI score by at least 70 points

* Patient population consisted of patients who failed or were intolerant to TNF blocker therapy

† Patient population consisted of patients who failed or were intolerant to corticosteroids or immunomodulators (e.g., 6-mercaptopurine, azathioprine, methotrexate) and previously received but not failed a TNF blocker or were never treated with a TNF blocker.

‡ Infusion dose of STELARA® using the weight-based dosage regimen specified in Table 1.

§ $0.001 \leq p < 0.01$

¶ $p < 0.001$

Study CD-3

The maintenance study (CD-3), evaluated 388 patients who achieved clinical response (≥100 point reduction in CDAI score) at Week 8 of induction with STELARA® in studies CD-1 or CD-2. Patients were randomized to receive a subcutaneous maintenance regimen of either 90 mg STELARA® every 8 weeks or placebo for 44 weeks (see Table 10).

Table 10: Clinical Response and Remission in CD-3 (Week 44; 52 weeks from initiation of the induction dose)

	Placebo* N=131†	90 mg STELARA® every 8 weeks N=128†	Treatment difference and 95% CI
Clinical Remission	47 (36%)	68 (53%)‡	17% (5%, 29%)
Clinical Response	58 (44%)	76 (59%)§	15% (3%, 27%)

Clinical remission is defined as CDAI score < 150; Clinical response is defined as reduction in CDAI of at least 100 points or being in clinical remission

* The placebo group consisted of patients who were in response to STELARA® and were randomized to receive placebo at the start of maintenance therapy.

† Patients who achieved clinical response to STELARA® at the end of the induction study.

‡ $p < 0.01$

§ $0.01 \leq p < 0.05$

¶ Patients in remission at the end of maintenance therapy who were in remission at the start of maintenance therapy. This does not account for any other time point during maintenance therapy.

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	Placebo* N=131†	90 mg STELARA® every 8 weeks N=128†	Treatment difference and 95% CI
Clinical Remission in patients in remission at the start of maintenance therapy¶	36/79 (46%)	52/78 (67%)‡	21% (6%, 36%)

Clinical remission is defined as CDAI score < 150; Clinical response is defined as reduction in CDAI of at least 100 points or being in clinical remission

* The placebo group consisted of patients who were in response to STELARA® and were randomized to receive placebo at the start of maintenance therapy.

† Patients who achieved clinical response to STELARA® at the end of the induction study.

‡ $p < 0.01$

§ $0.01 \leq p < 0.05$

¶ Patients in remission at the end of maintenance therapy who were in remission at the start of maintenance therapy. This does not account for any other time point during maintenance therapy.

At Week 44, 47% of patients who received STELARA® were corticosteroid-free and in clinical remission, compared to 30% of patients in the placebo group.

At Week 0 of Study CD-3, 34/56 (61%) STELARA® treated patients who previously failed or were intolerant to TNF blocker therapies were in clinical remission and 23/56 (41%) of these patients were in clinical remission at Week 44. In the placebo arm, 27/61 (44%) patients were in clinical remission at Week 0 while 16/61 (26%) of these patients were in remission at Week 44.

At Week 0 of Study CD-3, 46/72 (64%) STELARA® treated patients who had previously failed immunomodulator therapy or corticosteroids (but not TNF blockers) were in clinical remission and 45/72 (63%) of these patients were in clinical remission at Week 44. In the placebo arm, 50/70 (71%) of these patients were in clinical remission at Week 0 while 31/70 (44%) were in remission at Week 44. In the subset of these patients who were also naïve to TNF blockers, 34/52 (65%) of STELARA® treated patients were in clinical remission at Week 44 as compared to 25/51 (49%) in the placebo arm.

Patients who were not in clinical response 8 weeks after STELARA® induction were not included in the primary efficacy analyses for Study CD-3; however, these patients were eligible to receive a 90 mg subcutaneous injection of STELARA® upon entry into Study CD-3. Of these patients, 102/219 (47%) achieved clinical response eight weeks later and were followed for the duration of the study.

15 REFERENCES

[1] Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 6.6.2 Regs Research Data, Nov 2009 Sub (1973–2007) - Linked To County Attributes - Total U.S., 1969–2007 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2010, based on the November 2009 submission.

16 HOW SUPPLIED/STORAGE AND HANDLING

STELARA® (ustekinumab) Injection is a sterile, preservative-free, colorless to slightly yellow solution. STELARA® is available in single-dose prefilled syringes containing 45 mg or 90 mg or single-dose vials

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containing 45 mg of ustekinumab for subcutaneous use. Each prefilled syringe is equipped with a 27 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that contains dry natural rubber.

STELARA® is also available in single-dose vials containing 130 mg ustekinumab for intravenous use.

Subcutaneous Use	**NDC**
45 mg/0.5 mL single-dose prefilled syringe	57894-060-03
90 mg/mL single-dose prefilled syringe	57894-061-03
45 mg/0.5 mL single-dose vial	57894-060-02
Intravenous Infusion	**NDC**
130 mg/26 mL (5 mg/mL) single-dose vial	57894-054-27

Storage and Stability

STELARA® vials and prefilled syringes must be refrigerated at 2°C to 8°C (36°F to 46°F). Store STELARA® vials upright. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use)

Infections

Inform patients that STELARA® may lower the ability of their immune system to fight infections and to contact their healthcare provider immediately if they develop any signs or symptoms of infection *[see Warnings and Precautions (5.1)]*.

Malignancies

Inform patients of the risk of developing malignancies while receiving STELARA® *[see Warnings and Precautions (5.4)]*.

Hypersensitivity Reactions

- Advise patients to seek immediate medical attention if they experience any signs or symptoms of serious hypersensitivity reactions and discontinue STELARA® *[see Warnings and Precautions (5.5)]*.
- Inform patients the needle cover on the prefilled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions in individuals sensitive to latex *[see Dosage and Administration (2.4)]*

Immunizations

Inform patients that STELARA® can interfere with the usual response to immunizations and that they should avoid live vaccines *[see Warnings and Precautions (5.7)]*.

Pregnancy Registry

Inform patients that there is a pregnancy registry to monitor fetal outcomes of pregnant women exposed to STELARA® *[see Use in Specific Populations (8.1)]*.

Administration

Instruct patients to follow sharps disposal recommendations, as described in the Instructions for Use.

Prefilled Syringe Manufactured by: Janssen Biotech, Inc., Horsham, PA 19044, US License No. 1864 at Baxter Pharmaceutical Solutions, Bloomington, IN 47403 and at Cilag AG, Schaffhausen, Switzerland

Vial Manufactured by: Janssen Biotech, Inc., Horsham, PA 19044, US License No. 1864 at Cilag AG, Schaffhausen, Switzerland

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MEDICATION GUIDE
STELARA (stel ar' a)
(ustekinumab)
injection, for subcutaneous or intravenous use

What is the most important information I should know about STELARA?
STELARA is a medicine that affects your immune system. STELARA can increase your risk of having serious side effects, including:
Serious infections: STELARA may lower the ability of your immune system to fight infections and may increase your risk of infections. Some people have serious infections while taking STELARA, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses. Some people have to be hospitalized for treatment of their infection.

- Your doctor should check you for TB before starting STELARA.
- If your doctor feels that you are at risk for TB, you may be treated with medicine for TB before you begin treatment with STELARA and during treatment with STELARA.
- Your doctor should watch you closely for signs and symptoms of TB 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, sweat, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in 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 with 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. These infections 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 cancers. Tell your doctor if you have ever had any type of cancer. Some people who are receiving STELARA and have risk factors for skin cancer have developed certain types of skin cancers. During your treatment with STELARA, tell your doctor if you develop 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
- vision problems

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What is STELARA?
STELARA is a prescription medicine used to treat adults 18 years and older with:

- moderate or severe 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).
- active psoriatic arthritis. STELARA can be used alone or with methotrexate.
- moderately to severely active Crohn's disease in people who have already taken other medicine that did not work well enough or they could not tolerate it.

STELARA may improve your psoriasis, psoriatic arthritis or Crohn's disease, but may also lower the ability of your immune system to fight infections. Taking STELARA may also increase your risk for certain types of cancer.
It is not known if STELARA is safe and effective in children.

Do not take STELARA if you are allergic to ustekinumab or any of the ingredients in STELARA. See the end of this Medication Guide for a complete list of ingredients in STELARA.

Before you receive STELARA, tell your doctor if you:

- have any of the conditions or symptoms listed in the section "**What is the most important information I should know about STELARA**?"
- ever had an allergic reaction to STELARA. 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. Allergy shots may not work as well for you during treatment with STELARA. STELARA may also increase your risk of having an allergic reaction to an allergy shot.
- receive or have received phototherapy for your psoriasis.
- have any other medical conditions.
- are pregnant or planning to become pregnant. It is not known if STELARA can harm your unborn baby. You and your doctor should decide if you will take STELARA. There is a pregnancy registry for women who take STELARA during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. If you are pregnant or become pregnant while taking STELARA, talk to your doctor about how you can join this pregnancy registry or you may contact the registry at 1-877-311-8972 to enroll.
- are breastfeeding or plan to breastfeed. It is thought that STELARA passes into your breast milk in small amounts.
- 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.

How should I use STELARA?

- Use STELARA exactly as prescribed by your doctor.
- **The needle cover on the STELARA prefilled syringe contains latex. Do not handle the needle cover if you are sensitive to latex.**

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- Adults with Crohn's disease will receive the first dose of STELARA through a vein in the arm (intravenous infusion) in a healthcare facility by a healthcare provider. It takes at least 1 hour to receive the full dose of medicine. You will then receive STELARA as an injection under the skin (subcutaneous injection) 8 weeks after the first dose of STELARA, as described below.
- Adults with psoriasis or psoriatic arthritis will receive STELARA as an injection under the skin (subcutaneous injection) as described below.
- **Injecting STELARA under your skin**
  - 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 have been shown how to inject STELARA by your doctor or nurse.
  - Inject STELARA under the skin (subcutaneous injection) in your upper arms, buttocks, upper legs (thighs) or stomach area (abdomen).
  - Do not give an injection in an area of the skin that is tender, bruised, red or hard.
  - Use a different injection site each time you use STELARA.
  - If you inject more STELARA than prescribed, call your doctor right away.
  - Be sure to keep all of your scheduled follow-up appointments.
- **Read the detailed Instructions for Use at the end of this Medication Guide for instructions about how to prepare and inject a dose of STELARA, and how to properly throw away (dispose of) used needles and syringes.**

What should I avoid while using STELARA?
You should not receive a live vaccine while taking STELARA. See **"What should I tell my doctor before receiving STELARA?"**

What are the possible side effects of STELARA?
STELARA may cause serious side effects, including:

- See "**What is the most important information I should know about STELARA?**"
- **Serious allergic reactions.** Serious allergic reactions can occur with STELARA. Stop using STELARA and get medical help right away if you have any of the following symptoms of a serious allergic reaction:
  - feeling faint
  - swelling of your face, eyelids, tongue, or throat
  - chest tightness
  - skin rash

Common side effects of STELARA include:

- upper respiratory infections
- headache
- tiredness
- itching
- vomiting
- vaginal yeast infections
- urinary tract infections
- redness at the injection site

These are not all of the possible side effects of STELARA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
You may also report side effects to Janssen Biotech, Inc. at 1-800 JANSSEN (1-800-526-7736).

How should I store STELARA?

- Store STELARA prefilled syringes in a refrigerator between 36°F to 46°F (2°C to 8°C).
- Store STELARA in the original carton to protect it from light until time to use it.
- Do not freeze STELARA.
- Do not shake STELARA.

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Keep STELARA and all medicines out of the reach of children.

General information about the safe and effective use of STELARA.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use STELARA for a condition for which it was not prescribed. Do not give STELARA to other people, even if they have the same symptoms that you have. It may harm them.
You can ask your doctor or pharmacist for information about STELARA that was written for health professionals.

What are the ingredients in STELARA?
Active ingredient: ustekinumab
Inactive ingredients: single-dose prefilled syringe contains L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, and sucrose. **Single-dose vial** contains L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80 and sucrose.
Manufactured by: Janssen Biotech , Inc., Horsham, PA 19044, US License No. 1864
© 2016 Janssen Biotech, Inc.
For more information, go to *www.stelarainfo.com* or call 1-800-JANSSEN (1-800-526-7736).

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INSTRUCTIONS FOR USE
STELARA (stel ar' a**)**
(ustekinumab)
injection, for subcutaneous use

Instructions for injecting STELARA using a prefilled syringe.

Read this Instructions for Use before you start using STELARA. Your doctor or nurse should show you how to prepare and give your injection of STELARA the right way.

If you cannot give yourself the injection:
- ask your doctor or nurse to help you, or
- ask someone who has been trained by a doctor or nurse to give your injections.

Do not try to inject STELARA yourself until you have been shown how to inject STELARA by your doctor, nurse or health professional.

Important information:
- Before you start, check the carton to make sure that it is the right dose. You will have either 45 mg or 90 mg as prescribed by your doctor.
  - If your dose is 45 mg, you will receive one 45 mg prefilled syringe.
  - If your dose is 90 mg, you will receive either one 90 mg prefilled syringe or two 45 mg prefilled syringes. **If you receive two 45 mg prefilled syringes for a 90 mg dose, you will need to give yourself two injections, one right after the other.**
- Check the expiration date on the pre-filled syringe and carton. If the expiration date has passed, do not use it. If the expiration date has passed call your doctor or pharmacist, or call 1-800-JANSSEN (1-800-526-7736) for help.
- Make sure the syringe is not damaged.
- **The needle cover on the prefilled syringe contains latex. Do not handle the needle cover on the STELARA prefilled syringe if you are sensitive to latex.**
- Check your prefilled syringe for any particles or discoloration. Your prefilled syringe should look clear and colorless to light yellow with few white particles.
- Do not use if it is frozen, discolored, cloudy or has large particles. Get a new prefilled syringe.
- **Do not shake the prefilled syringe at any time.** Shaking your prefilled syringe may damage your STELARA medicine. If your prefilled syringe has been shaken, do not use it. Get a new prefilled syringe.
- To reduce the risk of accidental needle sticks, each prefilled syringe has a needle guard that is automatically activated to cover the needle after you have given your injection. Do not pull back on the

plunger at any time.

Gather the supplies you will need to prepare and to give your injection. (See Figure A)

You will need:

- antiseptic wipes
- cotton balls or gauze pads
- adhesive bandage
- your prescribed dose of STELARA **(See Figure B)**
- FDA-cleared sharps disposal container. **See "Step 4: Dispose of the syringe."**

Figure A

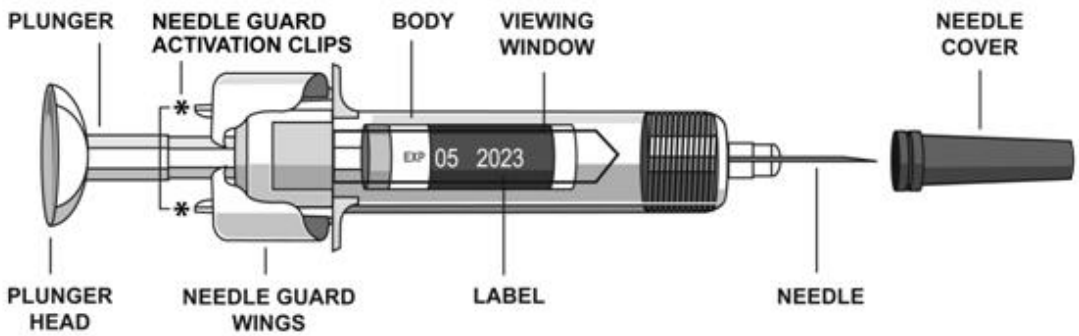
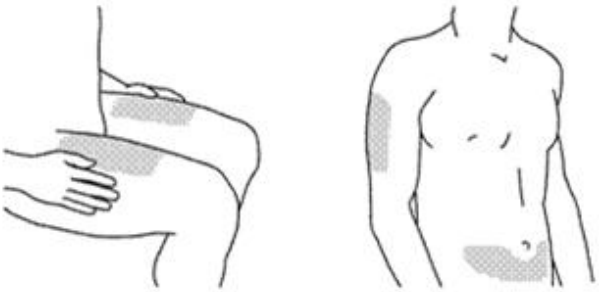


Figure B



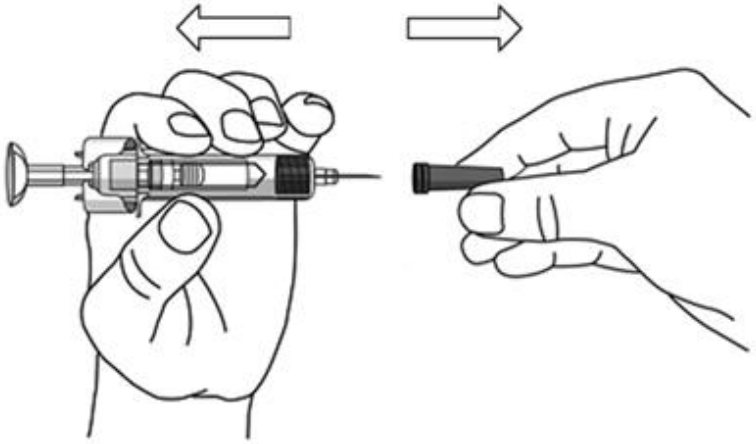
Step 1: Prepare the injection.

- Choose a well lit, clean, flat work surface.
- Wash your hands well with soap and warm water.
- Hold the prefilled syringe with the covered needle pointing upward.

Step 2: Prepare your injection site

- Choose an injection site around your stomach area (abdomen), buttocks, upper legs (thighs). If a caregiver is giving you the injection, the outer area of the upper arms may also be used. **(See Figure C)**
- **Use a different injection site for each injection. Do not** give an injection in an area of the skin that is tender, bruised, red or hard.
- Clean the skin with an antiseptic wipe where you plan to give your injection.
- **Do not** touch this area again before giving the injection. Let your skin dry before injecting.
- **Do not** fan or blow on the clean area.

Figure C



*Areas in gray are recommended injection sites.

Step 3: Inject STELARA

- Remove the needle cover when you are ready to inject your STELARA.
- **Do not** touch the plunger while removing the needle cover.
- Hold the body of the prefilled syringe with one hand, and pull the needle cover straight off. **(see Figure D)**
- Put the needle cover in the trash.
- You may also see a drop of liquid at the end of the needle. This is normal.
- **Do not** touch the needle or let it touch anything.
- **Do not** use the prefilled syringe if it is dropped without the needle cover in place. Call your doctor, nurse or health professional for instructions.

Figure D

- Hold the body of the prefilled syringe in one hand between the thumb and index fingers. **(See Figure E)**

Figure E

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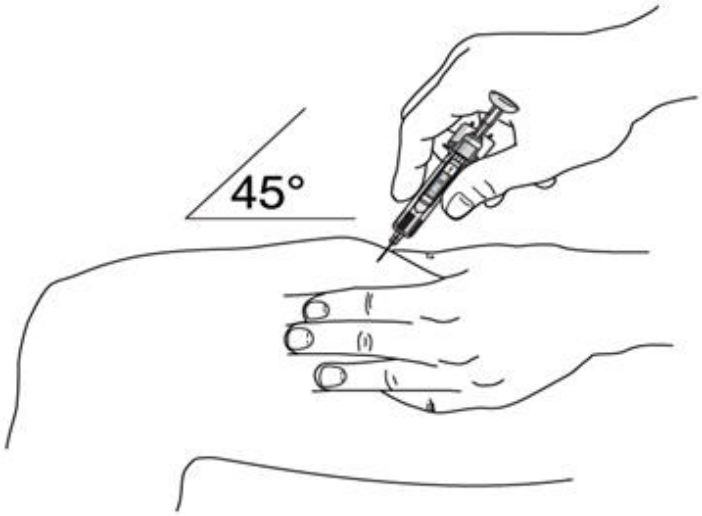
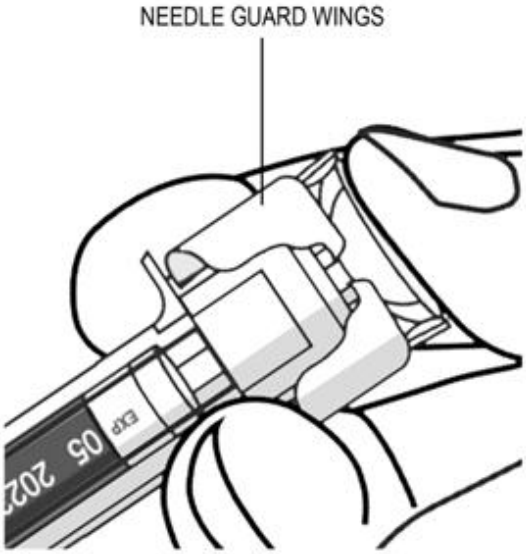


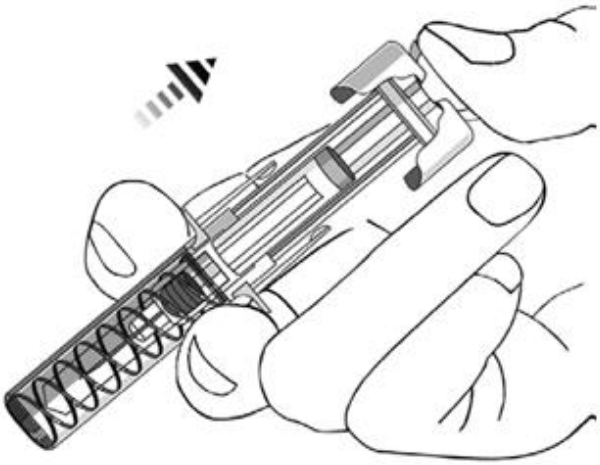
- **Do not** pull back on the plunger at any time.
- Use the other hand to gently pinch the cleaned area of skin. Hold firmly.
- Use a quick, dart-like motion to insert the needle into the pinched skin at about a 45-degree angle. **(See Figure F)**

Figure F



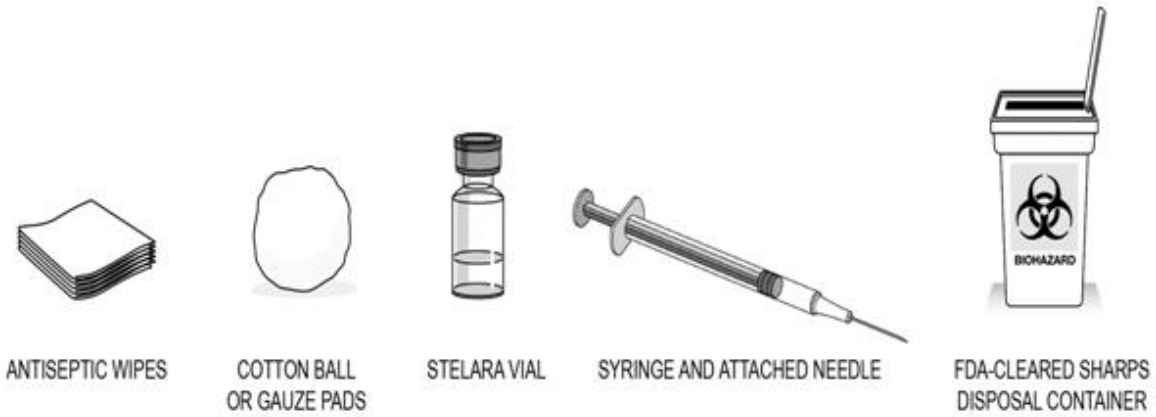
- Inject all of the liquid by using your thumb to push in the plunger until the plunger head is completely between the needle guard wings. **(See Figure G)**

Figure G



- When the plunger is pushed as far as it will go, keep pressure on the plunger head. Take the needle out of the skin and let go of the skin.
- Slowly take your thumb off the plunger head. This will let the empty syringe move up until the entire needle is covered by the needle guard. **(See Figure H)**

Figure H



- When the needle is pulled out of your skin, there may be a little bleeding at the injection site. This is normal. You can press a cotton ball or gauze pad to the injection site if needed. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if necessary.

Step 4: Dispose of the syringe.

- Put the syringe in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) loose syringes in your household trash.**
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of heavy-duty plastic.
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out.
  - upright and stable during use,
  - leak-resistant,
  - and properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be local or state laws about how to throw away syringes and needles. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your sharps disposal container.

- If you have any questions, talk to your doctor or pharmacist.

Keep STELARA and all medicines out of the reach of children.

Prefilled Syringe Manufactured by:
Janssen Biotech, Inc., Horsham, PA 19044, US License No. 1864 at Baxter Pharmaceutical Solutions, Bloomington, IN 47403 and at Cilag AG, Schaffhausen, Switzerland

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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PRINCIPAL DISPLAY PANEL - 45 mg/0.5 mL Vial Carton

Single use vial–
Discard unused portion

NDC 57894-060-02

Stelara®
(ustekinumab)

Injection

45 mg/0.5 mL

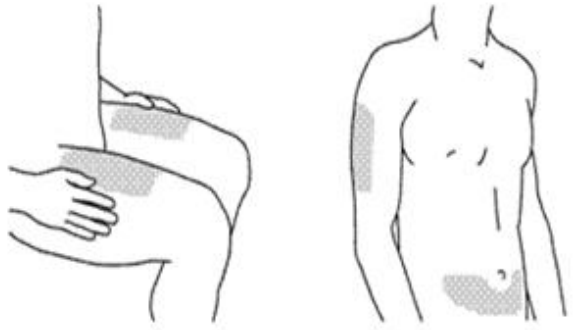
For subcutaneous use

Each vial contains 0.5 mL

Information for use and dosage–
See package insert

Rx only

ATTENTION: Dispense the enclosed Medication Guide to each patient.



PRINCIPAL DISPLAY PANEL - 90 mg/mL Syringe Carton

Stelara®
(ustekinumab)

Injection

90 mg/mL

For subcutaneous use

NDC 57894-061-03

Contains one 90 mg/mL syringe

Single dose prefilled syringe –
Discard unused portion

See package insert for dosing information

Rx only

ATTENTION: Dispense the enclosed Medication Guide to each patient.

PRINCIPAL DISPLAY PANEL - 130 mg/26 mL Vial Carton

NDC 57894-054-27

Single-Dose vial
Discard unused portion

Stelara®
(ustekinumab)
Injection

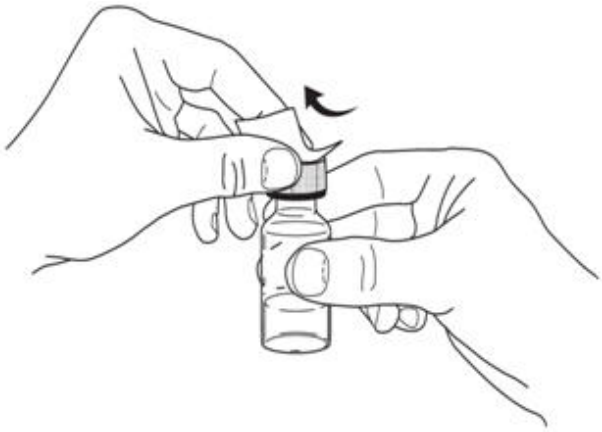
130 mg/26 mL
(5 mg/mL)

For Intravenous Infusion Only
Must be diluted

ATTENTION: Dispense the enclosed Medication Guide to each patient.

Rx only

janssen



STELARA

ustekinumab injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:57894-060
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ustekinumab (UNII: FU77B4U5Z0) (ustekinumab - UNII:FU77B4U5Z0)	ustekinumab	45 mg in 0.5 mL

Inactive Ingredients

Ingredient Name	Strength
sucrose (UNII: C151H8M554)	38 mg in 0.5 mL
polysorbate 80 (UNII: 6OZP39ZG8H)	0.02 mg in 0.5 mL
HISTIDINE (UNII: 4QD397987E)	0.5 mg in 0.5 mL
HISTIDINE MONOHYDROCHLORIDE MONOHYDRATE (UNII: X573657P6P)	
water (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:57894-060-02	1 in 1 CARTON	09/25/2009	
1		0.5 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product		
2	NDC:57894-060-03	1 in 1 CARTON	09/25/2009	
2		0.5 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		
3	NDC:57894-060-04	1 in 1 CARTON	09/25/2009	
3		0.5 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		

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Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125261	09/25/2009	

STELARA

ustekinumab injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:57894-061
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ustekinumab (UNII: FU77B4U5Z0) (ustekinumab - UNII:FU77B4U5Z0)	ustekinumab	90 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
sucrose (UNII: C151H8M554)	76 mg in 1 mL
polysorbate 80 (UNII: 6OZP39ZG8H)	0.04 mg in 1 mL
HISTIDINE (UNII: 4QD397987E)	1 mg in 1 mL
HISTIDINE MONOHYDROCHLORIDE MONOHYDRATE (UNII: X573657P6P)	
water (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:57894-061-02	1 in 1 CARTON	09/25/2009	
1		1 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product		
2	NDC:57894-061-03	1 in 1 CARTON	09/25/2009	
2		1 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		
3	NDC:57894-061-04	1 in 1 CARTON	09/25/2009	
3		1 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125261	09/25/2009	

STELARA
ustekinumab solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:57894-054
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ustekinumab (UNII: FU77B4U5Z0) (ustekinumab - UNII:FU77B4U5Z0)	ustekinumab	130 mg in 26 mL

Inactive Ingredients

Ingredient Name	Strength
Edetate Disodium (UNII: 7FLD91C86K)	0.52 mg in 26 mL
Histidine (UNII: 4QD397987E)	20 mg in 26 mL
Histidine Monohydrochloride Monohydrate (UNII: X573657P6P)	27 mg in 26 mL
Methionine (UNII: AE28F7PNPL)	10.4 mg in 26 mL
Polysorbate 80 (UNII: 6OZP39ZG8H)	10.4 mg in 26 mL
Sucrose (UNII: C151H8M554)	2210 mg in 26 mL

Product Characteristics

Color	YELLOW (colorless to slightly yellow)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:57894-054-27	1 in 1 BOX	09/23/2016	
1		26 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761044	09/23/2016	

Labeler - Janssen Biotech, Inc. (099091753)

Establishment

Name	Address	ID/FEI	Business Operations
Patheon Biologics LLC		965750420	API MANUFACTURE(57894-060, 57894-061) , ANALYSIS(57894-060, 57894-061)

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Establishment

Name	Address	ID/FEI	Business Operations
Cilag AG		483237103	MANUFACTURE(57894-060, 57894-061, 57894-054) , ANALYSIS(57894-060, 57894-061, 57894-054)

Establishment

Name	Address	ID/FEI	Business Operations
Janssen Biologics B.V.		409612918	ANALYSIS(57894-060, 57894-061, 57894-054) , API MANUFACTURE(57894-054)

Establishment

Name	Address	ID/FEI	Business Operations
Baxter Pharmaceutical Solutions		604719430	MANUFACTURE(57894-060, 57894-061)

Establishment

Name	Address	ID/FEI	Business Operations
Janssen Biologics (Ireland)		987061921	API MANUFACTURE(57894-060, 57894-061, 57894-054) , ANALYSIS(57894-060, 57894-061, 57894-054)

Establishment

Name	Address	ID/FEI	Business Operations
PPD Development Ireland Ltd.		985036175	ANALYSIS(57894-054)

Revised: 9/2016 Janssen Biotech, Inc.

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