PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]**Jamteki™**

(ustekinumab injection)

Solution for Subcutaneous Injection, 45 mg/0.5 mL and 90 mg/mL

Selective Immunomodulating Agent

JAMP Pharma Corporation

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Boucherville, Quebec

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Date of Initial Authorization:
November 9, 2023

Submission Control Number: 268742

RECENT MAJOR LABEL CHANGES

Not applicable.

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

Jamteki (ustekinumab injection) is a biosimilar biologic drug (biosimilar) to STELARA®. A biosimilar is a biologic drug that was granted authorization based on a demonstration of similarity to a version previously authorized in Canada, known as the reference biologic drug.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Indications have been granted on the basis of similarity between Jamteki and the reference biologic drug STELARA®.

Plaque Psoriasis

Jamteki (ustekinumab) is indicated in adult patients for the treatment of chronic moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Psoriatic Arthritis

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

1.1 Pediatrics

Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Evidence from clinical studies and experience suggests that use in the geriatric population is not associated with differences in safety or effectiveness (see 7.1.4 Geriatrics).

2 CONTRAINDICATIONS

- Patients with known hypersensitivity to ustekinumab or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- Patients with severe infections such as sepsis, tuberculosis and opportunistic infections (see 7 WARNINGS AND PRECAUTIONS, Infections).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Jamteki (ustekinumab) is intended for use under the guidance and supervision of a physician.

Subcutaneous Administration

Jamteki is supplied as 45 mg and 90 mg pre-filled syringes. A patient may self-inject with Jamteki if a physician determines that it is appropriate after proper training in subcutaneous injection technique and disposal (see PATIENT MEDICATION INFORMATION, How to use Jamteki).

Prior to subcutaneous administration, visually inspect the solution for particulate matter and discolouration. The product is colourless to slightly yellow and may contain a few small translucent or white particles of protein. This appearance is not unusual for proteinaceous solutions. The product

should not be used if solution is discoloured or cloudy, or if other particulate matter is present. Jamteki does not contain preservatives; therefore, any unused product remaining in syringe should not be used.

The needle cover on the pre-filled syringe is not made with natural rubber latex.

Patients should be instructed to inject the prescribed amount of Jamteki according to the directions provided in the PATIENT MEDICATION INFORMATION section (see Product Monograph, Part III: PATIENT MEDICATION INFORMATION).

4.2 Recommended Dose and Dosage Adjustment

Plaque Psoriasis

For the treatment of plaque psoriasis, Jamteki is administered by subcutaneous injection.

Adults

The recommended dose of Jamteki is 45 mg administered at Weeks 0 and 4, then every 12 weeks thereafter. Alternatively, 90 mg may be used in patients with a body weight greater than 100 kg. In patients weighing >100 kg, both 45 mg and 90 mg were shown to be efficacious. However, 90 mg was efficacious in a higher percentage of these patients than the 45 mg dose.

For patients who inadequately respond to dosing every 12 weeks, consideration may be given to treating as often as every 8 weeks.

Consideration should be given to discontinuing treatment in patients who have shown no response up to 12 weeks of treatment.

Re-treatment with a dosing regimen of Weeks 0 and 4 followed by 12-week dosing after interruption of therapy has been shown to be safe and effective (see 14.1 Clinical Trials - Reference Biologic Drug, Study Results, Efficacy of retreatment).

Psoriatic Arthritis - Adults

For the treatment of psoriatic arthritis, Jamteki is administered by subcutaneous injection. The recommended dose of Jamteki is 45 mg administered at Weeks 0 and 4, then every 12 weeks thereafter. Alternatively, 90 mg may be used in patients with a body weight greater than 100 kg.

Health Canada has not authorized an indication for pediatric use.

4.4 Administration

JAMP Care has been established to facilitate the administration of Jamteki. JAMP Care is staffed by qualified health professionals specially trained in the administration of Jamteki. JAMP Care is available across Canada.

Information about the JAMP Care can be obtained by calling 1-855-310-5102.

4.5 Missed Dose

Patients who miss their scheduled dose of Jamteki should be advised to contact their health professional for guidance.

5 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 (see 16 NON-CLINICAL TOXICOLOGY).

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous Injection	Sterile solution in single-use pre-filled syringe: 45 mg/0.5 mL, 90 mg/mL	L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose, and water for injection. Jamteki does not contain preservatives.

Jamteki: 45 mg or 90 mg Pre-filled Syringe

Jamteki is supplied as a single-use, sterile solution for subcutaneous injection in a Type 1 glass syringe with a fixed 29G, half-inch needle equipped with a passive safety device and a needle cover. The needle cover on the pre-filled syringe is not made with natural rubber latex.

The solution is clear to colourless to slightly yellow practically free from particles with a pH of 5.5 to 6.5. Each mL of Jamteki contains 90 mg of ustekinumab, and the following inactive ingredients: L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose, and water for injection. Jamteki does not contain preservatives.

There are two strengths of Jamteki available: 45 mg of ustekinumab in 0.5 mL and 90 mg of ustekinumab in 1.0 mL.

Jamteki is available in single unit packaging presentations.

Description

Ustekinumab is a fully human IgG1κ monoclonal antibody with an approximate molecular weight of 148,079 to 149,690 Daltons. Ustekinumab is produced by a recombinant cell line cultured by continuous perfusion and is purified by a series of steps that includes measures to inactivate and remove viruses.

7 WARNINGS AND PRECAUTIONS

General

Infections

Ustekinumab is a selective immunomodulator and may have the potential to increase the risk of infections and reactivate latent infections.

Jamteki should not be given to patients with any clinically important active infection. If a patient develops a serious infection they should be closely monitored and Jamteki should not be administered until the infection resolves or is adequately treated. Caution should be exercised when considering the use of Jamteki in patients with a chronic infection or a history of recurrent infection. Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur.

Prior to initiating treatment with Jamteki, patients should be evaluated for tuberculosis infection. Jamteki should not be given to patients with active tuberculosis. Treatment of latent tuberculosis infection should be initiated prior to administering Jamteki Anti-tuberculosis therapy should also be considered prior to initiation of Jamteki in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed. In clinical studies, patients with latent tuberculosis who were concurrently treated with isoniazid did not develop tuberculosis. Patients receiving Jamteki should be monitored closely for signs and symptoms of active tuberculosis during and after treatment.

In clinical studies, serious bacterial, fungal, and viral infections were observed in subjects receiving ustekinumab. Serious infections requiring hospitalization occurred in the clinical development programs. In the psoriasis and psoriatic arthritis programs serious infections included diverticulitis, cellulitis, pneumonia, appendicitis, cholecystitis and sepsis. Other clinically important infections included listeria meningitis and ophthalmic herpes which were reported in one patient each (see 8 ADVERSE REACTIONS).

Carcinogenesis and Mutagenesis

Malignancies

Ustekinumab is a selective immunomodulator. Immunomodulating agents have the potential to increase the risk of malignancy. Some patients who received ustekinumab in clinical studies developed malignancies (see 8 ADVERSE REACTIONS, Malignancies).

Ustekinumab injection has not been studied in patients with a history of malignancy. Caution should be exercised when considering the use of Jamteki in patients with a history of malignancy or when considering continuing treatment in patients who develop a malignancy.

All patients, in particular those greater than 60 years of age, those with a medical history of prolonged immunosuppressant therapy or those with a history of PUVA treatment, should be monitored for the appearance of skin cancer (see 8 ADVERSE REACTIONS).

Hepatic/Biliary/Pancreatic

Specific studies have not been conducted in patients with hepatic insufficiency.

Immune

Concomitant immunosuppressive therapy

In the Phase 3 psoriasis studies, the safety and efficacy of ustekinumab injection (ustekinumab) in combination with immunosuppressive agents or phototherapy have not been evaluated. In the Phase 3 psoriatic arthritis studies, concomitant methotrexate did not appear to influence the safety of ustekinumab injection. Caution should be exercised when considering concomitant use of immunosuppressive agents and Jamteki or when transitioning from other biologic agents (see 9 DRUG INTERACTIONS, Immunosuppressants).

Immunization

It is recommended that live viral or bacterial vaccines not be given concurrently with Jamteki (ustekinumab). No data are available on the secondary transmission of infection by live vaccines in patients receiving Jamteki. Caution is advised when administering some live vaccines to household contacts of patients receiving Jamteki because of the potential risk for shedding from the household contact and transmission to the patient. Patients receiving Jamteki may receive concurrent inactivated or non-live vaccinations (see 9 DRUG INTERACTIONS).

Prior to initiating therapy with Jamteki, patients should receive all immunizations appropriate for age as recommended by current immunization guidelines. Long term treatment with Jamteki does not appear to suppress the immune response to pneumococcal polysaccharide or tetanus vaccines polysaccharide or tetanus vaccines. During the long-term extension of a Phase 3 psoriasis study (PHOENIX 2), patients treated with Jamteki for at least 3.5 years mounted similar antibody responses to both pneumococcal polysaccharide and tetanus vaccines as a non-systemically treated psoriasis control group.

Similar proportions of patients developed protective levels of anti-pneumococcal and anti-tetanus antibodies and antibody titers were similar among ustekinumab-treated and control patients.

However, non-live vaccinations received during a course of Jamteki may not elicit an immune response sufficient to prevent disease.

Immunotherapy

Ustekinumab injection has not been evaluated in patients who have undergone allergy immunotherapy. Jamteki may affect allergy immunotherapy. Caution should be exercised in patients receiving or who have received allergy immunotherapy particularly for anaphylaxis.

Infant exposure *in utero*

For infants exposed *in utero* to ustekinumab, a six-month waiting period following birth is recommended before the administration of live vaccines. Administration of a live vaccine prior to 6 months of age may be considered if ustekinumab serum levels are undetectable in the infant, or the benefit of the vaccination clearly outweighs the risk of administration of live vaccines to the infant (see 7 WARNINGS AND PRECAUTIONS, Immune, Immunization).

Neurologic

Reversible Posterior Leukoencephalopathy Syndrome

One case of reversible posterior leukoencephalopathy syndrome (RPLS) was observed during the clinical development programs which included 6709 ustekinumab-treated subjects. The subject, who had received 12 doses of ustekinumab injection over approximately two and a half years, presented with headache, seizures and confusion in the setting of alcohol abuse. No additional ustekinumab injections were administered and the subject fully recovered with appropriate treatment.

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, acute hypertension, cytotoxic agents, immunosuppressive therapy and alcohol abuse. Fatal outcomes have been reported.

If RPLS is suspected, administer appropriate treatment and discontinue Jamteki.

Renal

Specific studies have not been conducted in patients with renal insufficiency.

Reproductive Health: Female and Male Potential

Women of Childbearing Potential: Women of childbearing potential initiating treatment with Jamteki should use effective methods of contraception and should receive preconception counselling before planning a pregnancy in accordance with disease specific clinical guidelines. Jamteki remains in the circulation for approximately 15 weeks after treatment. In clinical trials, women of childbearing potential were required to use effective methods of contraception during treatment and for at least 15 weeks after treatment (see also 7 WARNINGS AND PRECAUTIONS, Pregnant Women).

Sensitivity/Resistance

Hypersensitivity Reactions

Systemic

In post-marketing experience, serious allergic reactions, including anaphylaxis and angioedema, have been reported. If an anaphylactic or other serious allergic reaction occurs, institute appropriate therapy and discontinue administration of Jamteki (see 8 ADVERSE REACTIONS).

Respiratory

Cases of allergic alveolitis and eosinophilic pneumonia have been reported during post-approval use of ustekinumab. Clinical presentations included cough, dyspnoea, and interstitial infiltrates following one to three doses. Serious outcomes have included respiratory failure and prolonged hospitalisation. Improvement has been reported after discontinuation of ustekinumab and also, in some cases, administration of corticosteroids. If infection has been excluded and diagnosis is confirmed, discontinue ustekinumab and institute appropriate treatment.

7.1 Special Populations

7.1.1 Pregnant Women

There is no evidence from animal studies of teratogenicity, birth defects or developmental delays at dose levels up to approximately 45-fold higher than the highest equivalent dose intended to be administered to patients with psoriasis and psoriatic arthritis (see 7 WARNINGS AND PRECAUTIONS, 7.1.1 Pregnant Women; 16 NON-CLINICAL TOXICOLOGY, Reproductive Toxicology). However, animal reproductive and developmental studies are not always predictive of human response.

It is not known whether ustekinumab can cause fetal harm when administered to a pregnant woman or whether it can affect reproductive capacity. While it is known that human IgG antibodies, like ustekinumab, cross the placenta, no adequate and well-controlled studies have been conducted to evaluate if ustekinumab can cross the human placenta in pregnant women. In developmental toxicity studies in monkeys, ustekinumab was detected in fetal serum following repeated dosing of pregnant monkeys during the period of organogenesis. Although ustekinumab crossed the monkey placenta there was no evidence of teratogenicity in these studies. The decision to continue Jamteki during pregnancy should be carefully evaluated taking into consideration clinical practice guidelines to ensure the safety of the pregnant woman and the fetus. Jamteki should be given to a pregnant woman only if the benefit clearly outweighs the risk.

7.1.2 Breast-feeding

Limited data from published literature suggests that ustekinumab is excreted in human breast milk in small amounts and it is not known if ustekinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from ustekinumab, a decision should be made whether to discontinue nursing or to discontinue the drug.

7.1.3 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Geriatrics (> 65 years of age): Of the 6709 patients exposed to ustekinumab injection in clinical trials, a total of 353 were 65 years or older (including 183 patients with psoriasis and 69 patients with psoriatic arthritis). No major age-related differences in clearance or volume of distribution were observed in clinical studies. Although no overall differences in safety and efficacy were observed between older and younger patients in clinical studies in approved indications, the number of patients aged 65 and over is not sufficient to determine whether they respond differently from younger patients.

Patients over 60 years of age should be closely monitored for skin cancer (see 7 WARNINGS AND PRECAUTIONS, Carcinogenesis and Mutagenesis).

8 ADVERSE REACTIONS

The adverse drug reaction profiles reported in clinical studies that compared Jamteki to the reference biologic were comparable. The description of adverse reactions to this section is based on clinical experience with the reference biologic drug.

The following adverse reaction information is sourced from the Stelara Product Monograph, Approved on January 5, 2023.

8.1 Adverse Reaction Overview

The most common adverse reactions (>5%) in controlled periods of the clinical studies with ustekinumab injection among all indications were nasopharyngitis, and headache. Most were considered to be mild and did not necessitate drug discontinuation. Serious infections and malignancies were also reported in clinical studies (see 8.2 Clinical Trial Adverse Reactions; Infections and Malignancies).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Adults

The safety data described below reflect exposure to ustekinumab injection in 14 Phase 2 and Phase 3 studies in 6709 patients (4135 with psoriasis and/or psoriatic arthritis), including 4577 exposed for at

least 6 months, 3253 exposed for at least 1 year, 1482 exposed for at least 4 years and 838 for at least 5 years.

Psoriasis and Psoriatic Arthritis

The safety data described below reflect exposure to ustekinumab injection in 7 phase 2 and phase 3 studies in 4135 adult patients with psoriasis and/or psoriatic arthritis, including 3256 exposed for at least 6 months, 1482 exposed for at least 4 years and 838 for at least 5 years.

Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% in the Jamteki group during the placebo-controlled period of the Phase 3 studies (PHOENIX 1, PHOENIX 2, PSUMMIT 1 and PSUMMIT 2).

Table 2: Adverse reactions reported by > 1% of patients during the placebo controlled period of PHOENIX 1 and 2 and PSUMMIT 1 and 2*

	Placebo	Ustekinumab injection	
		45 mg	90 mg
Patients treated	974	972	974
Infections and infestations			
Nasopharyngitis	64 (6.6%)	72 (7.4%)	70 (7.2%)
Upper respiratory tract infection	44 (4.5%)	46 (4.7%)	40 (4.1%)
Dental Infection	2 (0.2%)	9 (0.9%)	10 (1.0%)
Nervous system disorders			
Headache	29 (3.0%)	48 (4.9%)	41 (4.2%)
Dizziness	9 (0.9%)	11 (1.1%)	13 (1.3%)
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	9 (0.9%)	16 (1.6%)	15 (1.5%)
Gastrointestinal disorders			
Diarrhea	15 (1.5%)	22 (2.3%)	18 (1.8%)
Nausea	10 (1.0%)	18 (1.9%)	15 (1.5%)
Skin and subcutaneous tissue disorders			
Pruritus	9 (0.9%)	14 (1.4%)	12 (1.2%)
Musculoskeletal and connective tissue disorders			
Arthralgia	23 (2.4%)	30 (3.1%)	26 (2.7%)
Back pain	9 (0.9%)	12 (1.2%)	19 (2.0%)
Myalgia	5 (0.5%)	8 (0.8%)	11 (1.1%)
General disorders and administration site conditions			
Fatigue	16 (1.6%)	24 (2.5%)	24 (2.5%)
Injection site erythema	6 (0.6%)	8 (0.8%)	16 (1.6%)

*Placebo controlled periods are through Week 12 in PHOENIX 1 AND 2 and through Week 16 in PSUMMIT 1 and 2.

Table 3 presents the rates at which the ustekinumab injection ADRs occurred in treatment groups in the ACCEPT trial.

Table 3 Adverse drug reactions reported by ≥1% of patients through Week 12 in ACCEPT

	ENBREL® (etanercept)	Ustekinumab injection	
		45 mg	90 mg
Patients treated	347	209	347
Infections and infestations			
Nasopharyngitis	29 (8.4%)	21 (10.0%)	34 (9.8%)
Upper respiratory tract infection	20 (5.8%)	13 (6.2%)	22 (6.3%)
Nervous system disorders			
Headache	38 (11.0%)	31 (14.8%)	41 (11.8%)
Dizziness	8 (2.3%)	3 (1.4%)	6 (1.7%)
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	14 (4.0%)	5 (2.4%)	14 (4.0%)
Gastrointestinal disorders			
Diarrhea	9 (2.6%)	8 (3.8%)	9 (2.6%)
Nausea	8 (2.3%)	8 (3.8%)	10 (2.9%)
Skin and subcutaneous tissue disorders			
Pruritus	14 (4.0%)	12 (5.7%)	16 (4.6%)
Musculoskeletal and connective tissue disorders			
Arthralgia	9 (2.6%)	11 (5.3%)	10 (2.9%)
Back pain	7 (2.0%)	14 (6.7%)	15 (4.3%)
Myalgia	7 (2.0%)	3 (1.4%)	7 (2.0%)
General disorders and administration site conditions			
Fatigue	13 (3.7%)	8 (3.8%)	19 (5.5%)
Injection site erythema	51 (14.7%)	2 (1.0%)	2 (0.6%)

Infections:

In placebo-controlled clinical studies, the rates of infection or serious infection were similar between ustekinumab injection-treated patients and those treated with placebo. In the placebo- controlled period of these clinical studies, the rate of infection was 1.36 per patient-year of follow-up in ustekinumab injection-treated patients, and 1.34 per patient-year of follow- up in placebo-treated patients. Serious infections occurred at a rate of 0.03 per patient-year of follow-up in ustekinumab injection-treated patients (30 serious infections in 930 patient- years of follow-up) and 0.03 per

patient-year of follow-up in placebo-treated patients (15 serious infections in 434 patient-years of follow-up) (see 7 WARNINGS AND PRECAUTIONS).

In the controlled and non-controlled portions of placebo-controlled clinical studies representing 11,581 patient-years of exposure in 6,709 patients, the median follow-up was 1.0 years (1.1 years for psoriatic disease studies). The rate of infection was 0.91 per patient-year of follow-up in ustekinumab injection-treated patients. The rate of serious infections was 0.02 per patient-year of follow-up in ustekinumab injection-treated patients (199 serious infections in 11581 patient-years of follow-up) and included pneumonia, sepsis, cellulitis, diverticulitis and viral infections.

Malignancies:

In the placebo-controlled period of the clinical studies, the incidence of non-melanoma skin cancer was 0.43 per 100 patient-years of follow-up for ustekinumab injection-treated patients (4 patients in 929 patient-years of follow-up) compared with 0.46 per 100 patient-years of follow-up for placebo- treated patients (2 patient in 433 patient-years of follow-up) during the placebo-controlled periods. In a Phase 3 clinical trial (ACCEPT) comparing ustekinumab and etanercept for the treatment of moderate to severe plaque psoriasis, 209 patients received ustekinumab 45 mg, 347 patients received ustekinumab 90 mg, and 347 patients received etanercept. Through Week 12, three (0.5%) subjects in the ustekinumab groups had a non-melanoma skin cancer detected in areas of psoriasis that had cleared with treatment. No skin cancers were observed in the etanercept group but due to the short treatment period, the possible pre-existing malignancies and the differences in efficacy (see 14 CLINICAL TRIALS section), the clinical relevance has not been established.

The incidence of malignancies excluding non-melanoma skin cancer was 0.11 per 100 patient- years of follow-up for ustekinumab injection-treated patients (1 patient in 929 patient- years of follow-up) compared with 0.23 per 100 patient-years of follow-up for placebo-treated patients (1 patient in 434 patient-years of follow-up) during the placebo-controlled periods. In the ACCEPT trial, through Week 12, one subject (0.2%) with a familial history of breast cancer was diagnosed with breast cancer versus no malignancies in the etanercept group.

In the controlled and non-controlled periods of clinical studies representing 11,561 patient-years of exposure in 6709 patients, the median follow-up was 1.0 years (1.1 years for psoriatic disease studies). Malignancies excluding non-melanoma skin cancers were reported in 62 patients in 11561 patient-years of follow-up. This represents an incidence of 0.54 per 100 patients-years of follow-up for ustekinumab injection-treated patients. This rate of malignancies reported in ustekinumab injection-treated patients was comparable to the rate expected in the general population (standardized incidence ratio = 0.93 [95% confidence interval: 0.71,1.20]). The most frequently observed malignancies, other than non-melanoma skin cancer, were prostate (16), colorectal (7), melanoma (6), and breast (5). The incidence of non-melanoma skin cancer was 0.49 per 100 patient-years of follow-up for ustekinumab injection-treated patients (56 patients in 11545 patient-years of follow-up). The ratio of patients with basal versus squamous cell skin cancers (3:1) is comparable with the ratio expected in the general population.

Among 1569 patients exposed to ustekinumab injection for at least 3 years, 0.9% (n= 14) of patients reported NMSC and 1.4% (n=22) of patients reported malignancies excluding NMSC. This represents an incidence of 0.18 and 0.29 per 100 patient-years of follow-up for NMSC and malignancies excluding NMSC, respectively.

Hypersensitivity and Infusion Reactions:

Subcutaneous Administration

During the controlled periods of the psoriasis and psoriatic arthritis clinical studies of ustekinumab, rash and urticaria have each been observed in <1% of patients.

Immunogenicity:

In psoriasis and psoriatic arthritis clinical studies, up to 12.4% of patients treated with ustekinumab developed antibodies to ustekinumab. No apparent association between the development of antibodies to ustekinumab and the development of injection site reactions was observed. 123 of 168 (73%) of psoriasis and psoriatic arthritis patients who were positive for antibodies to ustekinumab had neutralizing antibodies. Patients positive for antibodies to ustekinumab exhibited mean or median serum levels of ustekinumab that were consistently lower than those in patients negative or undetectable for antibodies to ustekinumab and tended to have lower efficacy; however, antibody positivity did not preclude a clinical response.

Immunogenicity tests are generally product-specific. Comparison of antibody rates to those from other products, or comparison of the incidence of antibodies between different tests without cross-validation is not appropriate.

8.3 Less Common Clinical Trial Adverse Reactions

The following adverse reactions occurred at rates less than 1% during the controlled period of ustekinumab injection clinical trials:

General disorders and administration site conditions: injection site reactions (including swelling, pruritus, induration, hemorrhage, hematoma), asthenia

Infections and infestations: cellulitis, herpes zoster, viral upper respiratory tract infections, vulvovaginal mycotic infections, dental infections

Psychiatric disorders: depression

Respiratory, thoracic and mediastinal disorders: nasal congestion

Skin and Subcutaneous tissue disorders: acne

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

During the placebo-controlled period of the Phase 2 and Phase 3 psoriasis studies (through week 12), an increase in non-fasting blood glucose levels was observed, as follows: Subjects with any abnormal value: 49 (6.7%) placebo vs. 83 (5.3%) in the combined ustekinumab group; Subjects with > 1 abnormal value: 9 (1.2%) placebo vs 35 (2.2%) in the combined ustekinumab group.

The clinical significance of these changes in glucose is unknown. No such increase in fasting blood glucose levels was observed in the same subjects.

8.5 Post-Market Adverse Reactions

Additional adverse events reported from worldwide post-marketing experience with ustekinumab are included below. Because these events 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 ustekinumab exposure.

Immune system disorders	Hypersensitivity reactions (including rash, urticaria) Serious allergic reactions (including anaphylaxis and angioedema)
Infections and infestations	Lower respiratory tract infection

Respiratory, thoracic and mediastinal disorders	Allergic alveolitis, eosinophilic pneumonia
Skin and subcutaneous tissue disorders	Pustular psoriasis Exfoliative dermatitis, erythrodermic psoriasis, hypersensitivity vasculitis

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Specific drug interaction studies have not been conducted with ustekinumab injection.

In population pharmacokinetic analysis, the effect of the most frequently used concomitant medications in patients with psoriasis (including paracetamol/acetaminophen, ibuprofen, acetylsalicylic acid, metformin, atorvastatin, naproxen, levothyroxine, hydrochlorothiazide, and influenza vaccine) on pharmacokinetics of ustekinumab was explored and none of the concomitant medications exerted significant impact. In psoriatic arthritis studies, concomitant MTX use did not appear to influence the pharmacokinetics of ustekinumab.

9.3 Drug-Behavioural Interaction

The pharmacokinetics of ustekinumab were not impacted by the use of tobacco or alcohol.

9.4 Drug-Drug Interactions

Live Vaccines

Live vaccines should not be given concurrently with Jamteki (ustekinumab) (see 7 WARNINGS AND PRECAUTIONS). Information regarding the administration of live vaccines in infants exposed to ustekinumab *in utero* is provided earlier in this product monograph (see 7 WARNINGS AND PRECAUTIONS, Immune, Infant exposure in utero).

Immunosuppressants

The safety and efficacy of ustekinumab injection in combination with immunosuppressive agents or phototherapy have not been evaluated (see 7 WARNINGS AND PRECAUTIONS).

CYP450 Substrates

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). The clinical significance of this is not known, although these results do not suggest the need for dose adjustments in patients who are receiving concomitant CYP450 substrates.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Ustekinumab is a fully human IgG1κ monoclonal antibody, a first-in-class agent that binds with specificity to the shared p40 protein subunit of human cytokines interleukin IL-12 and IL-23.

Ustekinumab inhibits the bioactivity of human IL-12 and IL-23 by preventing p40 from binding to the IL-12Rβ1 receptor protein expressed on the surface of immune cells. Ustekinumab cannot bind to IL-12 or IL-23 that is already bound to IL-12Rβ1 cell surface receptors. Thus, ustekinumab is not likely to contribute to complement or antibody- mediated cytotoxicity of cells expressing IL-12 and/or IL-23 receptors.

IL-12 and IL-23 are heterodimeric cytokines secreted by activated antigen-presenting cells, such as macrophages and dendritic cells. IL-12 stimulates natural killer (NK) cells and drives the differentiation of CD4+ T cells toward the T helper 1(Th1) phenotype and stimulates interferon gamma (IFNγ) production. IL-23 induces the T helper 17 (Th17) pathway and promotes secretion of IL-17A, IL-21, and IL-22. Levels of IL-12 and IL-23 are elevated in the skin and blood of patients with psoriasis, and serum IL12/23p40 distinguishes patients with psoriatic arthritis from healthy individuals, implicating IL-12 and IL-23 in the pathophysiology of psoriatic inflammatory diseases. Genetic polymorphisms in IL23A, IL23R, and IL-12B genes confer susceptibility to these disorders. Additionally, IL-12 and IL-23 are highly expressed in lesional psoriatic skin, and IL-12-mediated induction of IFNγ correlates with psoriasis disease activity. IL-23 responsive T-cells have been found in the entheses in a mouse model of inflammatory arthritis, where IL-23 drives entheseal inflammation. In addition, there is pre- clinical evidence implicating IL-23 and downstream pathways in bone erosion and destruction through up-regulation of receptor activator of nuclear factor-κB ligand (RANKL), which activates osteoclasts.

By binding the shared p40 subunit of IL-12 and IL-23, ustekinumab may exert its clinical effects in psoriasis and psoriatic arthritis through interruption of the Th1 and Th17 cytokine pathways, which have been implicated as contributors in the pathology of these diseases.

10.2 Pharmacodynamics

Treatment with ustekinumab resulted in significant improvement in histological measures of psoriasis including epidermal hyperplasia and cell proliferation. These results are consistent with the clinical efficacy observed. In patients with psoriasis and/or psoriatic arthritis ustekinumab injection had no apparent effect on the percentages of circulating immune cell populations including memory and naive T-cell subsets or circulating cytokine levels. Systemic markers of inflammation were measurable in the serum at baseline and 4 markers (MDC, VEGF, MCSF-1 and YKL-40) showed modest differences in concentration post-treatment in ustekinumab injection-treated patients as compared to placebo.

Treatment with ustekinumab resulted in a decrease in the gene expression of its molecular targets IL-12 and IL-23 as shown by analyses of mRNA obtained from lesional skin biopsies of psoriatic patients at baseline and up to two weeks post-treatment. In addition, ustekinumab down-regulated the gene expression of inflammatory cytokines and chemokines such as MCP-1, TNF-alpha, IP-10 and IL-8 in lesional skin biopsies. These results are consistent with the significant clinical benefit observed with ustekinumab treatment.

In psoriasis and psoriatic arthritis studies, clinical response (improvement in PASI or ACR measurements, respectively) appeared to be related to serum ustekinumab levels. Patients with psoriasis with higher PASI response had higher median serum concentrations of ustekinumab than those with lower clinical responses. In psoriasis studies, the proportion of patients with psoriasis who achieved PASI 75 response increased with increasing serum levels of ustekinumab. The proportion of patients who achieved PASI 75 response at Week 28 increased with increasing serum ustekinumab trough levels at Week 28. In psoriatic arthritis studies, patients achieving an ACR 20 response had higher median serum concentrations of ustekinumab than ACR 20 non-responders. The proportion of patients who achieved ACR 20 and ACR 50 response increased with increasing serum levels of ustekinumab.

10.3 Pharmacokinetics

The median pharmacokinetic parameters of ustekinumab following a single SC administration in adult patients with psoriasis are shown in Table 4. The pharmacokinetic parameters of ustekinumab (CL/F, V_z/F, and $t_{1/2}$) were generally comparable between 45 mg and 90 mg subcutaneous doses.

Table 4: Summary of Pharmacokinetic Parameters of Ustekinumab Following a Single 45 or 90 mg Subcutaneous Administration in Adult Patients with Psoriasis

Dose	45 mg			90 mg		
PK parameter	N	Median (Range)	Mean (± SD)	N	Median (Range)	Mean (± SD)
C_{max} (mcg/mL)	22	2.4 (1.0, 5.4)	2.7 (± 1.2)	24	5.3 (1.2, 12.3)	6.1 (± 3.6)
t_{max} (day)	22	13.5 (1.9, 58.2)	15.3 (± 13.5)	24	7.0 (2.9, 27.1)	9.9 (± 7.4)
AUC (mcg·day/mL)	18	84.9 (31.2, 1261.9)	196.7 (± 298.2)	21	226.9 (57.1, 755.5)	274.9 (± 206.5)
t1/2 (day)	18	19.8 (5.0, 353.6)	45.6 (± 80.2)	21	21.2 (13.6, 85.8)	26.7 (± 19.3)
CL/F (mL/day/kg)	18	5.3 (0.2, 12.9)	5.8 (± 3.5)	21	4.5 (1.5, 14.9)	5.7 (± 3.6)
V_z/F (mL/kg)	18	154.2 (32.6, 280.5)	160.5 (± 64.5)	21	160.5 (37.3, 354.1)	178.7 (± 85.2)

Source data: C0379T04 CSR

Absorption:

The median time to reach the maximum serum concentration (t_{max}) was 8.5 days after a single 90 mg subcutaneous administration in healthy subjects (n = 30). The median t_{max} values of ustekinumab following a single subcutaneous administration of either 45 mg or 90 mg in patients with psoriasis were comparable to that observed in healthy subjects.

The absolute bioavailability (F) of ustekinumab following a single subcutaneous administration was estimated to be 57.2% in patients with psoriasis (n = 17).

Distribution:

The median apparent volume of distribution during the terminal phase (V_z/F) following a single subcutaneous administration to patients with psoriasis ranged from 76 to 161 mL/kg (n = 4 to 21).

Metabolism:

The exact metabolic pathway for ustekinumab is unknown.

Elimination

The median apparent clearance (CL/F) following a single subcutaneous administration to patients with psoriasis ranged from 2.7 to 5.3 mL/day/kg. The median half-life ($t_{1/2}$) of ustekinumab was approximately 3 weeks in patients with psoriasis and/or psoriatic arthritis, ranging from 15 to 32 days across all psoriasis and psoriatic arthritis studies (n = 4 to 55).

Duration of Effect

Dose Linearity: The systemic exposure of ustekinumab (C_{max} and AUC) increased in a linear manner following a single subcutaneous administration at doses ranging from approximately 24 mg to 240 mg in patients with psoriasis.

Single Dose vs. Multiple Doses: Serum concentration-time profiles of ustekinumab were generally predictable after single or multiple subcutaneous dose administrations on the basis of a one-compartment model. In patients with psoriasis, steady-state serum concentrations of ustekinumab were achieved by Week 28 after initial subcutaneous doses at Weeks 0 and 4 followed by doses every 12 weeks. The median steady-state trough concentration ranged from 0.21 mcg/mL to 0.26 mcg/mL (45 mg; n = 242 to 390) and from 0.47 mcg/mL to 0.49 mcg/mL (90 mg; n = 236 to 386) in patients with psoriasis. There was no apparent accumulation in serum ustekinumab concentration over time when given subcutaneously every 12 weeks.

Special Populations and Conditions

Population Pharmacokinetic Analysis

Of the demographic factors (e.g., gender, race, age, body size), baseline patient physical or biochemical characteristics, medical or medication history, or concomitant medications evaluated in a population pharmacokinetic analysis, only body weight, diabetes comorbidity, and positive immune response to ustekinumab were found to be important covariates affecting the systemic exposure to ustekinumab in patients with moderate to severe psoriasis. Body weight and positive immune response to ustekinumab were also found to be important covariates affecting the systemic exposure to ustekinumab in subjects with psoriatic arthritis. Clinical relevance of the effects of these important covariates, however, needs to be evaluated concurrently with clinical efficacy and safety data.

- **Pediatrics (< 18 years of age):** Jamteki is not indicated for use in the pediatric population.
- **Geriatrics (> 65 years of age):** No specific studies have been conducted in elderly patients. A population pharmacokinetic analysis indicated there were no apparent changes in CL/F and V/F estimates in patients ≥ 65 years
- **Sex:** The apparent clearance of ustekinumab was not impacted by sex.
- **Genetic Polymorphism:** The apparent clearance of ustekinumab was not impacted by sex, age, or race.
- **Ethnic Origin**: The apparent clearance of ustekinumab was not impacted by race.
- **Hepatic Insufficiency:** No pharmacokinetic data are available in patients with impaired hepatic function.
- **Renal Insufficiency:** No pharmacokinetic data are available in patients with renal insufficiency.

- **Obesity:** Serum ustekinumab concentrations were affected by weight in patients with psoriasis and/or psoriatic arthritis. When given the same dose, patients of higher weight (> 100 kg) had lower median serum ustekinumab concentrations compared with those in patients of lower weight (≤ 100 kg). However, across doses, the median trough serum concentrations of ustekinumab in patients with higher weight (> 100 kg) in the 90 mg group were comparable to those in patients with lower weight (≤ 100 kg) in the 45 mg group.

11 STORAGE, STABILITY AND DISPOSAL

Jamteki must be refrigerated at 2 to 8°C. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake.

If needed, individual Jamteki pre-filled syringes may be stored at room temperature up to 30°C for a maximum single period of up to 30 days in the original carton with protection from light. Record the date when the pre-filled syringe is first removed from the refrigerator and the new expiry date on the carton in the space provided. The new expiry date must not exceed the original expiry date printed on the carton. Once a syringe has been stored at room temperature, it should not be returned to the refrigerator. Discard the syringe if not used within 30 days at room temperature storage. Do not use Jamteki after the expiration date on the carton or on the prefilled syringe.

12 SPECIAL HANDLING INSTRUCTIONS

Following administration of Jamteki, discard any unused portion. The syringe should be disposed of in a puncture-resistant container for syringes and needles. Patients or caregivers should be instructed in the technique as well as proper syringe and needle disposal, and not to reuse these items.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	ustekinumab
Chemical name:	ustekinumab
Molecular formula and molecular mass:	Ustekinumab is a fully human IgG1κ mAb, with an approximate molecular weight of 148,079 to 149,690 Daltons.
Physicochemical properties:	Jamteki is clear to opalescent, colourless to slightly yellow with a pH of approximately 5.5 to 6.5.

Product Characteristics:

Jamteki (ustekinumab) is supplied as a single-use, sterile solution for subcutaneous injection in a Type 1 glass syringe with a fixed 29G, half-inch needle equipped with a passive safety device and a needle cover. The needle cover on the pre-filled syringe is not made with natural rubber latex.

Jamteki is supplied as 2 dosage presentations at 45 mg in 0.5 mL volume as a pre-filled syringe or at 90 mg in a 1 mL volume as a pre-filled syringe. Each 1 mL of Jamteki solution contains 90 mg ustekinumab. No preservatives are present.

Viral Inactivation

Ustekinumab is produced by a recombinant cell line cultured by continuous perfusion and is purified by a series of steps that includes measures to inactivate and remove viruses.

14 CLINICAL TRIALS

14.5 Clinical Trials - Reference Biologic Drug

<u>Plaque Psoriasis - Adults</u>

The safety and efficacy of ustekinumab injection were assessed in two multicentre, randomized, double- blind, placebo-controlled studies (PHOENIX 1 and PHOENIX 2) in patients 18 years of age and older with chronic (>6 months) plaque psoriasis who had a minimum body surface area (BSA) involvement of 10%, and Psoriasis Area and Severity Index (PASI) score ≥12 and who were candidates for phototherapy or systemic therapy. Patients with guttate, erythrodermic, or pustular psoriasis were excluded from the studies. No concomitant anti-psoriatic therapies were allowed during the study with the exception of low-potency topical corticosteroids on the face and groin after Week 12. A total of 1996 patients were enrolled in the two studies. The safety and efficacy of ustekinumab injection beyond 5 years have not been established.

In addition, a multicenter, randomized, active-controlled study (ACCEPT) compared the safety and efficacy of ustekinumab injection and etanercept in patients 18 years of age and older with chronic (>6 months) plaque psoriasis who had a minimum BSA involvement of 10%, PASI score ≥12, Physician Global Assessment (PGA) score ≥ 3, who were candidates for phototherapy or systemic therapy, and who had had an inadequate response to, intolerance to, or contraindication to cyclosporine, methotrexate, or PUVA therapy. A total of 903 patients were enrolled in the study.

Study demographics and trial design

Baseline disease characteristics across PHOENIX 1 and 2 were similar (Table 5 and Table 6). In both studies, patients in all treatment groups had a median baseline PASI score ranging from 17 to 18. Approximately two-thirds of all patients 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 study patients had a history of psoriatic arthritis. Similar disease characteristics were also seen in the ACCEPT trial (Table 5 and Table 6).

Table 5: Summary of patient demographics for PHOENIX 1, PHOENIX 2 and ACCEPT

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n=number)	Mean age (Range)	Gender
C0743T08 (PHOENIX 1)	Double-Blind Placebo-Controlled	Fixed doses: Placebo (N = 255) Placebo → 45 mg SC regimen[a] (N = 123) Placebo → 90 mg SC regimen[a] (N = 120) 45 mg SC Weeks 0, 4 then q12w (N = 255) 90 mg SC Weeks 0, 4 then q12w (N = 256)	N=766	45.3 (19,76)	M=531 F=235
C0743T09 (PHOENIX 2)	Double-Blind Placebo-Controlled	Fixed doses: Placebo (N = 410)-Placebo → 45 mg SC regimen[a] (N = 197) Placebo → 90 mg SC regimen[a] (N = 195) 45 mg SC Weeks 0, 4 then q12w (N = 409) 90 mg SC Weeks 0, 4 then q12w (N = 411)	N=1230	46.2 (18, 86)	M=840 F=390
C0743T12 (ACCEPT)	Assessor-Blind Active-Comparator Controlled	Fixed doses: Etanercept 50 mg (N=347) twice weekly through Week 12 ustekinumab injection 45 mg (N=209) at Week 0 and 4 ustekinumab injection 90 mg (N=347) at Week 0 and 4	N= 903	45.0 (18, 81)	M = 613 F = 290

[a] The placebo groups crossed over to receive ustekinumab injection (45 mg or 90 mg) at Weeks 12 and 16 then q12w

Table 6: Baseline Disease Characteristics in PHOENIX 1, PHOENIX 2 and ACCEPT

	PHOENIX 1		PHOENIX 2		ACCEPT	
	Placebo	Ustekinumab injection	Placebo	Ustekinumab injection	Etanercept	Ustekinumab injection
Patients randomized at Week 0	N=255	N=511	N=410	N=820	N=347	N=556
Median BSA	22.0	21.0	20.0	21.0	19.0	20.0
BSA ≥ 20%	145 (57%)	276 (54%)	217 (53%)	445 (54%)	169 (49%)	289 (52%)
Median PASI	17.80	17.4	16.90	17.60	16.8	17.1
PASI ≥ 20	91 (36%)	169 (33%)	133 (32%)	300 (37%)	102 (29%)	205 (37%)
PGA of marked or severe	112 (44%)	223 (44%)	160 (39%)	328 (40%)	148 (43%)	242 (44%)
History of psoriatic arthritis	90 (35%)	168 (33%)	105 (26%)	200 (24%)	95 (27%)	157 (28%)
Prior phototherapy	150 (59%)	342 (67%)	276 (67%)	553 (67%)	224 (65%)	368 (66%)
Prior conventional systemic therapy excluding biologics[a]	142 (56%)	282 (55%)	241 (59%)	447 (55%)	199(57%)	311 (56%)
Prior conventional systemic or biologic therapy[a]	189 (74%)	364 (71%)	287 (70%)	536 (65%)	218(63%)	337 (61%)
Failed to respond to, had contraindication for, or intolerant to ≥ 1 conventional therapy[a]	139 (55%)	270 (53%)	254 (62%)	490 (60%)	347 (100%)	555 (100%)
Failed to respond to, had contraindication for, or intolerant to ≥ 3 conventional therapies[a]	30 (12%)	54 (11%)	66 (16%)	134 (16%)	52 (15%)	78 (14%)

[a] In PHOENIX 1 and 2, conventional systemic agents include acitretin, PUVA, methotrexate, and cyclosporine. In ACCEPT, conventional systemic agents included PUVA, methotrexate, and cyclosporine. All patients were required to be etanercept naïve at baseline in ACCEPT, but in PHOENIX 1 and 2 patients may have previously received etanercept.

PHOENIX 1 evaluated the safety and efficacy of ustekinumab injection versus placebo in 766 patients with plaque psoriasis. Patients were randomized in equal proportion to placebo, 45 mg or 90 mg of ustekinumab injection. Patients randomized to ustekinumab injection received 45 mg or 90 mg doses at Weeks 0 and 4 followed by the same dose every 12 weeks. Patients randomized to receive placebo at Weeks 0 and 4 crossed over to receive ustekinumab injection (either 45 mg or 90 mg) at Weeks 12 and 16 followed by the same dose every 12 weeks. To evaluate the efficacy of every 12-week dosing, patients who were PASI 75 responders at both Weeks 28 and 40 were re-randomized to either continue dosing of ustekinumab injection every 12 weeks or to placebo (i.e., withdrawal of therapy).

Patients withdrawn from ustekinumab injection at Week 40 reinitiated ustekinumab injection at their original dosing regimen when they experienced at least a 50% loss of their PASI improvement obtained at Week 40. Patients were followed for at least 76 weeks.

PHOENIX 2 evaluated the safety and efficacy of ustekinumab injection versus placebo in 1230 patients with plaque psoriasis. This study design was identical to PHOENIX 1 through Week 28.

Dose Adjustment (every 8 weeks)

At Week 28, PHOENIX 1 patients who were nonresponders (<PASI 50 response) discontinued treatment and patients who were partial responders (≥ PASI 50 response and <PASI 75 response) were adjusted to every-8-week dosing. PASI 75 responders at Week 28 who became partial responders or nonresponders at Week 40 were adjusted to every-8-week dosing.

In PHOENIX 2, patients who were partial responders at Week 28 were re-randomized to either continue every 12 weeks dosing of ustekinumab injection or to switch to every 8 weeks dosing.

All patients were followed for up to 76 weeks in PHOENIX 1 and up to 52 weeks in PHOENIX 2 following first administration of study treatment.

In both studies, the primary endpoint was the proportion of patients who achieved a reduction in score of at least 75% from baseline at Week 12 by the PASI (PASI 75). Patients achieving ≥ 90% improvement in PASI from baseline (PASI 90) were considered PASI 90 responders and patients with ≥ 50% improvement in PASI from baseline (PASI 50) were considered PASI 50 responders. Another key efficacy assessment was the Physician's Global Assessment (PGA), 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.

The Dermatology Life Quality Index (DLQI), a dermatology-specific quality of life instrument designed to assess the impact of the disease on a patient's quality of life, was assessed in both PHOENIX 1 and PHOENIX 2. Other efficacy assessments included the Nail Psoriasis Severity Index (NAPSI), a physician-assessed score that measures the severity of nail involvement (PHOENIX 1); the Itch Visual Analog Scale (VAS), used to assess the severity of itch at the time of the assessment (PHOENIX 1); the Hospital Anxiety and Depression Scale (HADS), a self- rating tool developed to evaluate psychological measures in patients with physical ailments (PHOENIX 2); and the Work Limitations Questionnaire (WLQ), a 25-item, self-administered questionnaire that was used to measure the impact of chronic health conditions on job performance and work productivity among employed populations (PHOENIX 2).

The ACCEPT trial compared the efficacy of ustekinumab injection to etanercept and evaluated the safety of ustekinumab injection and etanercept in moderate to severe psoriasis patients. The active-controlled portion of the study was from Week 0 to Week 12, during which the efficacy and safety of etanercept and 2 dose levels of ustekinumab injection were evaluated. This trial was powered to test the superiority of each dose level to etanercept and the primary endpoint was the proportion of patients who achieved a PASI 75 at week 12.

Study results

The results of PHOENIX 1 and PHOENIX 2 for key psoriasis clinical outcomes are presented in Table 7.

Efficacy at the Primary Endpoint, PHOENIX 1 and PHOENIX 2

The onset of action with ustekinumab injection was rapid and improvement was seen within 2 weeks of the first dose. In both the PHOENIX 1 and PHOENIX 2 studies, a significantly greater proportion of patients randomized to treatment with ustekinumab injection were PASI 75 responders compared with placebo at Week 12 (Table 7). In the PHOENIX 1 study, 67% and 66% of patients receiving ustekinumab injection 45 mg and 90 mg, respectively, achieved a PASI 75 response at Week 12 compared with 3% of patients receiving placebo. In the PHOENIX 2 study, 67% and 76% of patients receiving ustekinumab

injection 45 mg and 90 mg, respectively, achieved a PASI 75 response at Week 12 compared with 4% of patients receiving placebo.

All 3 components of the PASI (plaque thickness/induration, erythema, and scaling) contributed comparably to the improvement in PASI.

The efficacy of ustekinumab injection was significantly superior (p<0.001) to placebo across all subgroups defined by baseline demographics, clinical disease characteristics (including patients with a history of psoriatic arthritis) and prior medication usage. While pharmacokinetic modelling suggested a trend towards higher CL/F in patients with diabetes, a consistent effect on efficacy was not observed.

Table 7: Clinical Outcomes - PHOENIX 1 and PHOENIX 2

	PHOENIX 1			**PHOENIX 2**		
		Ustekinumab injection			**Ustekinumab injection**	
	Placebo	**45 mg**	**90 mg**	**Placebo**	**45 mg**	**90 mg**
Week 12						
Patients randomized	255	255	256	410	409	411
PASI response						
PASI 50 response[a]	26 (10%)	213 (84%)	220 (86%)	41 (10%)	342 (84%)	367 (89%)
PASI 75 response[a]	8 (3%)	171 (67%)	170 (66%)	15 (4%)	273 (67%)	311 (76%)
PASI 90 response[a]	5 (2%)	106 (42%)	94 (37%)	3 (1%)	173 (42%)	209 (51%)
PASI 100 response[a]	0 (0%)	33 (13%)	28 (11%)	0 (0%)	74 (18%)	75 (18%)
PGA of Cleared or Minimal[a]	10 (4%)	151 (59%)	156 (61%)	18 (4%)	277 (68%)	300 (73%)
Week 28						
Patients evaluated	--	250	243	--	397	400
PASI response						
PASI 50 response	--	228 (91%)	234 (96%)	--	369 (93%)	380 (95%)
PASI 75 response	--	178 (71%)	191 (79%)	--	276 (70%)	314 (79%)
PASI 90 response	--	123 (49%)	135 (56%)	--	178 (45%)	217 (54%)
PASI 100 response	--	52 (21%)	71(29 %)	--	74(19%)	118 (30%)
PGA of Cleared or Minimal	--	146 (58%)	160 (66%)	--	241(61%)	279 (70%)

[a] p < 0.001 for 45 mg or 90 mg comparison with placebo.

Other efficacy measures at Week 12

In both PHOENIX 1 and PHOENIX 2, compared with placebo, significantly greater proportions of patients randomized to 45 mg or 90 mg ustekinumab injection achieved a cleared or minimal PGA score, and significantly greater proportions of patients randomized to 45 mg or 90 mg ustekinumab injection were PASI 50, PASI 90 and PASI 100 responders at Week 12 (Table 7). In the PHOENIX 1 study,

60% and 62% of the patients treated with 45 mg and 90 mg ustekinumab injection, respectively, achieved PGA scores of cleared or minimal compared with 4% of placebo-treated patients. In PHOENIX 2, 68% and 73% of patients receiving 45 mg or 90 mg ustekinumab injection, respectively, had cleared or minimal PGA scores compared with 5% of the placebo patients. In PHOENIX 1, PASI 90 was achieved by 42% and 37% of the patients treated with 45 mg and 90 mg ustekinumab injection, respectively, compared with 2% of placebo-treated patients. In addition, a significantly higher proportion of subjects treated with either 45 mg (13%) or 90 mg (11%) achieved a PASI of 0 (i.e., PASI 100 response) compared with the placebo group (0.0%; $p<0.001$). In PHOENIX 2, the percentage of patients achieving PASI 100 and PASI 90 was 18% and 42%, respectively, in the 45 mg ustekinumab injection group, and 18% and 51%, respectively, in the 90 mg ustekinumab injection group versus 1% in the placebo group. The percentage of patients achieving PASI 50 in PHOENIX 1 was 84% and 86% in the 45 mg and 90 mg ustekinumab injection groups, respectively, compared with 10% in the placebo group. Similarly, 84% of patients treated with 45 mg ustekinumab injection, 89% of patients treated with 90 mg ustekinumab injection and 10% of patients treated with placebo reached PASI 50 in PHOENIX 2 (Table 7).

Response over time

In PHOENIX 1, significantly greater proportions of ustekinumab injection-treated patients had PASI 50 responses (9% and 10% for the 45 mg and 90 mg groups, respectively) compared with placebo (2%) by Week 2 ($p<0.001$). Significantly greater proportions of patients treated with ustekinumab injection achieved PASI 75 responses (9% and 12% for the 45 mg and 90 mg ustekinumab injection groups, respectively) compared with placebo (0.4%) by Week 4 ($p<0.001$). Maximum response was generally achieved by Week 24 in the 45 mg and 90 mg ustekinumab injection treatment groups, and response rates were generally sustained through Week 36 (Figure 2.1). In PHOENIX 1, PASI 75 rates at Week 24 were 76% for the 45 mg group, and 85% for the 90 mg group. Higher response rates were observed in patients receiving ustekinumab injection 90 mg than in those receiving ustekinumab injection 45 mg by Week 16 and these higher response rates were sustained through Week 36 (Figure 2.1). Similar results were observed in the PHOENIX 2 study through Week 28.

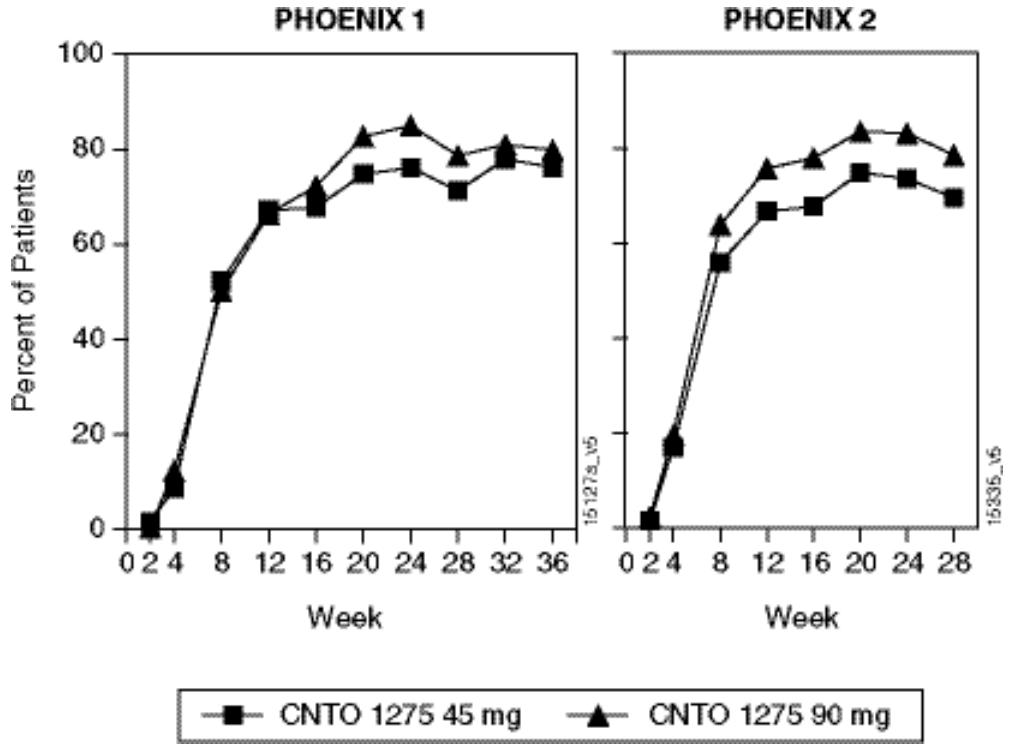


Figure 2.1: PASI 75 response over time in PHOENIX 1 and 2

In prespecified analyses of efficacy by body weight in PHOENIX 1 and PHOENIX 2, no consistent pattern of dose response was seen in patients ≤ 100 kg. In patients who weighed >100 kg, higher PASI 75 response rates were seen with 90 mg dosing compared with 45 mg dosing, and a higher proportion of patients receiving 90 mg dosing had PGA scores of cleared or minimal compared with patients receiving 45 mg dosing (Table 8).

Table 8: Clinical Outcomes by Weight – PHOENIX 1 and PHOENIX 2

Week 12						
	PHOENIX 1			**PHOENIX 2**		
	Placebo	**Ustekinumab injection**		**Placebo**	**Ustekinumab injection**	
		45 mg	**90 mg**		**45 mg**	**90 mg**
Patients randomized at Week 0	255	255	256	410	409	411
PASI 75 response by weight						
≤ 100 kg						
N	166	168	164	290	297	289
PASI 75 response	6 (4%)	124 (74%)	107 (65%)	12 (4%)	218 (73%)	225 (78%)
>100 kg						
N	89	87	92	120	112	121
PASI 75 response	2 (2%)	47 (54%)	63 (68%)	3 (3%)	55 (49%)	86 (71%)
PGA of Cleared or Minimal by weight						
≤ 100 kg						

Week 12						
	PHOENIX 1			**PHOENIX 2**		
	Placebo	**Ustekinumab injection**		**Placebo**	**Ustekinumab injection**	
		45 mg	**90 mg**		**45 mg**	**90 mg**
N	166	168	164	290	297	289
PGA response	7 (4%)	110 (65%)	104 (63%)	16 (6%)	219 (74%)	217 (75%)
>100 kg						
N	89	87	92	120	112	121
PGA response	3 (3%)	44 (51%)	54 (59%)	4 (3%)	59 (53%)	85 (70%)

Week 28				
	PHOENIX 1		**PHOENIX 2**	
	Ustekinumab injection		**Ustekinumab injection**	
	45 mg	**90 mg**	**45 mg**	**90 mg**
N	250	243	397	400
PASI 75 response by weight				
≤ 100 kg				
N	164	153	287	280
PASI 75 response	130 (79%)	124 (81%)	217 (76%)	226 (81%)
>100 kg				
N	86	90	110	119
PASI 75 response	48 (56%)	67 (74%)	59 (54%)	88 (74%)
PGA of Cleared or Minimal by weight				
≤ 100 kg				
N	164	153	287	280
PGA response	107 (65%)	107 (70%)	194 (68%)	208 (74%)
>100 kg				
N	86	90	110	119
PGA response	40 (47%)	54 (60%)	49 (45%)	71 (60%)

Therapeutic benefit of long-term continuous use

At Week 40 in PHOENIX 1, among patients who were PASI 75 responders at both weeks 28 and 40, 162 patients were re-randomized to receive ustekinumab injection at 45 mg and 90 mg given every 12 weeks (maintenance treatment) and 160 were re-randomized to receive placebo (treatment withdrawal). Maintenance of PASI 75 was significantly superior with continuous maintenance treatment compared with treatment withdrawal ($p<0.001$) through at least 1.5 years of follow-up. Similar results were seen with each dose of ustekinumab injection.

At 1 year (Week 52), 89% of patients re-randomized to maintenance treatment were PASI 75 responders compared with 63% of patients re-randomized to placebo (treatment withdrawal) ($p<0.001$) (Table 9). At Week 76, 84% of patients re-randomized to maintenance treatment were PASI 75 responders compared with 19% of patients re-randomized to placebo (treatment withdrawal)

(p<0.001). Through 18 months (Week 76), the proportion of subjects in the combined maintenance treatment group who were PASI 50 responders remained consistently at greater than 95%. By contrast, the proportion of PASI 50 responders in the combined withdrawal group progressively decreased over time such that by Weeks 52 and 76, only 50% and 31% remained as PASI 50 responders respectively. Among patients withdrawn from treatment, the rates of loss of the various PASI responses (PASI 50, 75, 90) were generally comparable in all groups regardless of dose. No rebound of psoriasis occurred in patients who were randomized to treatment withdrawal. Among the patients who reached PASI 75 response at weeks 28 and 40 and were re-randomized to maintenance treatment, 82% were PASI 75 responders at 3 years (Week 148). At 5 years (Week 244), 80% of patients (112/140) re-randomized to maintenance treatment were PASI 75 responders.

Table 9: Summary of PASI response from Week 40 through Week 76 in subjects randomized at Week 40 in PHOENIX 1

	Ustekinumab injection		**Ustekinumab injection**		**Ustekinumab injection**	
	45 mg		**90 mg**		**Combined**	
	Placebo	**q12 wks**	**Placebo**	**q12 wks**	**Placebo**	**q12 wks**
Patients randomized at Week 40	73	77	87	85	160	162
Week 52 N	73	77	86	85	159	162
≥90% improvement	27 (37.0%)	45 (58.4%)	33 (38.4%)	60 (70.6%)	60 (37.7%)	105 (64.8%)
≥75% improvement	47 (64%)	67 (87.0%)	53 (61.6%)	77 (90.6%)	100 (62.9%)	144 (88.9%)
≥50% improvement	63 (86%)	75 (97.4%)	71 (82.6%)	83 (97.6%)	134 (84.3%)	158 (97.5%)
Week 76 N	71	77	85	82	156	159
≥90% improvement	5 (7.0%)	38 (49.4%)	4 (4.7%)	52 (63.4%)	9 (5.8%)	90 (56.6%)
≥75% improvement	14 (19.7%)	63 (81.8%)	15 (17.6%)	71 (86.6%)	29 (18.6%)	134 (84.3%)
≥50% improvement	22 (31.0%)	74 (96.1%)	27 (31.8%)	79 (96.3%)	49 (31.4%)	153 (96.2%)

Efficacy of retreatment

In PHOENIX 1, after randomized withdrawal from therapy at week 40, patients reinitiated their original ustekinumab injection treatment regimen after a loss of ≥ 50% of PASI improvement.

Retreatment with ustekinumab injection resulted in 71% of evaluated patients regaining PASI 75 response within 8 weeks after reinitiating therapy and 85% of evaluated patients regaining PASI 75 response within 12 weeks after reinitiating therapy.

Dosing interval adjustment

In PHOENIX 1, Week 28 and Week 40 partial responders and Week 40 nonresponders were adjusted from every-12-week to every-8-week dosing. Approximately 40%-50% of Week 28 partial responders to every-12-week dosing achieved PASI 75 response after adjustment to every-8-week dosing and this proportion of PASI 75 responders was maintained through Week 52. A similar proportion of patients

who were PASI 75 responders at Week 28 and subsequently became partial responders or nonresponders at Week 40 achieved PASI 75 response following a dosing interval adjustment to every 8 weeks.

In PHOENIX 2, among patients initially randomized to 90 mg dosing who were partial responders at Week 28, dosing adjustment to every 8 weeks resulted in consistently superior efficacy as compared with continued every 12 weeks dosing: Partial responders randomized to 90 mg every 8 weeks achieved PASI 75 response at more visits between Weeks 40 and 52 than partial responders randomized to continue 90 mg every 12 weeks ($p = 0.014$), and a higher proportion of subjects achieved a PASI 75 response at Week 52 (68.8% with every 8 weeks dosing versus 33.3% with every 12 weeks dosing; $p = 0.004$). Among patients initially randomized to 45 mg dosing who were partial responders at Week 28, response rates were not higher among patients in whom dosing was adjusted to every 8 weeks compared with patients who continued every 12 weeks dosing.

Quality of life

In PHOENIX 1 and 2, the mean baseline DLQI scores ranged from 11 to 12. In PHOENIX 1, the mean baseline SF-36 Physical Component ranged from 47-49 and the mean baseline SF-36 Mental Component was approximately 50. Quality of life improved significantly in patients randomized to 45 mg or 90 mg ustekinumab injection compared with patients randomized to placebo as evaluated by DLQI in PHOENIX 1 and 2 and SF-36 in PHOENIX 1. Quality of life improvements were significant as early as 2 weeks in patients treated with ustekinumab injection ($p<0.001$) and these improvements were maintained over time with continued dosing.

In PHOENIX 1, 65% and 71% of patients treated with 45 mg and 90 mg of ustekinumab injection, respectively, showed a clinically meaningful reduction (5 or more points) in DLQI from baseline at week 12 compared to 18% in placebo group ($p<0.001$ for both groups compared with placebo). Furthermore, 33% and 34% of patients treated with 45 mg and 90 mg of ustekinumab injection, respectively, showed a DLQI score of 0 compared to 1% in the placebo group ($p<0.001$ for both groups compared with placebo), indicating no impairment in QOL from disease or treatment in these patients. In PHOENIX 2, 72% and 77% of patients treated with 45 mg and 90 mg of ustekinumab injection, respectively, showed a clinically meaningful reduction (5 or more points) in DLQI from baseline at Week 12 compared to 21% in placebo group ($p<0.001$ for both groups compared with placebo). In addition, 37% and 39% of patients treated with 45 mg and 90 mg of ustekinumab injection, respectively, showed a DLQI score of 0 compared to 1% in the placebo group ($p<0.001$ for both groups compared with placebo).

In PHOENIX 1, the median baseline NAPSI score for nail psoriasis was 4.0 and the median number of fingernails involved with psoriasis was 8.0. Nail psoriasis improved significantly in patients randomized to 45 mg or 90 mg ustekinumab injection compared with patients randomized to placebo when measured by the NAPSI score ($p\leq0.001$). Improvements in physical and mental component summary scores of the SF-36 and in the Itch Visual Analogue Scale (VAS) were also significant in each ustekinumab injection treatment group compared with placebo ($p<0.001$). In PHOENIX 2, the Hospital Anxiety and Depression Scale (HADS) and Work Limitations Questionnaire (WLQ) were also significantly improved in each ustekinumab injection treatment group compared with placebo ($p<0.001$).

ACCEPT

Significantly greater proportions of subjects treated with ustekinumab injection 45 mg (67%; $p = 0.012$) or 90 mg (74%; $p < 0.001$) were PASI 75 responders at Week 12 compared with the etanercept group (56.8%). PASI 90 response was observed in 36% and 45 % of patients in the ustekinumab injection 45 mg and 90 mg groups, respectively, compared with 23% of patients receiving etanercept ($p<0.001$ for

each comparison versus etanercept). PASI 100 response was observed in 12% and 21% of patients in the ustekinumab injection 45 mg and 90 mg groups, respectively, compared to 6% of patients receiving etanercept (Table 10). In addition, a greater proportion of patients in the ustekinumab injection 45 mg and 90 mg treatment groups achieved a PGA score of "cleared" or "minimal" (65 % and 71 %, respectively) compared with patients in the etanercept treatment group (49 %) (p<0.001 for each comparison versus etanercept).

Table 10: Clinical outcomes at Week 12: ACCEPT

	ACCEPT		
	Etanercept (50mg twice a week)	**Ustekinumab injection (at week 0 and week 4)**	
		45 mg	**90 mg**
Patients randomized	347	209	347
PASI response			
PASI 50 response	286 (82%)	181 (87%)	320 (92%)[a]
PASI 75 response	197 (57%)	141 (67%)[b]	256 (74%)[a]
PASI 90 response	80 (23%)	76 (36%)[a]	155 (45%)[a]
PASI 100 response	22 (6%)	25 (12%)[c]	74 (21%)[a]
PGA of Cleared or Minimal[a]	170 (49%)	136 (65%)[a]	245 (71%)[a]
PASI 75 RESPONSE BY WEIGHT			
≤ 100 kg			
N	251	151	244
PASI 75 response	154 (61%)	109 (72%)	189 (77%)
>100 kg			
N	96	58	103
PASI 75 response	43 (45%)	32 (55%)	67 (65%)
PGA OF CLEARED OR MINIMAL BY WEIGHT			
≤ 100 kg			
N	251	151	244
PGA response	131 (52%)	110 (73%)	185 (76%)
>100 kg			
N	96	58	103
PGA response	39 (41%)	26 (45%)	60 (58%)

[a] p <0.001 for ustekinumab injection 45 mg or 90 mg comparison with etanercept.

[b] p =0.012 for ustekinumab injection 45 mg comparison with etanercept.

[c] p =0.020 for ustekinumab injection 45 mg comparison with etanercept.

Greater proportions of subjects in the ustekinumab injection 45 mg and 90 mg groups achieved PASI 75 responses when compared with subjects in the etanercept group regardless of a subject's previous psoriasis medication history.

Psoriatic Arthritis

Study demographics and trial design

The safety and efficacy of ustekinumab injection was assessed in two multicenter, randomized, double-blind, placebo-controlled, phase 3 studies, PSUMMIT I and PSUMMIT II, in patients with active psoriatic arthritis. Patients were randomized to receive treatment with either ustekinumab injection 45 mg, 90 mg, or placebo subcutaneous injections at Weeks 0 and 4 followed by every 12 week (q12w) dosing. The primary endpoint in these studies was the reduction in the signs and symptoms of psoriatic arthritis (PsA) as measured by the percentage of ACR 20 responders at Week 24. Secondary endpoints included change from baseline in Disability Index of the Health Assessment Questionnaire (HAQ-DI), PASI 75, ACR 50, ACR 70 and change from baseline in total radiographic scores of the hands and feet at Week 24. Efficacy data were collected and analyzed through Week 52.

These studies included 927 adult patients (≥18 years) who had active psoriatic arthritis (≥5 swollen joints and ≥5 tender joints, despite disease modifying antirheumatic (DMARD) and/or nonsteroidal anti-inflammatory (NSAID) therapy. Methotrexate (MTX) use was allowed during the studies but was not mandatory. Approximately 50% of patients continued on stable doses of MTX (≤25 mg/week). In PSUMMIT I and PSUMMIT II, 80% and 86% of the patients, respectively, had been previously treated with DMARDs.

In PSUMMIT I patients, who had been previously treated with anti-TNFα therapy, prior to the first study dose, were excluded. In PSUMMIT II, the majority of patients (58%, n=180) had been previously treated with one or more an anti-TNFα agent(s) for at least 8 weeks (14 weeks with infliximab) or had discontinued anti-TNFα for intolerance at any time. Among the patients who had been previously treated with an anti-TNFα agent, over 70% had discontinued their anti-TNFα treatment for lack of efficacy or intolerance.

Patients with each subtype of psoriatic arthritis were enrolled, including polyarticular arthritis with no evidence of rheumatoid nodules (39%, N=362), spondylitis with peripheral arthritis (28%, N=255), asymmetric peripheral arthritis (21%, N=193), distal interphalangeal (DIP) arthritis (12%, N=112) and arthritis mutilans (0.5%, N=5). Over 70% and 40% of the patients in both studies had enthesitis and dactylitis at baseline, respectively.

Table 11: Summary of patient demographics in PSUMMIT I and PSUMMIT II

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n=number)	Mean age (Range)	Gender
CNTO1275 PSA3001 (PSUMMIT I)	Double-Blind Placebo-Controlled	Placebo SC (n=206): Placebo SC at Weeks 0, 4, 16, and 20 Placebo→45 mg SC at Weeks 24 and 28 followed by q12w dosing through Week 88 45 mg SC (n=205): 45 mg SC at Weeks 0 and 4 followed by q12w dosing through Week 88 90 mg SC (n=204): 90 mg SC at Weeks 0 and 4 followed by q12w dosing through Week 88	615	47.1 (18, 81)	M=330 F=285
CNTO1275 PSA3002 (PSUMMIT II)	Double-Blind Placebo-Controlled	Placebo SC (n=104): Placebo SC at Weeks 0, 4, 16, and 20 45 mg SC at Weeks 24 and 28 followed by q12w dosing through Week 40 45 mg SC (n=103): 45 mg SC at Weeks 0 and 4 followed by q12w dosing through Week 40 90 mg SC (n=105): 90 mg SC at Weeks 0 and 4 followed by q12w dosing through Week 40	312	48.0 (19, 75)	M=148 F=164

Study Results

Reduction in Signs and Symptoms

In both studies, a significantly greater proportion of patients achieved ACR 20 and ACR 50 responses at Week 24 in the ustekinumab injection 45 mg and 90 mg groups compared to placebo (see Table 12). In

PSUMMIT I, a significantly greater proportion of patients and in PSUMMIT II, a numerically greater proportion of patients (p=NS) achieved ACR 70 responses in the ustekinumab injection 45 mg and 90 mg groups compared to placebo (see Table 12).

Table 12: Number of patients who achieved ACR 20, ACR 50 and ACR 70 at Week 24

	PSUMMIT I			**PSUMMIT II**		
		Ustekinumab injection			**Ustekinumab injection**	
	Placebo (N=206)	**45 mg (N= 205)**	**90 mg (N= 204)**	**Placebo (N= 104)**	**45 mg (N= 103)**	**90 mg (N= 105)**
ACR 20	47 (23%)	87 (42%) [a]	101 (50%) [a]	21 (20%)	45 (44%)[a]	46 (44%) [a]
ACR 50	18 (9%)	51 (25%) [a]	57 (28%) [a]	7 (7%)	18 (17%) [b]	24 (23%) [a]
ACR 70	5 (2%)	25 (12%) [a]	29 (14%) [a]	3 (3%)	7 (7%) [c]	9 (9%) [c]

[a] p<0.001, [b] p<0.05, [c] p= NS

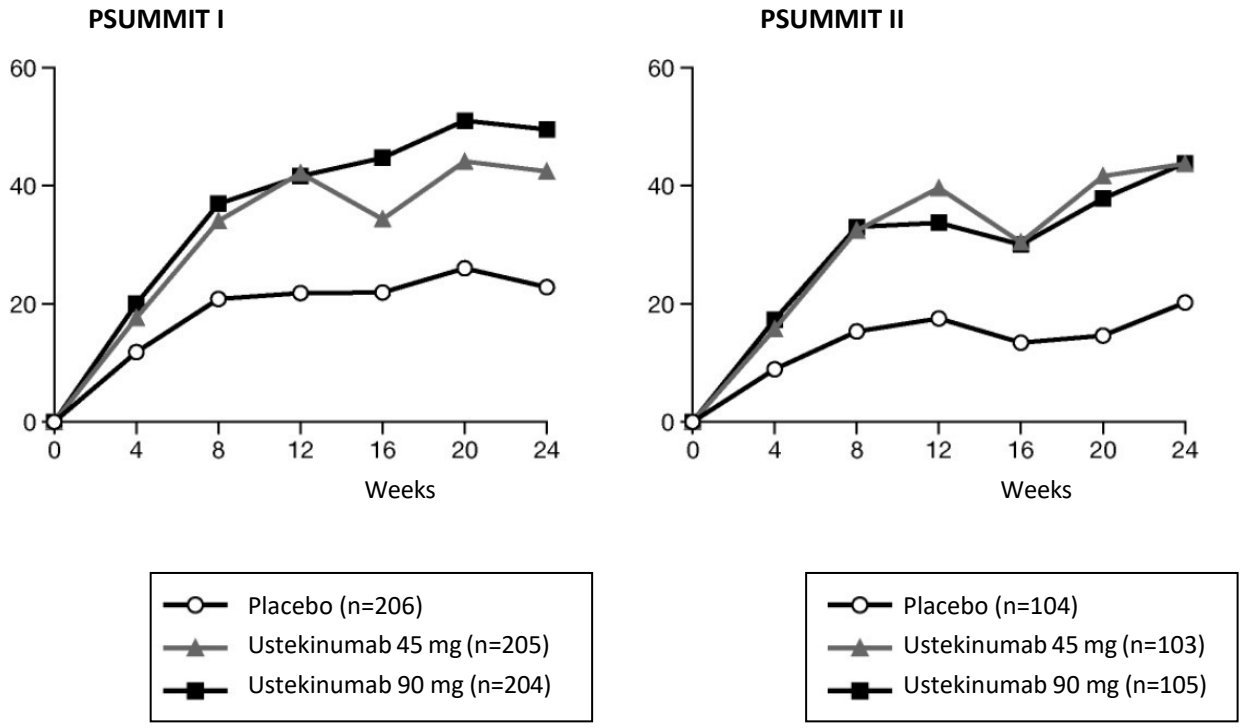
An ACR 20 response (Felson et al, 1995) was defined as:
1. ≥20% improvement in swollen joint count (66 joints) and tender joint count (68 joints); and
2. ≥20 % improvement in ≥3 of the following 5 assessments:

- Patient's assessment of pain [Visual Analog Scale (VAS)]
- Patient's global assessment of disease activity (VAS)
- Physician's global assessment of disease activity (VAS)
- Patient's assessment of physical function as measured by the HAQ-DI
- CRP

ACR 50 or ACR 70 are similarly defined.

The time course for ACR 20 response rates during the first 24 weeks in both studies for patients receiving ustekinumab injection or placebo are summarized in Figure 2.2. During the controlled phase of the studies, ACR 20 responses showed improvement at the first assessment (Week 4) and maximum responses were achieved at Week 20 or 24. ACR 20, 50 and 70 responses continued to improve or were maintained through Week 52.

Figure 2.2: Percent of patients achieving ACR 20 response through Week 24



In PSUMMIT I, of 205 subjects randomized to ustekinumab injection 45 mg, 153 continued the same dose and were available for evaluation at Week 52. Among those, ACR 20, 50 and 70 responses were achieved by 99 (64.7%), 57 (37.3%) and 34 (22.2%) subjects respectively. Of 204 subjects randomized to ustekinumab injection 90 mg, 185 were available for evaluation at Week 52. Among those, ACR 20, 50 and 70 responses were achieved by 120 (64.9%), 74 (40%) and 41 (22.2%) subjects respectively.

In PSUMMIT II, of 103 subjects randomized to ustekinumab injection 45 mg, 68 continued the same dose and were available for evaluation at Week 52. Among those, ACR 20, 50, and 70 responses were achieved by 41 (60.3%), 23 (33.8%) and 11 (16.2%) subjects respectively. Of 105 subjects randomized to ustekinumab injection 90 mg, 83 were available for evaluation at Week 52. Among those, ACR 20, 50 and 70 responses were achieved by 49 (59%), 26 (31.3%) and 17 (20.5%) subjects respectively.

Additionally, within each weight group (≤100 kg and >100 kg), ACR 20, ACR 50 and ACR 70 responses were consistently higher in the ustekinumab injection 45 mg and 90 mg groups than in the placebo group (see Table 13).

Table 13: Number of patients who achieved ACR 20, ACR 50 and ACR 70 responses by weight at Week 24

	PSUMMIT I			PSUMMIT II		
		Ustekinumab injection			Ustekinumab injection	
	Placebo (N=206)	45 mg (N= 205)	90 mg (N= 204)	Placebo (N= 104)	45 mg (N= 103)	90 mg (N= 105)
Patients randomized with weight ≤100 kg at baseline	154	153	154	74	74	73

Table 13: Number of patients who achieved ACR 20, ACR 50 and ACR 70 responses by weight at Week 24						
	PSUMMIT I			PSUMMIT II		
		Ustekinumab injection			Ustekinumab injection	
	Placebo (N=206)	45 mg (N= 205)	90 mg (N= 204)	Placebo (N= 104)	45 mg (N= 103)	90 mg (N= 105)
ACR 20	39 (25%)	67 (44%)	78 (51%)	17 (23%)	32 (43%)	34 (47%)
ACR 50	14 (9%)	38 (25%)	48 (31%)	6 (8%)	15 (20%)	21 (29%)
ACR 70	5 (3%)	20 (13%)	26 (17%)	3 (4%)	6 (8%)	8 (11%)
Patients randomized with weight >100 kg at baseline	52	52	50	30	29	31
ACR 20	8 (15%)	20 (38%)	23 (46%)	4 (13%)	13 (45%)	12 (39%)
ACR 50	4 (8%)	13 (25%)	9 (18%)	1 (3%)	3 (10%)	3 (10%)
ACR 70	0	5 (10%)	3 (6%)	0	1 (3%)	1 (3%)

Ustekinumab injection treatment resulted in significantly greater improvement compared with placebo for each ACR component at week 24 (see Table 14).

Table 14: Median percent improvement from baseline in ACR components at Week 24						
	PSUMMIT I			PSUMMIT II		
		Ustekinumab injection			Ustekinumab injection	
	Placebo (N=206)	45 mg (N= 205)	90 mg (N= 204)	Placebo (N=104)	45 mg (N= 103)	90 mg (N= 105)
Number of swollen joints [d]	21.54	58.82 [a]	60.00 [a]	0.00	52.94 [b]	50.00 [c]
Number of tender joints [e]	13.61	45.45 [a]	51.51 [a]	0.00	33.33 [a]	35.00 [c]
Patient's assessment of pain [f]	0.00	31.33 [a]	42.58 [a]	0.00	24.19 [a]	24.29 [a]
Patient global assessment [f]	4.11	32.84 [a]	42.44 [a]	0.00	21.25 [a]	22.54 [a]
Physician global assessment [f]	17.64	48.39 [a]	55.91 [a]	0.83	36.67 [a]	36.11 [a]
Disability index (HAQ-DI)g	0.00	22.22 a	32.46 a	0.00	12.50 a	14.29 a
CRP (mg/dL) h	0.00	38.56 a	48.30 a	0.00	25.61 c	33.69 a

[a] p<0.001

[b] p<0.05

[c] p<0.01

[d] Number of swollen joints counted (0-66)

[e] Number of tender joints counted (0-68)

[f] Visual analogue scale; 0= best, 10=worst.

[g] 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.

[h] CRP: (Normal Range 0.0-1.0 mg/dL)

In PSUMMIT I and PSUMMIT II, the proportion of subjects with good or moderate Disease Activity Index Score 28 using C-reactive protein (DAS28-CRP) responses and the proportion of subjects in DAS28 remission were greater in both ustekinumab injection-treated groups compared to placebo at Week 24. DAS28-CRP responses were maintained through Week 52.

Methotrexate Use

The proportion of patients achieving ACR responses were consistently greater in patients treated with ustekinumab injection than those treated with placebo regardless of concomitant MTX use.

Responses observed in the ustekinumab injection groups were similar in patients receiving or not receiving concomitant MTX. ACR responses were maintained through Week 52.

Table 15: Summary of patients achieving ACR 20, ACR 50 and ACR 70 responses through Week 24 by methotrexate usage

PSUMMIT I						
	Receiving MTX at baseline			*Not receiving MTX at baseline*		
		Ustekinumab injection			**Ustekinumab injection**	
	Placebo (N=206)	**45 mg (N= 205)**	**90 mg (N= 204)**	**Placebo (N=206)**	**45 mg (N= 205)**	**90 mg (N= 204)**
Patients randomized	96	99	101	110	106	103
ACR 20	25 (26%)	43 (43%)	46 (46%)	22 (20%)	44 (42%)	55 (53%)
ACR 50	8 (8%)	23 (23%)	27 (27%)	10 (9%)	28 (26%)	30 (29%)
ACR 70	2 (2%)	11 (11%)	13 (13%)	3 (3%)	14 (13%)	16 (16%)
PSUMMIT II						
	Receiving MTX at baseline			*Not receiving MTX at baseline*		
		Ustekinumab injection			**Ustekinumab injection**	
	Placebo (N=104)	**45 mg (N= 103)**	**90 mg (N= 105)**	**Placebo (N=104)**	**45 mg (N= 103)**	**90 mg (N= 105)**
Patients randomized	49	54	52	55	49	53
ACR 20	14 (29%)	27 (50%)	21 (40%)	7 (13%)	18 (37%)	25 (47%)
ACR 50	4 (8%)	10 (19%)	12 (23%)	3 (5%)	8 (16%)	12 (23%)
ACR 70	2 (4%)	4 (7%)	3 (6%)	1 (2%)	3 (6%)	6 (11%)

Prior Anti-TNFα therapy

PSUMMIT II evaluated 180 patients who were previously treated with one or more anti-TNFα agents for at least 8 weeks (14 weeks with infliximab) or had documented intolerance of anti- TNFα therapy at any time in the past.

Among patients previously treated with anti-TNFα agents, a greater proportion of ustekinumab injection- treated patients in both the 45 mg and 90 mg groups achieved an ACR 20 response at Week 24 compared to placebo (37% and 34% vs 15%). ACR 20 response was generally maintained through Week 52.

Enthesitis and Dactylitis

For patients with enthesitis and/or dactylitis at baseline, in PSUMMIT I, greater improvement in

enthesitis and dactylitis score was observed in the ustekinumab injection 45 mg and 90 mg groups compared to placebo. For enthesitis, the median improvement was 43% and 50% for each dose group respectively, compared to 0% for placebo. For dactylitis, the median improvement was 75% and 71% for each dose group respectively, compared to 0% for placebo. In PSUMMIT II, a greater improvement was observed in enthesitis score in both doses and in dactylitis score in the 90 mg group compared with the placebo group. In both studies, improvement in enthesitis score and dactylitis score were maintained at Week 52.

Psoriasis Skin Response

In PSUMMIT I and PSUMMIT II, the proportion of patients with psoriasis involvement of ≥3% BSA at baseline who achieved a ≥75% improvement in the PASI assessment at Week 24 was significantly greater in the ustekinumab injection 45 mg and 90 mg groups compared with the placebo group (see Table 16). In both studies the proportion of patients achieving the PASI 75 response was maintained through Week 52.

Table 16: Number of patients who achieved PASI 75, PASI 90 and PASI 100 responses at Week 24

	PSUMMIT I			**PSUMMIT II**		
		Ustekinumab injection [a]			**Ustekinumab injection [a]**	
	Placebo (N= 206)	**45 mg (N=205)**	**90 mg (N=204)**	**Placebo (N= 104)**	**45 mg (N=103)**	**90 mg (N=105)**
Patients with ≥3% BSA psoriasis skin involvement at baseline	146	145	149	80	80	81
PASI 75	16 (11%)	83 (57%)	93 (62%)	4 (5%)	41 (51%)	45 (56%)
PASI 90	4 (3%)	60 (41%)	65 (44%)	3 (4%)	24 (30%)	36 (44%)
PASI 100	2 (1%)	29 (20%)	41 (28%)	1 (1%)	13 (16%)	17 (21%)

[a] $p<0.001$ for 45 mg or 90 mg comparison with placebo.

Additionally, within each weight group (≤100 kg and >100 kg), PASI 75, 90 and 100 responses were consistently higher in the ustekinumab injection 45 mg and 90 mg groups than in the placebo group. In both studies, the proportion of patients who achieved a PASI 75 response at Week 24 was consistently higher in ustekinumab injection 45 mg and 90 mg groups compared with placebo regardless of concomitant MTX use. PASI 75 responses were maintained through Week 52.

Radiographic Response

Structural damage in both hands and feet was assessed by readers unaware of treatment group and order of visits, and expressed as change in total van der Heijde-Sharp score (vdH-S score), modified for PsA by addition of hand distal interphalangeal (DIP) joints, compared to baseline. A pre-specified major secondary endpoint based on the integrated analysis combining data from 927 subjects in both PSUMMIT I and PSUMMIT II was performed. At Week 24, based on this integrated analysis, patients treated with either ustekinumab injection 45 mg (n=308, mean change in total vdH-S score=0.40) or 90 mg (n=309, mean change=0.39) demonstrated significantly less progression of structural damage compared to placebo (n=310, mean change=0.97), $p<0.05$ and $p<0.001$ for the 45 mg and 90 mg groups, respectively. This effect was demonstrated irrespective of concomitant MTX use, and was maintained through Week 52.

Similar results were seen in PSUMMIT I for patients treated with either ustekinumab injection 45 mg (n=205, mean change=0.28) or 90 mg (n=204, mean change=0.17) compared to placebo (n=206, mean change=1.20). In PSUMMIT II, the mean change was 0.66 for 45 mg (n=103), 0.81 for 90 mg (n=105) and 0.51 for placebo (n=104).

Physical Function and Health-Related Quality of Life

In PSUMMIT I and PSUMMIT II, physical function and health-related quality of life were assessed using the Disability Index of the Health Assessment Questionnaire (HAQ-DI) and the SF-36 health survey.

Patients treated with ustekinumab injection 45 mg and 90 mg showed significant improvement in physical function as assessed by the HAQ-DI at Week 24 as compared to placebo in both PSUMMIT I and PSUMMIT II. The proportion of patients achieving a clinically meaningful ≥0.3 improvement in HAQ-DI score from baseline at Week 24 was also significantly greater in the ustekinumab injection groups when compared with placebo. Improvement was observed at the first assessment (Week 4), reached maximum at Week 12 and was maintained through Week 24. In both studies the improvement in HAQ-DI at Week 24 was consistently greater in the ustekinumab injection 45 mg and 90 mg groups compared with placebo regardless of concomitant MTX use. Improvement in HAQ-DI score from baseline was maintained at Week 52.

Table 17: Improvement in physical function as measured by HAQ-DI at Week 24

	PSUMMIT I			**PSUMMIT II**		
		Ustekinumab injection			**Ustekinumab injection**	
	Placebo (N= 206)	**45 mg (N=205)**	**90 mg (N=204)**	**Placebo (N= 104)**	**45 mg (N=103)**	**90 mg (N=105)**
HAQ-DI Baseline Score						
N	204	205	204	104	103	104
Mean (SD)	1.24 (0.647)	1.22 (0.610)	1.22 (0.634)	1.25 (0.723)	1.34 (0.704)	1.29 (0.666)
Median	1.25	1.25	1.25	1.25	1.38	1.25
Improvement in HAQ-DI						
N[c]	206	205	204	104	103	105
Mean (SD)	0.10 (0.390)	0.31 (0.521)	0.40 (0.514)	0.03 (0.380)	0.21 (0.461)	0.22 (0.436)
Median	0.00	0.25 [a]	0.25 [a]	0.00	0.13 [b]	0.25 [a]
HAQ-DI Responders*	58 (28%)	98 (48%)[a]	97 (48%)[a]	17 (16%)	35 (34%)[b]	40 (38%)[a]

[a] p<0.001

[b] p<0.01

[c] Includes all randomized subjects

*achieving a ≥0.3 improvement from baseline

In PSUMMIT I, of 205 subjects randomized to ustekinumab injection 45 mg, 153 continued the same dose and were available for evaluation at Week 52. Among those, the HAQ-DI response was achieved by 83 (54.2%) subjects. Of 204 subjects randomized to ustekinumab injection 90 mg, 185 were available for evaluation at Week 52. Among those, HAQ-DI response was achieved by 102 (55.1%) subjects.

In PSUMMIT II, of 103 subjects randomized to ustekinumab injection 45 mg, 68 continued the same dose and were available for evaluation at Week 52. Among those, the HAQ-DI response was achieved

by 29 (42.6%) subjects. Of 105 subjects randomized to ustekinumab injection 90 mg, 83 were available for evaluation at Week 52. Among those, HAQ-DI response was achieved by 44 (53%) subjects.

In both PSUMMIT I and PSUMMIT II, at Week 24, the change from baseline in the SF-36 physical component summary (PCS) scores was significantly greater in the ustekinumab injection 45 mg and 90 mg groups compared with the placebo group. In both studies, the change from baseline in the SF-36 mental component summary (MCS) scores at Week 24 was greater in both ustekinumab injection groups compared with the placebo group. In both studies, the change from baseline in the SF-36 PCS and MCS scores was maintained at Week 52.

The DLQI was assessed by comparing the change in DLQI scores from baseline for those patients with ≥3% BSA at baseline. In both studies at Week 24, there was a greater improvement from baseline in DLQI scores in both the ustekinumab injection 45 mg and 90 mg groups as compared with placebo and the improvement was maintained at Week 52.

In PSUMMIT II, the improvement from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores at Week 24 was greater in the ustekinumab injection 45 mg and 90 mg groups compared with the placebo group. Similarly, the percentage of patients with clinically meaningful improvement in fatigue from baseline (4 points in FACIT-F) was greater in both dose groups compared with the placebo group. The change from baseline in the FACIT-F scores was maintained at Week 52.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

The toxicity of ustekinumab was specifically evaluated in a number of nonclinical studies. An overview of these toxicity studies is provided in Table 18.

General Toxicology: In repeated-dose toxicity studies in cynomolgus monkeys, ustekinumab was well tolerated following IV doses up to 45 mg/kg/week for up to 1 month and following twice-weekly SC doses up to 45 mg/kg for 6 months. There were no ustekinumab-related findings in the immunotoxicity and cardiovascular safety pharmacology evaluations. In histopathology evaluations there were no preneoplastic changes observed. No evidence of ustekinumab-related local intolerance was observed in examinations of subcutaneous injection sites in a local tolerance study and in the chronic subcutaneous toxicity study.

The 45 mg/kg dose is approximately 45-fold higher than the highest equivalent dose intended to be administered to patients with psoriasis (based on administration of a 90 mg SC dose to a 90 kg patient) and the average C_{max} value observed following the last SC 45 mg/kg dose in the 6-month chronic toxicity study in cynomolgus monkeys was approximately 118-fold higher than the median C_{max} value of ustekinumab observed following 4 weekly 90 mg SC doses in psoriasis patients.

Carcinogenicity: No carcinogenicity studies have been conducted with ustekinumab.

Genotoxicity: No genotoxicity studies have been conducted with ustekinumab.

Reproductive and Developmental Toxicology: Three developmental toxicity studies were conducted in cynomolgus monkeys. No ustekinumab-related maternal toxicity, abortions, still-births, embryotoxicity, developmental delays, malformations or birth defects were observed at doses up to 45 mg/kg following weekly or twice weekly administration of ustekinumab via the IV or SC routes, respectively. In neonates

born from pregnant monkeys treated with ustekinumab, no adverse effects on growth or functional development were observed and no deficits were observed in immunotoxicity evaluations. In a male fertility study in cynomolgus monkeys, no ustekinumab-related effects on mating behaviour, sperm parameters, or serum concentrations of male hormones were observed following twice weekly subcutaneous administration of ustekinumab at doses up to 45 mg/kg.

A female fertility toxicity study was conducted in mice using an analogous antibody that binds to and inhibits IL-12 and IL-23 activity in mice. Twice weekly subcutaneous administration of the anti-mouse IL-12/23 antibody was well tolerated at doses up to 50 mg/kg and no adverse effects on female fertility parameters were observed.

Table 18: Non-Clinical Toxicology Studies with ustekinumab

Study	Species/ Strain	Route	Duration of Dosing	Doses(mg/kg)	Results
Repeat-Dose Toxicity					
Subchronic toxicity	Monkey/ Cynomolgus	IV	1 month	9, 45 weekly	No treatment-related signs of toxicity.
Subchronic toxicity	Monkey/ Cynomolgus	IV	1 month	9, 45 weekly	No treatment-related signs of toxicity.
Chronic toxicity	Monkey/ Cynomolgus	SC	6 months	22.5, 45 twice weekly	No treatment-related signs of toxicity. No preneoplastic changes observed on histopathology.
Reproductive and Developmental Toxicity					
Embryofetal Development	Monkey/ Cynomolgus	IV	Pregnant females: gestation day 20 to gestation day 50	9, 45 weekly	No maternal or fetal abnormalities were observed.
Embryofetal Development	Monkey/ Cynomolgus	SC	Pregnant females: gestation day 20 – gestation day 51	22.5, 45 twice weekly	A statistically significant increase in maternal 17ß-estradiol levels relative to the control group was observed on days 80 and 100 of gestation in the 22.5 and 45 mg/kg groups. However, foetal 17ß-estradiol levels were not affected, and there were no other treatment-related maternal or foetal abnormalities observed at either dose level.
Male fertility	Monkey/ Cynomolgus	SC	Males: 13 weeks	22.5, 45 twice weekly	No changes in fertility parameters observed.
Female fertility	Mouse/Crl CD-1	SC	beginning 15 days before cohabitation and continuing through day 7 of presumed gestation	25, 50 twice weekly	No maternal or fetal abnormalities were observed.
Embryofetal and pre- and postnatal development	Monkey/ Cynomolgus	SC	Pregnant females: gestation day 20 – postpartum day 30	22.5, 45 twice weekly	No effects on pregnancy or delivery; or morphological, functional and immunological developmental parameters of offspring. Ustekinumab was detected in the

					milk of lactating monkeys.
Local Tolerance					
Pharmacokinetics and injection site irritation	Monkey/ Cynomolgus	SC	18 days	45 twice weekly	Minimal signs of local irritation at injection sites were observed, with no associated histopathologic findings.
Other Toxicity Studies					
Tissue cross-reactivity	Human Tissues	In vitro		1.13,11.3, 113, 225 mg/mL	No binding to nontarget normal human tissues.
Tissue cross-reactivity	Human Tissues	In vitro		1.13,11.3, 113, 225 mg/mL	No binding to nontarget normal human tissues
Asthma model	Monkey/ Cynomolgus	IV	Single dose	9, 45	No exacerbation of pulmonary function or cellular responses.
Asthma model	Monkey/ Cynomolgus	IV	1 week	45	No exacerbation of pulmonary function or cellular responses.

17 SUPPORTING PRODUCT MONOGRAPHS

1. PrSTELARA® (ustekinumab injection, 45 mg/0.5 mL. 90 mg/ 1.0 mL), submission control 267288, Product Monograph Janssen Inc. [January 5, 2023]

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]Jamteki™

Ustekinumab injection, Solution for Subcutaneous Injection

Read this carefully before you start taking **Jamteki** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Jamteki**.

Jamteki is a biosimilar biologic drug (biosimilar) to the reference biologic drug Stelara®. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.

What is Jamteki used for?

Adults with Plaque Psoriasis

Jamteki is a prescription medicine that is approved for adults with moderate to severe plaque psoriasis that is chronic (doesn't go away).

Adults with Psoriatic Arthritis

Jamteki is a prescription medicine that is approved for adults with active psoriatic arthritis.

Psoriatic arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. If you have active psoriatic arthritis, you will be given Jamteki by injection under the skin, alone or in combination with methotrexate, to reduce signs and symptoms of your arthritis, help improve your ability to perform daily activities (such as dressing, walking and climbing stairs) and improve your psoriasis.

How does Jamteki work?

Jamteki blocks the action of two proteins in your body called interleukin 12 (IL-12) and interleukin 23 (IL-23). In people with psoriasis or psoriatic arthritis, their immune system may attack parts of their body and that attack uses IL-12 and IL-23. Ustekinumab can block the IL-12 and IL-23 from causing the immune system to attack the skin, nails or joints.

What are the ingredients in Jamteki?

Medicinal ingredient: ustekinumab

Non-medicinal ingredients: L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose, and water for injection. No preservatives are present.

Jamteki comes in the following dosage forms:

Pre-filled Syringe:

- 45 mg / 0.5 mL
- 90 mg / mL

Do not use Jamteki if:

- you have a serious infection such as tuberculosis, infections caused by bacteria or fungi, and bacterial infections that have spread throughout the body (sepsis).

- you have had an allergic reaction to Jamteki, or any of the other ingredients in Jamteki including components of the container. The needle cover on the pre-filled syringe is not made with natural rubber latex. See above for a complete list of ingredients in Jamteki.
- after the expiration date on the label.
- the seal is broken.
- the liquid is discoloured, cloudy or you can see other particulate matter floating in it.
- you know or think that it may have been exposed to extreme temperatures (such as accidentally frozen or heated).

You should not receive a live vaccine while taking Jamteki.

If you used Jamteki while pregnant, tell your baby's healthcare professional about your Jamteki use before the baby receives any vaccine, including live vaccines, such as the BCG vaccine (used to prevent tuberculosis), rotavirus vaccine, or any other live vaccines.

Always keep medicine out of the reach and sight of children.

To help avoid side effects and ensure proper use, talk to your health care professional before you take Jamteki. Talk about any health conditions or problems you may have, including if you:

- ever had an allergic reaction to Jamteki. Ask your doctor if you are not sure.
- have any kind of infection even if it is very minor.
- have an infection that won't go away or a history of infection that keeps coming back.
- have burning when you urinate.
- have diarrhea or abdominal pain.
- have had TB (tuberculosis), notice blood in your phlegm or if you have recently been near anyone who might have TB.
- have or have had any type of cancer.
- have any new or changing skin lesions.
- have recently received or are scheduled to receive a vaccine. Tell your doctor if anyone in your house needs a vaccine. The viruses in some vaccines can spread to people with a weakened immune system and can cause serious problems.
- are receiving or have received "allergy shots", especially for serious allergic reactions.
- are pregnant, think you might be pregnant, planning to become pregnant, or breastfeeding. Jamteki may pass into your breast milk in small amounts.

Your doctor will assess your health before each treatment.

Contact your doctor immediately:

- if you develop signs of a serious allergic reaction such as skin rash, swollen face, lips, mouth, throat, wheezing, dizziness, trouble swallowing or breathing.
- if you develop headache, vision problems, seizures or change in mental status (for example, confusion).

There is limited experience with Jamteki in pregnant and breastfeeding women. If you are a woman of childbearing potential, you should use effective contraception when starting Jamteki and talk to your doctor before planning to conceive a child. If you are pregnant or breastfeeding, your doctor will help you decide whether or not to use Jamteki.

Tell your health care professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Jamteki:

- Jamteki may change the way the body responds to live vaccines.
- Jamteki may interact with other medications that decrease the activity of the immune system.

Know the medicines you take. Keep a list of your medicines and show them to your doctor and pharmacist when you get a new medicine.

If you have questions, ask your health care provider.

How to take Jamteki:

Instructions for injecting Jamteki under the skin yourself:

Jamteki may be injected by your healthcare provider.

However, your doctor may decide that it is right for you or your caregiver to learn how to inject Jamteki under the skin (subcutaneously) yourself. Before you self-inject Jamteki, you must be trained by a healthcare professional. If you or your caregiver have not been trained, please contact your healthcare provider to schedule a training session. Call your healthcare provider if you have any questions about giving yourself an injection. Jamteki is not to be mixed with other liquids for injection.

INSTRUCTIONS FOR INJECTING JAMTEKI USING A PRE-FILLED SYRINGE

To reduce the risk of accidental needle sticks to users, each pre- filled syringe is equipped with a needle guard that is automatically activated to cover the needle after complete delivery of the syringe content.

Do not shake Jamteki at any time. Prolonged vigorous shaking may damage the product. If the product has been shaken vigorously, don't use it.

1: PREPARING FOR PRE-FILLED SYRINGE USE

Take the Syringe out of the Refrigerator

If your dose amount is 90 mg and you receive two 45 mg packages, you need to give a second injection right after the first. Choose a different site for the second injection.

Check Expiration Date

Open the box and remove the pre-filled syringe. Check the expiration date on the pre-filled syringe and the label of the box. If the expiration date has passed, or if the pre-filled syringe has been kept at room temperature up to 30°C for longer than 30 days or if the pre-filled syringe has been stored above 30°C, DO NOT use the pre-filled syringe.

Assemble Additional Supplies

Assemble the additional supplies you will need for your injection. These include an antiseptic wipe, a cotton ball or gauze, and a sharps container for syringe disposal.

Check Solution in Syringe

Hold the pre-filled syringe with the covered needle pointing upward. Make sure the syringe is not damaged. Look at the solution or liquid in the syringe to make sure that it is clear to slightly opalescent and colourless to slightly yellow. DO NOT use if it is frozen, discoloured, cloudy or contains particles and contact your healthcare provider for assistance.

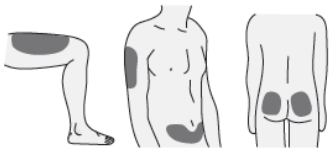
DO NOT remove the needle cover from the pre-filled syringe.

DO NOT pull back on the plunger head at any time.

2: CHOOSING AND PREPARING THE INJECTION SITE

Choose the Injection Site*

Good sites are the top of the thigh and around the tummy (abdomen) but about 2 inches away from the belly button (navel). Avoid, if possible, skin involved with psoriasis. If your caregiver is giving you the injection, they may use the upper arms or buttocks as well.

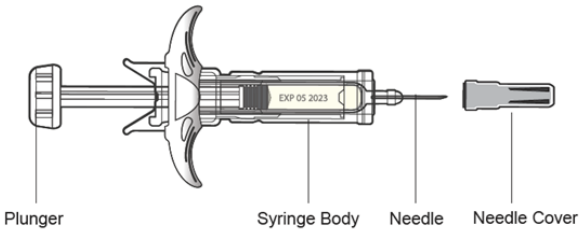


Areas in Dark Grey are recommended injection sites.

Prepare the Injection Site

Thoroughly wash your hands with soap and warm water. Wipe the injection site with an antiseptic wipe. DO NOT touch this area again before giving the injection.

3: INJECTING THE MEDICATION



Remove the Needle Cover

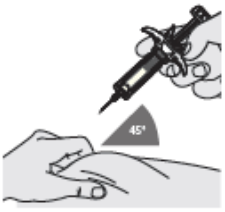
When you are ready to inject, pick up the pre-filled syringe, hold the SYRINGE BODY and remove the NEEDLE-COVER. **Do not hold the PLUNGER while removing the NEEDLE COVER or the PLUNGER may move. Do not use the pre-filled syringe if it is dropped without the NEEDLE COVER in place.**

Inject the Medication

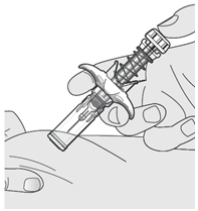
Gently pinch the cleaned skin between your thumb and index finger. Don’t squeeze it.

Push the syringe needle into the pinched skin.

- Inject all of the medication by pushing in the PLUNGER until the pre-filled syringe is empty. **Injection of the entire prefilled syringe contents is necessary to activate the passive safety device guard.**



After injection, maintain the pressure on the PLUNGER and remove the needle from the skin. Slowly take your thumb off the PLUNGER. The PLUNGER will move up with your thumb and retract the needle into the needle guard, as shown by the illustration below.



4: AFTER THE INJECTION

Dispose of the Empty Syringe

Immediately dispose of the empty syringe into the sharps container. For your safety and health and for the safety of others, needles and syringes **must NEVER** be re-used. Dispose of sharps container according to your local regulations.

Use a Cotton Ball or Gauze

There may be a small amount of blood or liquid at the injection site, which is normal. You can press a cotton ball or gauze over the injection site and hold for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if necessary.

Usual dose:

Psoriasis

For treatment of psoriasis, Jamteki is given by injection under the skin.

Adults:

The recommended dose of Jamteki is 45 mg at Weeks 0 and 4 then every 12 weeks thereafter. Your doctor may consider treating you as often as every 8 weeks.

90 mg may be used in patients with a body weight greater than 100 kg.

Psoriatic Arthritis

Adults:

For treatment of psoriatic arthritis, Jamteki is given by injection under the skin. The recommended dose of Jamteki is 45 mg at Weeks 0 and 4 then every 12 weeks thereafter.

Alternatively, 90 mg may be used in patients with a body weight greater than 100 kg.

JAMP Care has been established to facilitate the administration of Jamteki. JAMP Care is staffed by qualified health care professionals specially trained in the administration of Jamteki. Contact your doctor if you have any questions.

Overdose:

Call your doctor if you accidentally inject Jamteki more frequently than instructed.

If you think you, or a person you are caring for, have taken too much Jamteki, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose, contact your health care provider for guidance.

What are possible side effects from using Jamteki?

These are not all the possible side effects you may have when taking Jamteki. If you experience any side effects not listed here, tell your health care professional.

The most common side effects of Jamteki are:

- Upper respiratory tract infections such as the common cold
- Infection of the nose and throat
- Dizziness
- Headache
- Sore throat
- Diarrhea
- Nausea
- Vomiting
- Itching
- Back pain
- Muscle aches
- Joint pain
- Feeling very tired
- Redness of the skin where the injection is given
- Pain where the injection is given
- Sinus infection

Jamteki is a medicine that affects your immune system. It can increase your risk of getting serious side effects including:

Serious Infections

- Jamteki may lower your ability to fight infections. Some infections could become serious and lead to hospitalization. If you have an infection or have any open cuts, tell your health care provider before you start using Jamteki. If you get an infection, have any sign of an infection such as fever, feel very tired, cough, flu-like symptoms, or warm, red, or painful skin or sores on your body, tell your health care provider right away. These may be signs of infections such as chest infections, or skin infections or shingles that could have serious complications.

- Your doctor will examine you for tuberculosis (TB) and perform a test to see if you have TB. If your doctor feels that you are at risk for TB, you may be treated with medicine for TB before you begin treatment with Jamteki and during treatment with Jamteki.

Cancers

- Jamteki may decrease the activity of your immune system, and increase the risk for certain types of cancer. Tell your doctor if you notice any unusual changes to your skin or health status while receiving Jamteki treatment.

Serious Skin Conditions

Shedding of skin – increase in redness and shedding of skin over a larger area of the body may be symptoms of erythrodermic psoriasis or exfoliative dermatitis, which are serious skin conditions. You should contact your doctor immediately if you notice any of these signs.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your health care professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON (>10%)			
Infected nose, sinuses or throat (cold)	√		
COMMON (≥1% and <10%)			
Sore throat, nasal congestion	√		
Allergic reaction (skin rash)		√	
UNCOMMON (≥0.1% and <1%)			
Cellulitis (skin infection)		√	
Vaginal yeast infections	√		
Tooth abscess/tooth infection		√	
RARE (≥0.01% and <0.1%)			
Serious allergic reactions (e.g.: swollen face or trouble breathing; symptoms such as cough, shortness of breath, and fever may also be a sign of an allergic lung reaction)			√
Increase in redness and shedding of skin		√	

This is not a complete list of side effects. For any unexpected effects while taking Jamteki, contact your doctor or pharmacist.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your health care professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

If you are using Jamteki at home, it is important to store the product in your refrigerator at 2-8°C although not in the freezer compartment. Jamteki should not be frozen. Keep the product in the original carton to protect from light until the time of use. Do not shake.

If needed, individual Jamteki pre-filled syringes may also be stored at room temperature up to 30°C for a maximum single period of up to 30 days in the original carton with protection from light. Record the date when the pre-filled syringe is first removed from the refrigerator and the new expiry date on the carton in the spaces provided. The new expiry date must not exceed the original expiry date printed on the carton. Once a syringe has been stored at room temperature, it should not be returned to the refrigerator. Discard the syringe if not used within 30 days at room temperature storage.

Always keep medicine out of the reach and sight of children.

If you want more information about Jamteki:

- Talk to your health care professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by calling 1-866-399-9091.

This leaflet was prepared by JAMP Pharma Corporation.

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