PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrSILIQ®

Brodalumab Injection
Solution for Subcutaneous Injection, 140 mg/mL

Biological Response Modifier

Bausch Health, Canada Inc.
2150 St-Elzear Blvd. West
Laval, Quebec
H7L 4A8

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RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS, Immune, Hypersensitivity	10/2023

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

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

- SILIQ brodalumab injection) is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

1.1 Pediatrics (< 18 years of age)

The safety and efficacy of SILIQ in children below the age of 18 years have not yet been established. No data are available.

1.2 Geriatrics (≥ 65 years of age)

No dose adjustment is recommended in geriatric patients (see 10 CLINICAL PHARMACOLOGY).

2 CONTRAINDICATIONS

SILIQ (brodalumab) is contraindicated in:

- patients who are hypersensitive to brodalumab or to any ingredient in the formulation or component of the container. For a complete listing, see the 6 DOSAGE FORMS, COMPOSITION AND PACKAGING section of the product monograph.
- patients with Crohn's disease (see 7 WARNINGS AND PRECAUTIONS).

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

Suicidal ideation and behavior, including completed suicides, have occurred in patients treated with SILIQ. A causal association between treatment with SILIQ and increased risk of suicidal ideation and behaviour has not been established. Prior to prescribing SILIQ, weigh the potential risks and benefits in patients with a history of depression and/or suicidal ideation or behavior. Patients with new or worsening suicidal ideation and behavior should be referred to a mental health professional, as appropriate. Advise patients and caregivers to seek medical attention for manifestations of suicidal ideation or behavior, new onset or worsening depression, anxiety, or other mood changes (see 7 WARNINGS AND PRECAUTIONS, Psychiatric).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

SILIQ (brodalumab injection) is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject SILIQ when deemed appropriate by a healthcare professional and after proper training in subcutaneous injection technique using the prefilled syringe. Patients should be instructed to inject the full dose of SILIQ according to the instructions provided in the package leaflet. Comprehensive instructions for administration are

given in the package leaflet (see PATIENT MEDICATION INFORMATION).

If an adequate response has not been achieved after 12 to 16 weeks of treatment with SILIQ, consider discontinuing therapy. Continued treatment beyond 16 weeks in patients who have not achieved an adequate response is not likely to result in greater success.

4.2 Recommended Dose and Dosage Adjustment

The recommended SILIQ dose is 210 mg administered by subcutaneous injection at Weeks 0, 1, and 2 followed by 210 mg every 2 weeks.

Each 210 mg dose is given as one subcutaneous injection of single-use prefilled syringe (1.5 mL).

4.4 Administration

SILIQ is administered subcutaneously (SC). Each prefilled syringe is for single use only.

Do not inject SILIQ into areas where the skin is tender, bruised, red, hard, thick, scaly, or affected by psoriasis.

Instruction on Injection Technique

- Advise patients to read the 'Instructions for Use' before administration.
- Instruct the patient to perform the first self-injection under the guidance and supervision of a qualified healthcare professional for proper training in subcutaneous injection technique. Assess a patient or their caregiver's ability to inject subcutaneously (see PATIENT MEDICATION INFORMATION).
- Instruct patients who are self-administering to inject the full dose of SILIQ (see PATIENT MEDICATION INFORMATION).

5 OVERDOSAGE

Doses up to 700 mg intravenously have been administered in clinical trials with no evidence of dose limiting toxicity. In the event of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required.

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

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous injection	Sterile solution in single-use prefilled syringe / 210 mg of brodalumab in 1.5 mL solution.	Glutamate, Polysorbate 20, Proline, and Water for injections

Description

Brodalumab is a human monoclonal immunoglobulin (Ig) G2 antibody directed against human interleukin 17 Receptor A (IL-17RA). It is expressed in a Chinese Hamster Ovary (CHO) cell line. Brodalumab is comprised of 1312 amino acids and has an estimated molecular mass of 144,000 Daltons.

SILIQ is a sterile solution that is clear to slightly opalescent, colorless to slightly yellow liquid, practically free from particles.

Each SILIQ single-use prefilled syringe contains 210 mg of brodalumab.

SILIQ is supplied as:

- 1.5 mL solution (140 mg/mL brodalumab) in a single-use syringe made from type 1 glass with stainless steel 27G x ½" needle.
- SILIQ single-use prefilled syringe is formulated in Proline (36 mg / 2.4% w/v), Glutamate (6.5 mg / 30 mM), Polysorbate 20 (0.15 mg / 0.01% w/v), and Water for Injections (to target volume). The resulting pH is 4.8.
- SILIQ 210 mg solution for injection in a pre-filled syringe is available in a pack containing 2 pre-filled syringes.
- SILIQ does not contain preservatives.

7 WARNINGS AND PRECAUTIONS

General

The SILIQ Patient Support Program is a comprehensive program that supports patients and healthcare professionals with the prescribing, administration, and monitoring of patients who receive SILIQ treatment. Prescribers are to register in the SILIQ Patient Support Program before prescribing SILIQ (brodalumab injection). Prescribers are educated regarding the appropriate use of SILIQ and are expected to educate patients on the benefits and risks of treatment, especially the risk of suicidal ideation and behavior.

Patients who are prescribed SILIQ are to enroll in the SILIQ Patient Support Program by filling in the program enrollment form or by calling at 844 852 6967.

Carcinogenesis and Mutagenesis

Carcinogenicity studies have not been conducted for brodalumab.

Gastrointestinal

Crohn's Disease

There are limited data in patients with a history of Crohn's disease. SILIQ is contraindicated in patients with Crohn's disease.

In psoriasis trials, which excluded subjects with active Crohn's disease, Crohn's disease occurred in one subject during treatment with SILIQ and led to discontinuation of therapy. In other trials, exacerbation of Crohn's disease was observed with SILIQ use.

Discontinue SILIQ if the patient develops Crohn's disease while taking SILIQ.

Hepatic/Biliary/Pancreatic

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

Immune

Hypersensitivity

Hypersensitivity reactions have been identified in post-marketing data; the reactions are mostly cutaneous manifestations, and most reported events included rashes, eczema, urticaria and dermatitis.

Cases of anaphylaxis including anaphylactic shock have been also reported. If an anaphylactic or other serious allergic reaction occurs, administration of SILIQ should be discontinued immediately and appropriate therapy initiated. In clinical trials, there were no serious reports of hypersensitivity occurring within 1 day of SILIQ administration.

Infections

SILIQ may increase the risk of infections.

During the 12-week placebo-controlled clinical trial period in patients with psoriasis, serious infections were observed in 0.5% of patients receiving SILIQ and 0.2% of patients receiving placebo (see 8.1 Adverse Reaction Overview).

Exercise caution when considering the use of SILIQ in patients with a chronic infection or a history of recurrent infection. Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and SILIQ should be discontinued until the infection resolves (see 8.1 Adverse Reaction Overview).

Pre-treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with SILIQ. Do not administer SILIQ to patients with active TB infection. Initiate treatment for latent TB prior to administering SILIQ.

Consider anti-TB therapy prior to initiation of SILIQ in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving SILIQ should be monitored closely for signs and symptoms of active TB.

Vaccinations

It is recommended that patients be brought up to date with all immunizations in accordance with local immunization guidelines prior to initiating treatment with SILIQ.

Live vaccines should not be given concurrently with SILIQ. No data are available on the response to live vaccines or the risk of infection, or transmission of infection after the administration of live vaccines to patients receiving SILIQ.

Patients receiving SILIQ may receive concurrent inactivated or non-live vaccinations. Non-live vaccines received during SILIQ treatment may not elicit an immune response sufficient to prevent disease.

Psychiatric

Suicidal Ideation and Behavior

Suicidal ideation and behavior, including 4 completed suicides, occurred in subjects treated with SILIQ in the psoriasis clinical trials.

Patients with psoriasis are in general at an increased risk of suicidal ideation and behaviour. Suicidal ideation and behavior, including completed suicide, have been reported in patients treated with SILIQ. The majority of patients with suicidal behaviour had a history of depression and/or suicidal ideation or behaviour. A causal association between treatment with SILIQ and increased risk of suicidal ideation and behaviour has not been established.

Carefully weigh the risk and benefit of treatment with SILIQ for patients with a history of depression and/or suicidal ideation or behaviour, or patients who develop such symptoms while on SILIQ. Patients, caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal ideation, anxiety, or other mood changes, and they should contact their healthcare provider if such events occur.

Because of the observed suicidal ideation and behavior in subjects treated with SILIQ, if an adequate response to SILIQ has not been achieved within 12 to 16 weeks, consider discontinuing therapy.

Renal

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

Reproductive health: Female and male potential

Fertility

No data are available on the effect of SILIQ on human fertility. Studies in sexually mature cynomolgus monkeys did not show any effects on fertility endpoints (see 16 NON-CLINICAL TOXICOLOGY).

7.1 Special Populations

7.1.1 Pregnant Women

There are no adequate and well-controlled studies of SILIQ in pregnant women. No effects on embryo-fetal or pre- postnatal development were observed in infants from pregnant monkeys administered brodalumab by subcutaneous injection during organogenesis to near parturition up to 26 times the maximum human recommended dose (on a mg/kg basis of 90 mg/kg/week) (see 16 NON-CLINICAL TOXICOLOGY).

7.1.2 Breast-feeding

There is no information regarding the presence of SILIQ in human breast milk, the effects on breastfed infants, or the effects on milk production. Because many drugs and immunoglobulins are excreted in human milk, caution should be exercised when SILIQ is administered to a nursing woman. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from SILIQ therapy, taking into account the benefits of breast feeding for the child and the benefit of therapy for the woman.

7.1.3 Pediatrics (< 18 years of age)

The safety and efficacy of SILIQ in children below the age of 18 years have not yet been established. No data are available.

7.1.4 Geriatrics (≥ 65 years of age)

Data in geriatric patients are limited. Of the 3066 plaque psoriasis patients initially randomized to SILIQ in clinical studies, 192 (6%) were ≥ 65 years old and no patients were ≥ 75 years old. The overall rate of AEs was higher in the ≥ 65-year-old age group than in those < 65. Exposure-adjusted event rates were 314.0 and 288.6 per 100 subject-years, respectively. No differences in efficacy were observed in elderly (≥ 65 years) patients compared to the overall population.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most commonly reported adverse reactions in SILIQ-treated patients were headache, arthralgia, fatigue, oropharyngeal pain, and diarrhea (see Table 1). The proportion of SILIQ-treated patients who discontinued treatment in the first 12 weeks of treatment due to adverse events was similar (about 1%) in all treatment arms.

The following adverse reactions are discussed elsewhere in the label:

- Crohn's Disease (see 7 WARNINGS AND PRECAUTIONS, Gastrointestinal, Crohn's Disease)
- Infections (see 7 WARNINGS AND PRECAUTIONS, Immune, Infections)

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.

Data from three phase 3 clinical trials and one phase 2 trial in plaque psoriasis were pooled to evaluate the safety of SILIQ (brodalumab injection) in comparison to placebo up to 12 weeks after treatment initiation (see 14 CLINICAL TRIALS).

These data included 4558 patients (3066 SILIQ, 613 ustekinumab, 879 placebo) in controlled clinical trials and open-label extension studies representing 5401.6 patient-years of exposure. Of these, 4461 patients received at least one dose of SILIQ, 3072 patients were exposed for at least 1 year.

During the 12-week placebo-controlled period of these studies, the subject incidence of serious adverse events was 1.6% in patients who received SILIQ, 1% in patients that received ustekinumab, and 1.7% in patients who received placebo.

Table 1 summarizes all adverse reactions that occurred in at least 1% of all patients receiving SILIQ and at a higher rate than in the placebo group during the 12-week placebo-controlled period:

Table 1 - Adverse Reactions Reported in at least 1% of all Patients with Plaque Psoriasis Receiving SILIQ through Week 12 in Three Phase 3 and One Phase 2 Clinical Trials and at a Higher Rate than Placebo

	SILIQ 210 mg every 2 weeks (N=1496) n (%)	Placebo (N=879) n (%)	Ustekinumab (N=613) n (%)
General			
Fatigue	39 (2.6)	10 (1.1)	16 (2.6)
Ear/Nose /Throat			
Oropharyngeal pain	31 (2.1)	10 (1.1)	8 (1.3)
Gastrointestinal			
Diarrhea	33 (2.2)	10 (1.1)	5 (0.8)
Nausea	28 (1.9)	10 (1.1)	6 (1.0)
Hematologic			
Neutropenia	15 (1.0)	4 (0.5)	5 (0.8)

	SILIQ 210 mg every 2 weeks (N=1496) n (%)	Placebo (N=879) n (%)	Ustekinumab (N=613) n (%)
Musculoskeletal and Connective Tissue			
Arthralgia	71 (4.7)	29 (3.3)	15 (2.4)
Myalgia	26 (1.7)	3 (0.3)	4 (0.7)
Neurology			
Headache	64 (4.3)	31 (3.5)	23 (3.8)
Respiratory			
Influenza	19 (1.3)	4 (0.5)	7 (1.1)
Skin			
Injection site reactions (pain, erythema, bruising, hemorrhage, pruritus)	23 (1.5)	11 (1.3)	12 (2.0)
Tinea infections (tinea pedis, versicolor, cruris)	15 (1.0)	2 (0.2)	3 (0.5)

Suicidal Ideation and Behaviour

During the 12-week randomized treatment period in the pooled trials, one subject in the SILIQ group attempted suicide and none in the placebo or ustekinumab groups. From initiation through Week 52 of the trials, suicidal ideation or behavior occurred in 7 of 4019 subjects (0.2 per 100 subject-years) treated with SILIQ and in 2 of 613 subjects (0.4 per 100 subject-years) treated with ustekinumab. During the course of the clinical trials for plaque psoriasis, suicidal ideation or behavior occurred in 34 of 4464 subjects treated with SILIQ (0.37 per 100 subject-years). Eight of the 10 subjects who attempted or completed suicide had a history of depression and/or suicidal ideation or behavior.

Infections

During the 12-week placebo-controlled trial period in plaque psoriasis, infections were reported in 25.4% of patients treated with SILIQ compared with 23.4% of patients treated with placebo. The majority of infections consisted of nasopharyngitis, upper respiratory tract infection, pharyngitis, urinary tract infections, bronchitis, and influenza, which did not necessitate treatment discontinuation. Serious infections occurred in 0.5% of patients treated with SILIQ and in 0.2% of patients treated with placebo. Higher rates of fungal infections, primarily non-serious skin and mucosal candida infections were observed in SILIQ patients compared to placebo patients, 1.8% vs 0.9%, respectively, and one serious case of cryptococcal meningitis was observed in SILIQ-treated patients (see 7 WARNINGS AND PRECAUTIONS, Immune, Infections).

Through week 52, the exposure-adjusted event rates (per 100 patient-years) for infections were 114.6 for patients treated with SILIQ and 118.1 for patients treated with ustekinumab. The exposure-adjusted event rates (per 100 patient-years) for serious infections were 1.3 for patients

treated with SILIQ and 1.0 for patients treated with ustekinumab.

Neutropenia

During the 12-week randomized treatment period, neutropenia occurred in 0.7% of subjects in the SILIQ group. Most adverse reactions of neutropenia were transient. In subjects with normal absolute neutrophil count (ANC) at baseline, a reduction in ANC occurred in 6.8% of subjects in the SILIQ group, compared to 3.3% in the ustekinumab group, and 3.6% in the placebo group. Neutropenia ≥ Grade 3 (< 1000/mm3) occurred in 0.5% of subjects in the SILIQ group compared to 0.2% of subjects in the ustekinumab group and none in the placebo group. From Week 0 to end of trial, the exposure-adjusted rate of treatment-emergent neutropenia was 0.4 per 100 subject-years (0.1 per 100 subject-years were ≥ Grade 3). No serious infections were associated with cases of neutropenia.

Immunogenicity

Antibodies to brodalumab developed in 2.7% (122/4461) of patients treated with SILIQ for up to 52 weeks in psoriasis clinical studies (0.3% of patients had anti-brodalumab antibodies at baseline). Of these patients, none had neutralizing antibodies.

No evidence of altered pharmacokinetic profile, clinical response, or safety profile was associated with anti-brodalumab antibody development.

8.3 Less Common Clinical Trial Adverse Reactions

Adverse reactions that occurred in less than 1% of all patients receiving SILIQ through week 12 were conjunctivitis and candida infections (including oral, genital, and esophageal).

8.5 Post-Market Adverse Reactions

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

- ***Hypersensitivity reactions (mostly cutaneous manifestations):*** pruritus, rashes, eczema, urticaria, dermatitis, and anaphylaxis, including anaphylactic shock with unknown frequency.

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Live vaccines should not be given concurrently with SILIQ (see 7 WARNINGS AND PRECAUTIONS, Immune, Vaccinations)

9.4 Drug-Drug Interactions

CYP450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Although a role for IL-17A and IL-

17RA in the regulation of CYP450 enzymes has not been reported, the effect of brodalumab on CYP3A4/3A5 activity was evaluated in a disease-drug-drug interaction study.

In subjects with moderate to severe plaque psoriasis, a single subcutaneous dose of 210 mg SILIQ (brodalumab injection) increased the exposure of midazolam metabolized by CYP3A4/3A5 by 24%. Based on the magnitude of change in exposure of midazolam, no dose adjustment of CYP3A4/3A5 substrates is necessary when administered concomitantly with SILIQ. Consider monitoring in patients taking CYP3A4/3A5 substrates with narrow therapeutic indices.

9.5 Drug-Food Interactions

Interactions with herbal products 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

Brodalumab is a human monoclonal IgG2 antibody that selectively binds to human IL-17RA and blocks its interactions with cytokines IL-17A, IL-17F, IL17C, IL-17A/F heterodimer and IL-25. IL-17RA is a protein expressed on the cell surface and is a required component of receptor complexes utilized by multiple IL-17 family cytokines. IL-17 family cytokine concentrations have been reported to be increased in psoriasis. Blocking IL-17RA inhibits IL-17 cytokine-induced responses.

10.2 Pharmacodynamics

Elevated levels of IL-17A, IL-17C and IL-17F are found in psoriatic plaques. Treatment with SILIQ (brodalumab injection) in psoriasis patients has been shown to decrease levels of IL-17A. The relationship between the pharmacodynamic effect and mechanism(s) by which brodalumab exerts its clinical effects is unknown.

10.3 Pharmacokinetics

Absorption

In moderate to severe plaque psoriasis patients following a single subcutaneous administration of SILIQ at 210 mg, the mean (±SD) maximum SILIQ serum concentration (Cmax) was 13.4 mcg/mL (±7.29 mcg/mL). The median time to maximum SILIQ concentration (Tmax) was 3.0 days (range: 2.0 to 4.0 days). The mean (±SD) area-under-the-concentration-time curve (AUClast) of SILIQ was 111 mcg•day/mL (±64.4 mcg•day/mL).

Following multiple subcutaneous doses of 210 mg SILIQ every 2 weeks (plus a week 1 loading dose), steady state was achieved by Week 4. Mean (±SD) steady-state area-under-the-concentration-time curve over the dosing interval (AUCtau) of SILIQ was 243 mcg•day/mL (±234 mcg•day/mL) as measured at Week 10.

The subcutaneous bioavailability of brodalumab estimated by population pharmacokinetic analysis is 54.7%. The accumulation ratio after 6 weeks of every other week administration of 210 mg brodalumab was 1.5-fold.

Immunogenicity

The pharmacokinetics of SILIQ was not affected by the formation of anti-brodalumab antibodies.

Distribution

Following a single subcutaneous administration of brodalumab 210 mg in subjects with plaque psoriasis, the mean (±SD) apparent volume of distribution (Vz/F) of brodalumab was 8.9 (±9.4) L.

Metabolism

The metabolic pathway of brodalumab has not been characterized. As an IgG2 human monoclonal antibody, brodalumab is expected to be degraded into small peptides and amino acids via catabolic pathways in a manner similar to endogenous IgG.

Elimination

Following a single subcutaneous administration of brodalumab 210 mg in plaque psoriasis patients, the apparent clearance (CL/F) is 2.95 L/day. The clearance of brodalumab increased with decreasing doses due to nonlinear elimination.

Based on population pharmacokinetic modeling, the estimated half-life of SILIQ was 10.9 days at steady state after every other week subcutaneous dose of 210 mg.

Weight

Impact of weight on pharmacokinetics: Population pharmacokinetic analysis indicated that exposure decreased as body weight increased, however, no dose adjustment is recommended.

Special Populations and Conditions

- **Pediatrics (< 18 years of age):** The safety and efficacy of SILIQ have not been evaluated in pediatric patients.
- **Geriatrics (≥ 65 years of age):** Data in geriatric patients are limited. Of the 3066 plaque psoriasis patients initially randomized to SILIQ in clinical studies, 192 (6%) were ≥ 65 years old and no patients were ≥ 75 years old. The overall rate of AEs was higher in the ≥ 65-year-old age group than in those < 65. Exposure-adjusted event rates were 314.0 and 288.6 per 100 subject-years, respectively. Although no differences in efficacy were observed between older and younger patients, the number of patients aged 65 years and

older was not sufficient to determine whether they responded differently from younger patients.

Population pharmacokinetic analysis indicated that age did not have an effect on brodalumab pharmacokinetics.

No dose adjustment is recommended in geriatric patients.

- **Sex:** Population pharmacokinetic analysis indicated that sex did not have an effect on brodalumab pharmacokinetics.
- **Hepatic Insufficiency:** No pharmacokinetic data are available in patients with impaired hepatic function.
- **Renal Insufficiency:** No pharmacokinetic data are available in patients with impaired renal function.

11 STORAGE, STABILITY AND DISPOSAL

- Store refrigerated at 2°C to 8°C in the original carton.
- For convenience, prefilled syringes can be stored at room temperature between 20°C to 25°C in the original carton for a maximum single period of 14 days with protection from light and sources of heat. Once the prefilled syringe has reached room temperature, it should not be placed back into the refrigerator. If not used within 14 days at room temperature, the prefilled syringe should be discarded.
- Keep in original carton to protect from light and physical damage during storage.
- Keep out of the sight and reach of children.
- Do not freeze.
- Do not shake.

12 SPECIAL HANDLING INSTRUCTIONS

SILIQ is a sterile, preservative-free solution. Each pre-filled syringe is for single use only. Consult the ‘Instructions for Use’ for detailed instructions on administration of SILIQ.

To avoid discomfort at the site of injection, allow at least 30 minutes for the pre-filled syringe to reach room temperature before injecting. Do not warm in any other way. Do not remove the grey needle cap on the pre-filled syringe while allowing to reach room temperature.

Visually inspect SILIQ for particles and discolouration prior to administration. SILIQ is a clear to slightly opalescent, colourless to slightly yellow liquid, practically free from particles. Do not use SILIQ if it is cloudy or discoloured or contains large lumps, flakes, or coloured particles.

Do not use the prefilled syringe if it has been dropped on hard surface.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

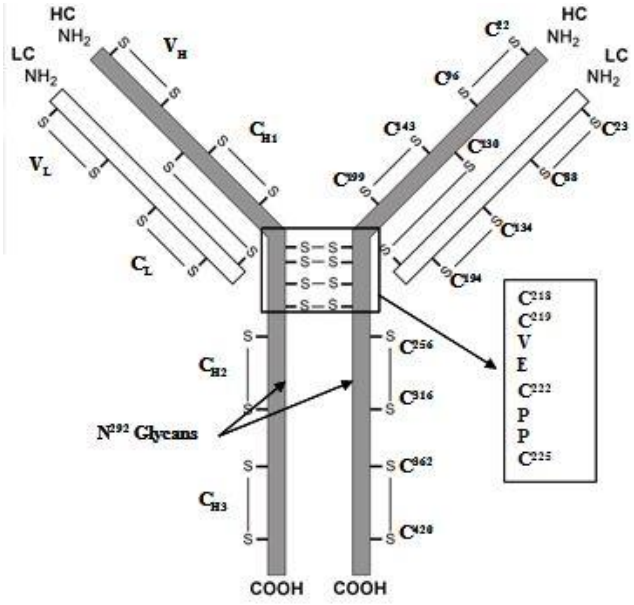
Proper name: Brodalumab Injection

Chemical name: Brodalumab

Molecular formula: The molecule is a heterotetramer consisting of 2 heavy chains (HC) of the lgG2 subclass and 2 light chains (LC) of the kappa subclass that are covalently linked through disulfide bonds.

Molecular mass: Brodalumab is comprised of 1312 amino acids and has an estimated molecular mass of 144,000 Daltons.

Structural formula:



Schematic representation of Brodalumab:

Heavy chains are shown in grey and light chains in white.

VH Variable region, heavy chain

CH Constant domain, heavy chain

VL Variable region, light chain

CL Constant domain, light chain.

Physicochemical properties

Description:	SILIQ (brodalumab injection) solution is clear to slightly opalescent, colorless to slightly yellow liquid.

Viral Inactivation

SILIQ is produced by a recombinant cell line culture and is purified by a series of steps that includes measures to inactivate and remove viruses.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Three multicenter, randomized, double-blind, controlled trials (Trials 1, 2, and 3) enrolled a total of 4373 subjects 18 years of age and older with at least a 6-month history of moderate to severe plaque psoriasis, defined as having a minimum affected body surface area (BSA) of 10%, a Psoriasis Area and Severity Index (PASI) score ≥ 12, a static Physician's Global Assessment (sPGA) score ≥ 3 in the overall assessment (plaque thickness/induration, erythema, and scaling) of psoriasis on a severity scale of 0 to 5, and who were candidates for systemic therapy or phototherapy. All three trials included a 12-week placebo-controlled induction phase, a double-blind duration of 52 weeks, and an open-label long-term extension. Subjects randomized to SILIQ (brodalumab injection) or placebo received subcutaneous treatment at Weeks 0, 1, and 2, followed by the same dose every 2 weeks through Week 12. In Trials 2 and 3, subjects randomized to ustekinumab received the 45 mg dose for subjects weighing less than 100 kg and the 90 mg dose for subjects weighing greater than 100 kg at Weeks 0, 4, and 16, followed by same dose every 12 weeks.

In all trials, the co-primary endpoints (compared to placebo) were the proportion of subjects who achieved a PASI score of 75% (PASI 75) and sPGA success (clear [0] or almost clear [1]) at Week 12. The primary endpoint (compared to ustekinumab) for trials 2 and 3, included the proportion of patients who received SILIQ 210 mg and achieved PASI score of 100% (PASI 100) at Week 12.

Other evaluated outcomes included the proportion of subjects who achieved a reduction in PASI score of 90% (PASI 90) and sPGA 0 (clear) at Week 12, and maintenance of efficacy to Week 52. Proportion of subjects who achieved Psoriasis Symptom Inventory (PSI) score of 0 (not at all) or 1 (mild) on every item (itch, redness, scaling, burning, stinging, cracking, flaking, and pain) through week 52, and the proportion of subjects who achieved Dermatology Life Quality Index (DLQI) response through Week 52 were also evaluated.

Baseline Demographics and Characteristics

Baseline demographics and disease characteristics were generally consistent across all treatment groups in all three studies. Subjects were predominantly men (69%) and white (91%), with a mean age of 45 years. The mean baseline body weight was 90.5 kg and 28% of patients had body weight greater than 100 kg. The baseline PASI score ranged from 9.4 to 72 (median: 17.4) and baseline BSA ranged from 10 to 97 (median: 21). Baseline sPGA score ranged from "3 (moderate)" (58%) to "5 (very severe)" (5%).

Approximately 21% of subjects had a history of psoriatic arthritis. Approximately 30% of subjects had previously received a biologic, 26% had not received systemic therapy or phototherapy and 12% of subjects were biologic failures.

Table 2 - Summary of Patient Demographics for Clinical Trials in Specific Indication

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
Trial 1 (20120102)	Double-blind, Placebo-controlled Multicenter	INDUCTION PHASE Placebo, brodalumab 140 mg or 210 mg: SC at week 0, 1 and 2 followed by same dose Q2W through week 12. 140 mg: n = 219 210 mg: n = 222 Placebo = 220	N = 661	46 (19, 75)	M = 323 F = 118
Trial 2 (20100103)	Double-blind, Double-dummy, Placebo-controlled Active comparator-controlled Multicenter	INDUCTION PHASE Placebo, Brodalumab 140 mg or 210 mg: SC at week 0, 1 and 2 followed by same dose Q2W through week 12. Placebo, Ustekinumab 45 mg (≤100kg) or 90 mg (>100kg): SC at week 0 and 4 210 mg = 612 140 mg = 610 Ustekinumab = 300 Placebo = 309	N = 1831	44.6 (18, 75)	M = 1258 F = 573

Trial 3 (20120104)	Double-blind, Double-dummy, Placebo-controlled Active comparator-controlled Multicenter	INDUCTION PHASE Placebo, Brodalumab 140 mg or 210 mg: SC at week 0, 1 and 2 followed by same dose Q2W through week 12. Placebo, Ustekinumab 45 mg (≤100kg) or 90 mg (>100kg): SC at week 0 and 4 210 mg = 624 140 mg = 629 Ustekinumab = 313 Placebo = 315	N = 1881	44.8 (18, 75)	M = 1288 F = 593
Q2W = every two weeks					

14.2 Study Results

Table 3 - Baseline Disease Characteristics in Trials 1, 2, and 3

	Trial 1			**Trial 2**				**Trial 3**			
	Place-bo	**Broda-lumab 140 mg Q2W**	**Broda-lumab 210 mg Q2W**	**Place-bo**	**Broda-lumab 140 mg Q2W**	**Broda-lumab 210 mg Q2W**	**Uste ki-numa b**	**Place-bo**	**Brod a-luma b 140 mg Q2W**	**Broda-lumab 210 mg Q2W**	**Usteki-numab**
N	220	219	222	309	610	612	300	315	629	624	313
PSA Mean (SD)	26.9 (17.1)	27.4 (17.1)	25.1 (15.3)	27.9 (17.0)	27.1 (17.4)	26.0 (16.3)	27.0 (19.3)	27.7 (17.4)	28.6 (18.4)	28.3 (17.7)	28.1 (17.6)
PASI n (SD)	19.7 (7.7)	20.0 (7.4)	19.4 (6.6)	20.4 (8.2)	20.5 (8.2)	20.3 (8.3)	20.0 (8.4)	20.1 (8.7)	20.1 (8.5)	20.4 (8.3)	20.1 (8.4)
Psoriasis disease duration (years) Mean (SD)	20.7 (12.1)	19.4 (12.5)	20.4 (13.2)	17.6 (12.3)	18.8 (11.9)	18.7 (12.1)	19.1 (12.7)	17.9 (11.7)	17.0 (11.6)	18.1 (12.4)	18.0 (11.7)

	Trial 1			Trial 2				Trial 3			
	Place-bo	**Broda-lumab 140 mg Q2W**	**Broda-lumab 210 mg Q2W**	**Place-bo**	**Broda-lumab 140 mg Q2W**	**Broda-lumab 210 mg Q2W**	**Uste ki-numa b**	**Place-bo**	**Brod a-luma b 140 mg Q2W**	**Broda-lumab 210 mg Q2W**	**Usteki-numab**
N	220	219	222	309	610	612	300	315	629	624	313
History of psoriatic arthritis n (%)	63 (28.8	60 (27.4)	58 (26.1)	51 (16.5)	125 (20.5)	114 (18.6)	50 (16.7)	59 (18.7)	134 (21.3)	127 (20.4)	64 (20.4)
Prior systemic therapy n (%)	164 (74.5)	143 (65.3)	155 (69.8)	182 (58.9)	375 (61.5)	378 (61.8)	187 (62.3)	162 (51.4)	334 (53.1)	332 (53.2)	168 (53.7)
Prior biologic therapy n (%)	101 (45.9)	99 (45.2)	105 (47.3)	90 (29.1)	179 (29.3)	177 (28.9)	84 (28.0)	76 (24.1)	160 (25.4)	157 (25.2)	75 (24.0)
Prior failure of biologic therapy n (%)	41 (18.6)	37 (16.9)	44 (19.8)	40 (12.9)	77 (12.6)	85 (13.9)	40 (13.3)	24 (7.6)	67 (10.7)	65 (10.4)	22 (7.0)

Clinical Response

The percentages of subjects treated with SILIQ 210 mg every 2 weeks achieving PASI 75 and PASI 100 responses as well sPGA success (clear or almost clear) in all three trials are presented in Table 4. In all three trials, subjects treated with SILIQ 210 mg every 2 weeks had higher rates of PASI 75 and PASI 100 response as well as sPGA success versus placebo at Week 12. In Trials 2 and 3, a statistically significant difference in PASI 100 responses were observed for the SILIQ 210 mg every 2 weeks dose compared to ustekinumab treatment.

Onset of response as measured by PASI 75 was observed within 2 weeks of treatment with SILIQ 210 mg every 2 weeks in all three clinical trials.

Table 4 - Clinical Outcomes at Week 12 in Adults with Plaque Psoriasis in Trials 1, 2, and 3

Trial 1			
Endpoint	**SILIQ[a] 210 mg (N=222) n (%)**	**Placebo (N=220) n (%)**	**SILIQ vs Placebo % (95% CI)**
PASI 75 response	185 (83) [a]	6 (3)	80.6 (75.3, 86.0)
PASI 100 response	93 (42) [a]	1 (<1)	41.4 (34.9, 48.0)
sPGA success clear (0) or almost clear (1)	168 (76) [a]	3 (1)	74.3 (68.5, 80.2)

Trial 2					
Endpoint	**SILIQ 210 mg (N=612) n (%)**	**Ustekinumab (N=300) [c] n (%)**	**Placebo (N=309) n (%)**	**Difference SILIQ vs Placebo % (95% CI)**	**Difference SILIQ vs Ustekinumab % (95% CI)**
PASI 75 response	528 (86) [a]	210 (70)	25 (8)	78.2 (74.1, 82.3)	16.3 (10.4, 22.1)
PASI 100 response	272 (44) [a, b]	65 (22)	2 (1)	43.8 (39.8, 47.8)	22.8 (16.7, 28.9)
sPGA success clear (0) or almost clear (1)	481 (79) [a]	183 (61)	12 (4)	74.7 (70.8, 78.6)	17.6 (11.2, 24.0)

Trial 3					
Endpoint	**SILIQ 210 mg (N=624) n (%)**	**Ustekinumab (N=313) [c] n (%)**	**Placebo (N=315) n (%)**	**Difference SILIQ vs Placebo % (95% CI)**	**Difference SILIQ vs Ustekinumab % (95% CI)**
PASI 75 response	531 (85) [a, b]	217 (69)	19 (6)	79.1 (75.2, 82.9)	15.8 (9.9, 21.6)
PASI 100 response	229 (37) [a, b]	58 (19)	1 (0.3)	36.4 (32.5, 40.2)	18.2 (12.4, 23.9)
sPGA success clear (0) or almost clear (1)	497 (80) [a]	179 (57)	13 (4)	75.5 (71.7, 79.4)	22.5 (16.1, 28.8)

[a] Adjusted p-value (vs placebo) < 0.05
[b] Adjusted p-value (vs ustekinumab) <0.05
[c] Ustekinumab 45 mg for patients ≤ 100kg and 90 mg for patients >100kg

Note: Type I error controlled using a combination of parallel and sequential testing
Non-responder imputation (NRI) is used to impute missing data

Higher rates of PASI 90 response at Week 12 were observed with SILIQ 210 mg every 2 weeks compared to placebo (Trial 1: 70% (156/222) versus 1% (2/220); Trial 2: 70% (430/612) versus 3% (10/309); Trial 3: 69% (429/624) versus 2% (5/315)). These PASI 90 response rates were also higher than those observed for ustekinumab at Week 12 (Trial 2: 47% (141/300); Trial 3: 48% (149/313)).

Examination of age, gender, race, use of prior systemic or phototherapy, use of prior biologics, and biologic failures did not identify differences in response to SILIQ among these subgroups.

Maintenance of Effect

In Trial 1, subjects randomized to receive SILIQ and who were responders at Week 12 (i.e., sPGA of 0 or 1) were re-randomized to receive either placebo or SILIQ. Among responders at Week 12, 83% (69/83) of subjects re-randomized to continued treatment with SILIQ 210 mg Q2W maintained this response (sPGA of 0 or 1) at Week 52 compared to none (0/84) who were re-randomized to placebo and withdrawn from SILIQ. In addition, 87% (72/83) of subjects re-randomized to continued treatment with SILIQ 210 mg Q2W achieved PASI 75 response at Week 52 compared to none (0/84) who were re-randomized to placebo and withdrawn from SILIQ.

Trials 2 and 3 included a re-randomized phase during which subjects originally randomized to receive SILIQ during the first 12 weeks were re-randomized to one of four SILIQ regimens at the Week 12 visit and placebo subjects were crossed over to receive SILIQ 210 mg Q2W. Subjects receiving ustekinumab continued the same treatment until crossed over at Week 52 to SILIQ 210 mg Q2W. Of the subjects who received continuous SILIQ Q2W dosing or ustekinumab Q12W dosing, PASI 100 was achieved by 51% of SILIQ-treated subjects and by 28% of ustekinumab-treated subjects. For sPGA 0 or 1 responders at Week 12, the percentage of subjects who maintained this response at Week 52 was 79% for subjects treated with SILIQ 210 mg Q2W. For PASI 100 responders at Week 12, 72% of the subjects who continued on SILIQ 210 mg Q2W maintained the response at Week 52.

Psoriasis Symptom Inventory

At Week 12, a greater proportion of subjects in SILIQ 210 mg Q2W group achieved a Psoriasis Symptom Inventory (PSI) score of 0 (not at all) or 1 (mild) on every item (itch, redness, scaling, burning, stinging, cracking, flaking, pain).

Dermatology Life Quality Index (DLQI)

DLQI was assessed to evaluate the effect of psoriasis on the quality of the patient's life. The percentage of subjects with no impairment/effect on quality of life (DLQI 0 or 1 score) at week 12 assessed in Trials 1, 2 and 3 was 43%, 61%, and 59%, respectively in the brodalumab 210 mg every 2 weeks compared with placebo 5%, 5%, and 7%, respectively.

In Trials 2 and 3, the percentage of subjects with DLQI scores of 0 or 1 at week 12 was higher in the brodalumab 210 mg every 2 weeks group compared with ustekinumab group.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology

No significant effects, including any organ toxicity or undesirable effects on immune function (e.g., peripheral blood immunophenotyping and T-cell dependent antibody response) were observed in cynomolgus monkeys administered brodalumab by subcutaneous injection up to dose levels of 90 mg/kg/week for 6 months (26 times the MRHD on a mg/kg basis). Brodalumab related effects were limited to injection site reactions and mucocutaneous inflammation that was consistent with pharmacologic modulation of host surveillance to commensal microflora.

Carcinogenicity

Carcinogenicity and mutagenicity studies with brodalumab have not been conducted.

Reproductive and Developmental Toxicology

In cynomolgus monkeys there were no effects on fertility endpoints such as reproductive organ weight or sperm analysis following administration of brodalumab at dose levels up to 90 mg/kg/week for 6 months.

No effects on embryo-fetal toxicity or postnatal development (up to 6 months of age), including morphological and immunological development, were observed in infants from pregnant cynomolgus monkeys administered brodalumab by subcutaneous injection from the period of organogenesis to parturition up to dose levels of 90 mg/kg/week.

Brodalumab was detected in milk of exposed animals for up to 14 days after birth at concentrations that were approximately 1000-fold lower than those measured in maternal serum.

PATIENT MEDICATION INFORMATION
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrSILIQ®
Brodalumab Injection

Read this carefully before you start taking **SILIQ** 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 **SILIQ**.

Serious Warnings and Precautions

Suicidal thoughts or behaviour have happened in some people treated with SILIQ. Some people have ended their own lives. It has not been proven that SILIQ causes suicidal thoughts or behaviour. Your risk of suicidal thoughts and behaviour may be increased if you have a history of suicidal thoughts or depression. Seek medical attention if you have thoughts of suicide, dying, or hurting yourself, new onset or worsening depression, anxiety, or other mood changes.

What is SILIQ used for?

SILIQ is used to treat a skin condition called “plaque psoriasis”, which causes inflammation and scaly plaque formation on the skin. SILIQ reduces the inflammation and other symptoms of the disease. SILIQ is used in adults with moderate to severe plaque psoriasis that involves large areas of the body, who may benefit from taking injections, pills, or phototherapy.

Using SILIQ will benefit you by leading to improvements of skin clearance, possible total skin clearance, and by reducing signs and symptoms such as itch, redness, scaling, burning, stinging, cracking, flaking, and pain.

It is not known if SILIQ is safe and effective in children.

How does SILIQ work?

SILIQ contains the active substance brodalumab. Brodalumab is a monoclonal antibody. Monoclonal antibodies are proteins that recognize and bind specifically to certain proteins in the body.

SILIQ belongs to a group of medicines called interleukin (IL) inhibitors. The medicine works by blocking the activity of IL-17 proteins, which are present at increased levels in diseases such as psoriasis.

What are the ingredients in SILIQ?

Medicinal ingredients: brodalumab

Non-medicinal ingredients: Glutamate, Polysorbate 20, Proline, and Water for injections

SILIQ comes in the following dosage forms:

SILIQ is supplied as a single-use prefilled syringe. Each syringe contains one 210 mg dose of SILIQ. **Each SILIQ prefilled syringe can only be used once.**

Do not use SILIQ if:

- you are allergic to brodalumab or any of the ingredients in SILIQ. See **What are the ingredients in SILIQ?** for a complete list of ingredients in SILIQ.

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

- currently have Crohn's disease or if you have a history of Crohn's disease;
- have or have had suicidal thoughts or actions, depression, anxiety, or mood problems;
- have an infection at the moment or often get infections;
- if you have long-term (chronic) infections;
- have tuberculosis, have had a positive tuberculosis test, or have been in close contact with someone with tuberculosis. You may need to be treated with another medicine for tuberculosis before you begin treatment with SILIQ;
- have recently received or are scheduled to receive a vaccination. You should not be given certain types of vaccines (called 'lives vaccines') while being treated with SILIQ.

Other warnings you should know about:

Tell your doctor or pharmacist immediately if you get any of these symptoms during treatment with SILIQ:

- if you have suicidal thoughts or actions, depression, anxiety, or mood problems;
- if you think you have an infection or have symptoms of an infection such as:
  - fever, sweats, or chills;
  - muscle aches;
  - cough;
  - shortness of breath;
  - sore throat or difficulty swallowing;
  - warm, red, or painful skin or sores on your body;
  - diarrhea or stomach pain;
  - burning when you urinate or urinate more often than normal;
- if you have been told you have tuberculosis.

Children and adolescents (below the age of 18 years): SILIQ is not recommended for children and adolescents (under 18 years of age) because it has not been studied in this age group.

Pregnancy and breast-feeding: before using SILIQ, tell your healthcare provider if you:

- are pregnant or plan to become pregnant. It is not known if SILIQ can harm your unborn baby. You and your healthcare provider should decide if you should use SILIQ;
- are breastfeeding or plan to breastfeed. It is not known if SILIQ passes into your breast milk.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines. Know the medicines you take. Keep a list of your medicines with you and show it to your healthcare provider when you get a new medicine.

The following may interact with SILIQ:

Tell your doctor or pharmacists if you recently had or are going to have a vaccination. You should not have certain types of vaccines (called 'live vaccines') while using SILIQ.

How to take SILIQ:

- **Read "Instructions for Use" all the way through before use.**
- Use SILIQ exactly as your healthcare provider has told you. Check with your healthcare provider if you are not sure.
- SILIQ is given as an injection under the skin (known as a subcutaneous or SC injection).
- SILIQ is available as a single-use prefilled syringe that you or your caregiver may use at home to give injections.
- If your healthcare provider decides that you or a caregiver can give the injections of SILIQ at home, you or your caregiver should receive training on the right way to prepare and inject SILIQ. Do not try to inject SILIQ until you or your caregiver has been shown how to inject SILIQ by your healthcare provider.
- SILIQ is injected in your upper legs (thighs) or stomach area (abdomen) by you or a caregiver. A caregiver may also give you an injection of SILIQ in your upper outer arm.
- **Do not** give an injection in an area of the skin that is tender, bruised, red, hard, or in an area of skin that is affected by psoriasis.

Usual dose:

- Your doctor will decide how much SILIQ you need and for how long. The recommended dose is 210 milligram (mg) each injection. Make sure to discuss with your doctor when you will receive injections and to come in for all your schedules follow-up appointments.
- After the first dose you will need to take an injection at Week 1 (one week after first dose) and Week 2 (two weeks after first dose). After that, you will need to take an injection every two weeks.
- SILIQ is for long term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

Instructions for Use:

SILIQ is supplied as a single-use prefilled syringe. Each syringe contains one 210 mg dose of SILIQ. Your healthcare provider has prescribed SILIQ and will tell you how often it should be injected. **Each SILIQ prefilled syringe can only be used once.**

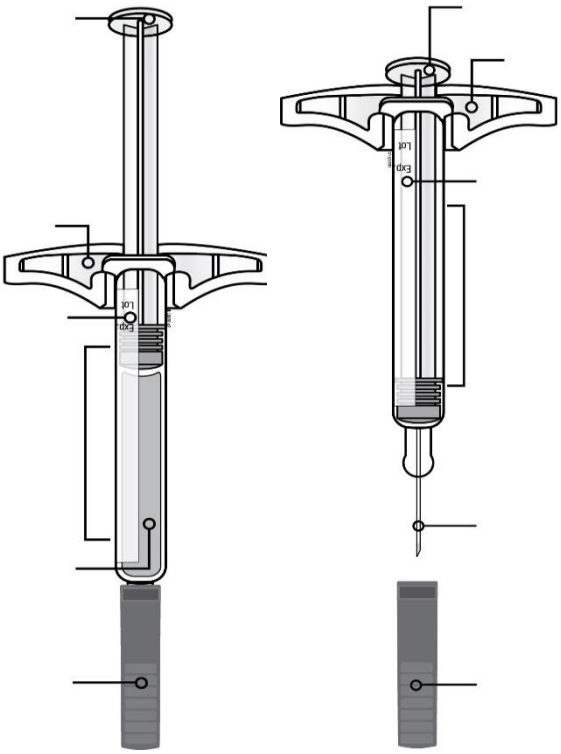
If your healthcare provider decides that you or a caregiver may be able to give your injections of SILIQ at home, you should receive training on the right way to prepare and

inject SILIQ. Do not try to inject yourself until you have been shown the right way to give the injections by your healthcare provider.

Please read all of the instructions before using the SILIQ syringe. Call your healthcare provider if you or your caregiver have any questions about the right way to inject SILIQ.

Guide to parts:

Before use **After use**



Important: Needle is inside

Before you use a SILIQ prefilled syringe, read this important information:

Storing your SILIQ prefilled syringes

- Keep the SILIQ prefilled syringe out of the reach of children.
- Keep the SILIQ prefilled syringe in the original carton to protect from light or physical damage.
- The SILIQ prefilled syringe should be kept in the refrigerator (2˚C to 8˚C).
- If needed, you may store the SILIQ prefilled syringe at room temperature at 20°C to 25°C for up to 14 days. Throw away SILIQ that has been stored at room temperature after 14 days.
- **Do not** store the SILIQ prefilled syringe in extreme heat or cold. For example, avoid storing in your vehicle's glove box or trunk. **Do not** freeze.

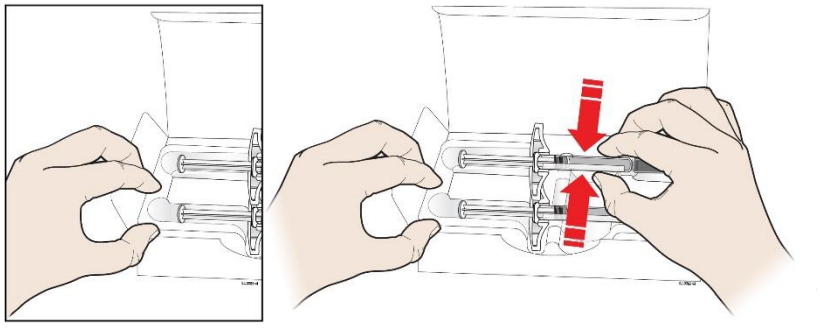
Using your SILIQ prefilled syringe

- It is important that you do not try to give the injection unless you or your caregiver has received training from your healthcare provider.
- **Do not** use a SILIQ prefilled syringe after the expiration date on the label.
- **Do not** shake the SILIQ prefilled syringe.
- **Do not** remove the gray needle cap from the SILIQ prefilled syringe until you are ready to inject.
- **Do not** freeze or use the SILIQ prefilled syringe if it has been frozen.
- **Do not** use a SILIQ prefilled syringe if it has been dropped on a hard surface. Part of the SILIQ prefilled syringe may be broken even if you cannot see the break.

Step 1: Prepare

A) Remove the SILIQ prefilled syringe from the package.

Grab the syringe barrel to remove the syringe from the tray.



Place finger or thumb on edge of tray to secure it while you remove syringe.

Grab Here

Put the original package with any unused syringes back in the refrigerator.

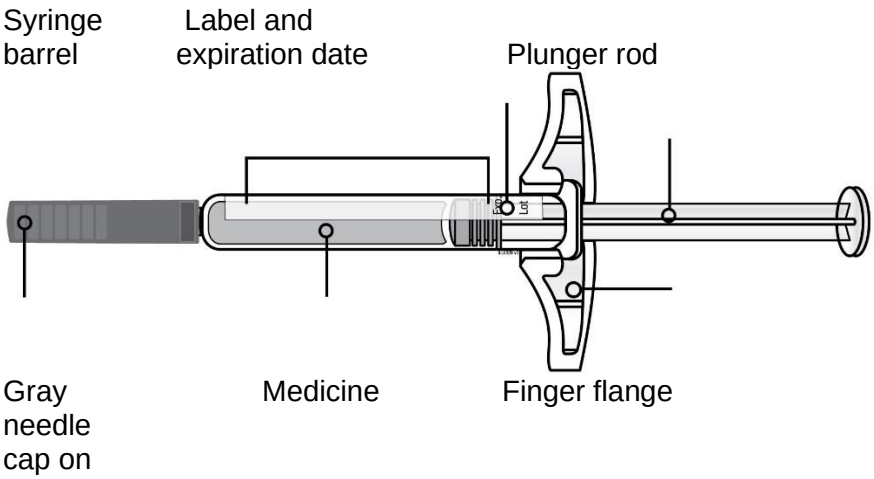
For safety reasons:

- **Do not** grasp the plunger rod.
- **Do not** grasp the gray needle cap.
- **Do not** remove the gray needle cap until you are ready to inject.
- **Do not** remove the finger flange. This is part of the syringe.

Leave the syringe at room temperature for at least 30 minutes before injecting.

- **Do not** put the syringe back in the refrigerator once it has reached room temperature.
- **Do not** try to warm the syringe by using a heat source such as hot water or microwave.
- **Do not** leave the syringe in direct sunlight.
- **Do not** shake the syringe.

B) Inspect the SILIQ prefilled syringe.



Always hold the syringe by the syringe barrel.

Make sure the medicine in the syringe is clear and colorless to slightly yellow.

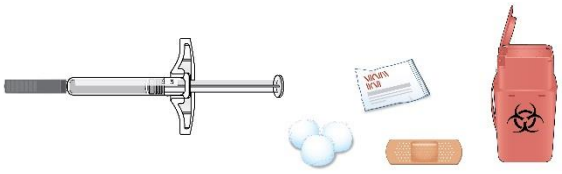
- **Do not** use the syringe if:
  - The medicine is cloudy or discolored or contains flakes or particles.
  - Any part appears cracked or broken.
  - The gray needle cap is missing or not securely attached.
  - The expiration date printed on the label has passed.

C) Gather all materials needed for your injection.

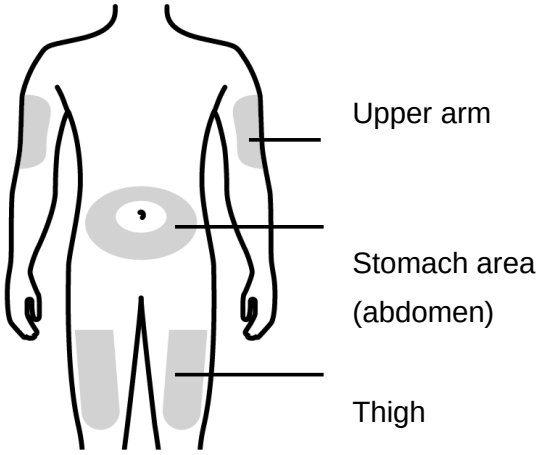
Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the:

- New syringe
- Alcohol wipes
- Cotton ball or gauze pad
- Adhesive bandage
- Sharps disposal container



D) Prepare and clean your injection site.



You can use:

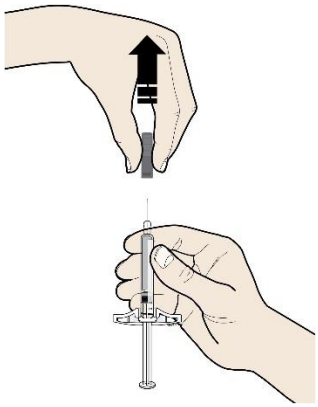
- Your thigh
- Stomach area (abdomen), except for a 2-inch area right around your navel
- Outer area of upper arm (only if someone else is giving you the injection)

Clean your injection site with an alcohol wipe. Let your skin dry.

- **Do not** touch this area again before injecting.
- If you want to use the same injection site, make sure it is not the same spot on the injection site you used for a previous injection.
- Do not inject into areas where the skin is tender, bruised, red, or hard.
- Avoid injecting into areas with scars or stretch marks.
- Avoid injecting directly into raised, thick, red, or scaly skin patch or lesion.

<u>Step 2: Get ready</u>

E) Pull gray needle cap straight out and away from your body when you are ready to inject.



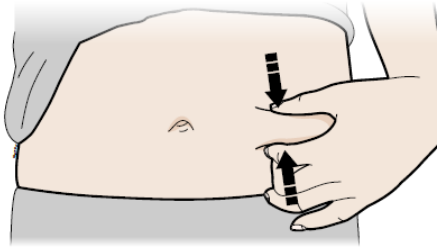
It is normal to see a drop of liquid at the end of the needle.

- **Do not** twist or bend the gray needle cap.
- **Do not** put the gray needle cap back onto the syringe.
- **Do not** remove the gray needle cap from the syringe until you are ready to inject.

Important: Throw the needle cap into the sharp's disposal container.

F) Pinch your injection site to create a firm surface.

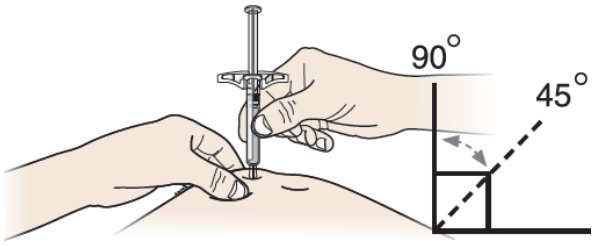
Pinch skin firmly between your thumb and fingers, creating an area of about 2 inches wide.



Important: Keep skin pinched while injecting.

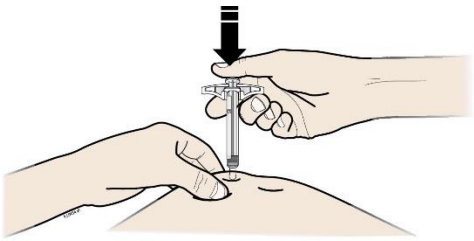
<u>Step 3: Inject</u>

G) Hold the pinch. With the gray needle cap off, insert the syringe into your skin at 45 to 90 degrees.

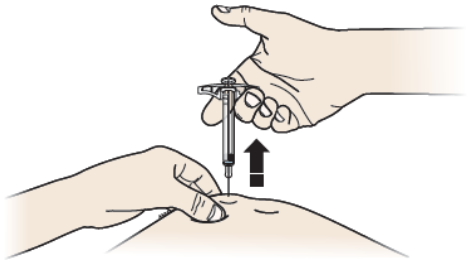


Do not place your finger on the plunger rod while inserting the needle.

H) Using slow and constant pressure, push the plunger rod all the way down until it stops moving.



I) When done, release your thumb, and gently lift the syringe off of your skin.



Important: When you remove the syringe, if it looks like the medicine is still in the syringe barrel, this means you have not received a full dose. Call your healthcare provider immediately.

Step 4: Finish

J) Discard the used syringe and the gray needle cap.

- **DO NOT** put the needle cap back on. Immediately throw away the used SILIQ syringe in a sharp's disposal container. **Do not** throw away (dispose of) the syringe in your household trash.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharp's disposal container. There may be provincial or local laws about how you should throw away used needles and syringes.
- **NEVER** reuse the syringe.
- **Do not** recycle the syringe or sharps disposal container or throw them into household trash.

Important: Always keep the sharps disposal container out of the reach of children.

K) Examine the injection site.

If there is blood, press a cotton ball or gauze pad on your injection site. **Do not** rub the injection site. Apply an adhesive bandage if needed.

Overdose:

If you use more SILIQ than prescribed or take the dose sooner than required, tell your doctor.

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

Missed Dose:

If you have forgotten to inject a dose of SILIQ, inject the next dose as soon as you can after the missed dose. Then, talk to your doctor about when you should inject the next dose.

What are possible side effects from using SILIQ?

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

Common side effects of SILIQ include:

- Headache
- Joint pain
- Feeling tired
- Mouth or throat pain
- Diarrhea

Serious side effects and what to do about them			
Symptoms / effects	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNKNOWN			
Allergic reactions (angioedema, anaphylaxis): sudden low blood pressure, which can cause dizziness or light-headedness, difficulty swallowing or breathing; wheezing; swollen face, lips, tongue, throat, hands and feet, genitals; hives or rash; severe itching of the skin, with red rash or raised bumps			√
Hypersensitivity reactions: rashes, eczema, urticaria and dermatitis		√	

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 healthcare 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:

- Store SILIQ in a refrigerator at 2°C to 8°C.
- Keep SILIQ in the original carton to protect from light and physical damage during storage.
- SILIQ can be kept at controlled room temperature between 20°C to 25°C in the original carton for 14 days. Discard SILIQ if it is not used within 14 days of storage at room temperature.
- Keep SILIQ out of sight and reach of children.
- Do not freeze SILIQ.
- Do not shake SILIQ.
- Do not use SILIQ beyond the expiration date on the label of the prefilled syringe.
- Do not throw away any medicines via wastewater or household waste. Ask your healthcare provider how to throw away medicines you no longer use.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use SILIQ for a condition for which it was not prescribed. Do not give SILIQ to other people even if they have the same symptoms that you have. It may harm them.

If you want more information about SILIQ:

- Talk to your healthcare 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; the manufacturer's website www.bauschhealth.ca, or by calling 1-800-361-4261.

This leaflet was prepared by Bausch Health, Canada Inc.

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