

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrSKYRIZI™

risankizumab injection

75 mg in 0.83 mL sterile solution (90 mg/mL) subcutaneous injection

Interleukin-23 (IL-23) inhibitor

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SKYRIZI™

risankizumab injection

PART I: HEALTH PROFESSIONAL INFORMATION

1. INDICATIONS

SKYRIZI (risankizumab injection) is indicated for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

1.1. Pediatrics (< 18 years of age):

SKYRIZI is not indicated in the pediatric population, as the efficacy and safety of SKYRIZI have not been evaluated in patients less than 18 years of age.

1.2. Geriatrics (≥ 65 years of age):

Limited data are available to Health Canada regarding this age group. Of the 2234 patients with plaque psoriasis exposed to SKYRIZI in Phase 2 and Phase 3 clinical trials, 243 (11%) were 65 years or older and 24 (1%) patients were 75 years or older (see **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Geriatrics**).

2. CONTRAINDICATIONS

SKYRIZI is contraindicated in patients who are hypersensitive to risankizumab or to any ingredient in the formulation or component of the container. For a complete listing, see the **DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING**.

3. DOSAGE AND ADMINISTRATION

SKYRIZI (risankizumab injection) should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of plaque psoriasis and familiar with the SKYRIZI efficacy and safety profile.

3.1. Dosing Considerations

Patients may self-inject SKYRIZI if their physician determines that it is appropriate and with medical follow-up, as necessary, after proper training in subcutaneous injection technique.

Patients should be instructed to inject 2 pre-filled syringes for the full 150 mg dose and to read the **Instructions for Use** before administration. Each pre-filled syringe is for single use only.

3.2. Recommended Dose and Dosage Adjustment

The recommended dose of SKYRIZI is 150 mg (two 75 mg injections) administered by subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter.

Pediatrics (< 18 years of age)

SKYRIZI is not indicated in the pediatric population, as the efficacy and safety of SKYRIZI have not been evaluated in patients less than 18 years of age.

Geriatrics (≥ 65 years of age)

Limited data are available to Health Canada regarding this age group. No dosage adjustment is required (see **INDICATIONS, Geriatrics** and **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Geriatrics**).

Renal or Hepatic Impairment

No specific studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of SKYRIZI (see **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Renal and Hepatic Insufficiency**).

3.3. Administration

SKYRIZI is administered by subcutaneous injection. For each dose, the injections should be administered at different anatomic locations (such as upper arms, thighs or abdomen), and not into areas where the skin is tender, bruised, erythematous, indurated or affected by psoriasis. SKYRIZI is intended for use under the guidance and supervision of a physician. SKYRIZI may be administered by a healthcare professional or a patient or caregiver after proper training in subcutaneous injection technique.

3.4. Preparation for Use

For a more comfortable injection, patients may remove the carton from the refrigerator before injecting and allow to reach room temperature out of direct sunlight (15 to 30 minutes) without removing the pre-filled syringes from the carton.

Visually inspect SKYRIZI for particulate matter and discolouration prior to administration. SKYRIZI is a colourless to slightly yellow and clear to slightly opalescent solution. It may contain a few translucent to white product-related particles. Do not use if the solution is cloudy or discoloured, or contains large particles.

3.5. Missed Dose

If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time.

4. OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

Single intravenous doses up to 1200 mg and single subcutaneous doses up to 300 mg of risankizumab have been administered in clinical trials without dose-limiting toxicity (see **DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment**).

5. DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Route of Administration	Dosage Form/ Strength/ Composition	Non-medicinal Ingredients
subcutaneous	Solution for injection/ 90 mg/mL/ 75 mg risankizumab in 0.83 mL solution	disodium succinate hexahydrate, polysorbate 20, sorbitol, succinic acid, and water for injection

SKYRIZI (risankizumab injection) is supplied as a solution for injection in a pre-filled syringe with needle guard. Each pre-filled syringe contains 75 mg risankizumab in 0.83 mL sterile solution. SKYRIZI does not contain preservatives; therefore, each pre-filled syringe is for single use only.

SKYRIZI is available in cartons containing 2 pre-filled syringes.

Not made with natural rubber latex.

6. WARNINGS AND PRECAUTIONS

Infections

SKYRIZI (risankizumab injection) may increase the risk of infections (see **ADVERSE REACTIONS, Clinical Trial Adverse Drug Reactions, Infections**).

SKYRIZI should not be given to patients with any clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, the risks and benefits should be considered prior to prescribing SKYRIZI. Patients should be instructed to seek medical advice if signs or symptoms of a clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy for the infection, the patient should be closely monitored and SKYRIZI should not be administered until the infection resolves.

In clinical trials, infections were reported in 22% of patients in the SKYRIZI 150 mg group versus 15% of patients in the placebo group through 16 weeks of treatment. The most common type of infection reported in patients that received SKYRIZI 150 mg were upper respiratory tract infections (see **ADVERSE REACTIONS, Clinical Trial Adverse Drug Reactions, Infections**).

Tuberculosis

SKYRIZI must not be given to patients with active tuberculosis (TB). Evaluate patients for TB infection according to the Canadian Tuberculosis Standards prior to initiating treatment with SKYRIZI. Initiate treatment of latent TB prior to initiating SKYRIZI. Consider anti-TB therapy prior to initiating SKYRIZI in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving SKYRIZI should be monitored for signs and symptoms of active TB during and after the treatment.

Immune

Vaccinations

Prior to initiating therapy with SKYRIZI, completion of all appropriate immunizations should be considered according to current immunization guidelines. SKYRIZI should not be used with live vaccines. No data are available on the response to live or inactive vaccines.

If a patient has received live vaccination (viral or bacterial), it is recommended to wait at least four weeks prior to starting treatment with SKYRIZI.

Hypersensitivity

As with all therapeutic proteins including SKYRIZI, there is potential for anaphylaxis. If an anaphylactic or other serious allergic reaction occurs, immediately discontinue the administration of SKYRIZI and initiate appropriate medical treatment.

Inform patients/caregivers of the signs and symptoms of anaphylaxis and hypersensitivity reactions, and instruct them to seek immediate medical care if signs and symptoms occur.

Sexual Health

Fertility

The effect of SKYRIZI on human fertility has not been studied. In addition, no dedicated fertility studies have been conducted in animals. In 26-week repeat-dose toxicity studies conducted in cynomolgus monkeys, no adverse effects on male or female reproductive organs or on male fertility-related parameters were observed (see **NON-CLINICAL TOXICOLOGY, Reproductive and Developmental Toxicology**).

6.1. Special Populations

6.1.1. Pregnant Women

The use of SKYRIZI in pregnant women has not been studied.

In an enhanced pre- and post-natal developmental study conducted in cynomolgus monkeys, fetal losses and neonatal deaths were observed following weekly subcutaneous injections of risankizumab to pregnant monkeys from the beginning of organogenesis until parturition at exposure values that were 13- to 99-fold greater than the human exposure levels. No adverse developmental effects were observed in surviving monkey infants. In addition, risankizumab was detected in monkey infant serum (see **NON-CLINICAL TOXICOLOGY, Reproductive and Developmental Toxicology**).

Animal studies are not always predictive of human response; therefore, it is unknown whether SKYRIZI can cause fetal harm when administered to a pregnant woman.

Women of childbearing potential should use adequate contraception while using SKYRIZI and for at least 20 weeks after the last SKYRIZI dose.

6.1.2. Breast-feeding

There are no data on the presence of risankizumab in human milk, the effects on the breastfed infant, or the effects on milk production. Because human immunoglobulin G (IgG) is secreted into human milk, precaution should be exercised. The developmental and health benefits of breast-feeding should be considered, as well as any potential adverse effects on the breastfed infant.

6.1.3. Pediatrics (< 18 years of age)

SKYRIZI is not indicated in the pediatric population, as the efficacy and safety of SKYRIZI have not been evaluated in patients less than 18 years of age.

6.1.4. Geriatrics (≥ 65 years of age)

Limited data are available regarding this age group (see **INDICATIONS, Geriatrics and DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment, Geriatrics**).

7. ADVERSE REACTIONS

7.1. Adverse Drug Reaction Overview

Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 20.0.

The most frequently ($\geq 10\%$) reported adverse drug reactions (ADRs), through the 16-week placebo-controlled period in the SKYRIZI (risankizumab injection) 150 mg group were upper respiratory tract infections (13%) compared with 10% in the placebo group. Most of the reactions were mild or moderate in severity.

The proportion of patients treated with SKYRIZI 150 mg who discontinued treatment due to adverse events was 1.8% (29/1590).

Serious adverse events (SAEs) were reported in 2.4% (31/1306) of SKYRIZI 150 mg-treated patients and 4.0% (12/300) of placebo-treated patients through 16 weeks.

7.2. Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

A total of 2234 patients were treated with SKYRIZI in clinical development studies in plaque psoriasis, representing 2167 patient years of exposure. Of these, 1208 (54%) patients with psoriasis were exposed to SKYRIZI for at least one year.

Data from placebo- and active-controlled studies were pooled to evaluate the safety of SKYRIZI for up to 16 weeks. In total, 1306 patients were evaluated in the SKYRIZI 150 mg group.

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the SKYRIZI group than the placebo group during the 16-week controlled period of pooled clinical studies.

Table 1. Adverse Reactions Occurring in $\geq 1\%$ of Patients with Plaque Psoriasis through Week 16

	SKYRIZI¹ N = 1306 n (%)	Placebo² N = 300 n (%)	Ustekinumab³ N = 199 n (%)	Adalimumab⁴ N = 304 n (%)
General Disorders and Administration Site Conditions				
Fatigue ⁵	33 (2.5)	3 (1.0)	5 (2.5)	8 (2.6)
Injection site reactions ⁶	19 (1.5)	3 (1.0)	5 (2.5)	17 (5.6)
Infections and Infestations				
Upper respiratory tract infections ⁷	170 (13.0)	29 (9.7)	25 (12.6)	42 (13.8)
Urinary tract infection	14 (1.1)	2 (0.7)	5 (2.5)	3 (1.0)
Tinea infections ⁸	14 (1.1)	1 (0.3)	0 (0)	2 (0.7)
Nervous System Disorders				
Headache ⁹	46 (3.5)	6 (2.0)	7 (3.5)	20 (6.6)
Skin and Subcutaneous Tissue Disorders				
Pruritus	19 (1.5)	4 (1.3)	3 (1.5)	10 (3.3)
1 Includes data from ULTIMMA-1, ULTIMMA-2, IMMSTANCE and IMMVENT studies. Patients received SKYRIZI 150 mg at Week 0 and Week 4.				
2 Includes data from ULTIMMA-1, ULTIMMA-2 and IMMSTANCE studies. Patients received placebo at Week 0 and Week 4.				
3 Includes data from ULTIMMA-1 and ULTIMMA-2 studies. Patients received a weight-based dose of ustekinumab: 45 mg (weight ≤ 100 kg) or 90 mg (weight > 100 kg) at Week 0 and Week 4.				
4 Includes data from IMMVENT study. Patients received adalimumab 80 mg at Week 0, 40 mg at Week 1, then every other week (q2wk) thereafter.				
5 Includes: fatigue, asthenia				
6 Includes: injection site bruising, erythema, extravasation, hematoma, hemorrhage, infection, inflammation, irritation, pain, pruritus, reaction, swelling, warmth				
7 Includes: respiratory tract infection (viral, bacterial, or unspecified), sinusitis (including acute), rhinitis, nasopharyngitis, pharyngitis (including viral), tonsillitis				
8 Includes: tinea pedis, tinea cruris, body tinea, tinea versicolor, tinea manuum, tinea infection				
9 Includes: headache, tension headache, sinus headache, cervicogenic headache				

Infections

In the first 16 weeks, infections occurred in 22.1% (288/1306) of the SKYRIZI 150 mg group (90.8 events per 100 patient-years) compared to 14.7% (44/300) of the placebo group (56.5 events per 100 patient-years). The majority of cases were non-serious and mild to moderate in severity and did not lead to discontinuation of SKYRIZI. Serious infections were reported in 5 (0.4%) SKYRIZI 150 mg-treated patients and in 1 (0.3%) placebo-treated patient (see **WARNINGS AND PRECAUTIONS, Infections**).

Over the entire psoriasis program including long-term exposure to SKYRIZI 150 mg, the rate of infections was 48% (759/1590, 79 events per 100 patient-years); the rate of serious infections was 1.4% (22/1590, 1.6 events per 100 patient-years).

Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity with SKYRIZI. Immunogenicity tests are generally product-specific and are highly dependent on the sensitivity and specificity of the assay. Comparison of incidence of antibodies between products by different tests may be misleading.

For patients treated with SKYRIZI at the recommended clinical dose for up to 52 weeks in psoriasis clinical trials, treatment-emergent anti-drug antibodies were detected in 24% (263/1079) of evaluated patients. Of the patients who developed antidrug antibodies, approximately 57% had antibodies that were classified as neutralizing which equates to 14% (150/1079) of all patients treated with SKYRIZI.

Antibodies to risankizumab including neutralizing antibodies were not generally associated with changes in clinical response or safety. Among the few patients (approximately 1%; 7/1000 at Week 16 and 6/598 at Week 52) with high antibody titers (> 128), clinical response appeared to be reduced.

7.3. Less Common Clinical Trial Adverse Drug Reactions (< 1%)

Infections and Infestations: Folliculitis

8. DRUG INTERACTIONS

8.1. Serious Drug Interactions Box

Not applicable.

8.2. Overview

SKYRIZI (risankizumab injection) is not expected to undergo metabolism by hepatic enzymes or renal elimination. Drug interactions between SKYRIZI and substrates/inhibitors/inducers of drug metabolizing enzymes are not expected.

8.3. Drug-Drug Interactions

Live Vaccines

Live vaccines should not be given while a patient is undergoing therapy with SKYRIZI (see **WARNINGS and PRECAUTIONS, Immune, Vaccinations**).

Immunosuppression Therapy

The safety and efficacy of SKYRIZI in combination with immunosuppressant drugs, including biologics, or with phototherapy, have not been evaluated.

Interactions with CYP450 Substrates

The formation of cytochrome P450 (CYP) enzymes can be altered by increased levels of certain cytokines (e.g., interleukin [IL]- β , IL-6, tumor necrosis factor, and interferon) during chronic inflammation. A drug interaction study was conducted in patients with plaque psoriasis to assess the effect of repeated administration of risankizumab injection on the pharmacokinetics of cytochrome P450 (CYP) sensitive probe substrates. The exposure of caffeine (CYP1A2 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate) and midazolam (CYP3A substrate) following administration of risankizumab injection were comparable to their exposures prior to risankizumab injection, indicating no interactions through these enzymes.

Population pharmacokinetic analyses indicated that risankizumab exposure was not impacted by concomitant medications (metformin, atorvastatin, lisinopril, amlodipine, ibuprofen, acetylsalicylate and levothyroxine) used by some patients with plaque psoriasis during the clinical studies.

8.4. Drug-Food Interactions

Interactions with food have not been studied.

8.5. Drug-Herb Interactions

Interactions with herbal products have not been studied.

8.6. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been studied.

9. ACTION AND CLINICAL PHARMACOLOGY

9.1. Mechanism of Action

Risankizumab is a humanized immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds with high affinity to the p19 subunit of human interleukin 23 (IL-23) cytokine and inhibits IL-23 signalling in cell-based assays, including the release of the pro-inflammatory cytokine, IL-17. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Risankizumab was shown to not bind to human IL-12 *in vitro*.

9.2. Pharmacokinetics

Risankizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure across dose ranges of 18 to 300 mg and 0.25 to 1 mg/kg administered subcutaneously, and 200 to 1200 mg and 0.01 to 5 mg/kg administered intravenously.

Absorption

Following subcutaneous dosing of risankizumab, peak plasma concentrations were achieved between 3 to 14 days after dosing with an estimated absolute bioavailability of 89% based on population pharmacokinetic analyses.

Following a single 300 mg subcutaneous injection in healthy Caucasian subjects, risankizumab reached a mean (\pm SD) maximum plasma concentration (C_{max}) of 20.4 ± 8.02 mcg/mL by approximately 7 days post dose.

With the dosing regimen in patients with psoriasis (150 mg at Week 0, Week 4, and every 12 weeks thereafter), population pharmacokinetic estimated mean (\pm SD) steady-state peak and trough plasma concentrations are 11.9 ± 3.06 and 1.91 ± 1.17 mcg/mL, respectively.

Distribution

Based on population pharmacokinetic analyses, in a typical 90 kg patient with psoriasis, the steady-state volume of distribution (V_{ss}) was 11.2 L.

Metabolism

The exact pathway through which risankizumab is metabolized has not been characterized. Therapeutic IgG monoclonal antibodies are typically degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgGs.

Elimination

Based on population pharmacokinetic analyses, the systemic clearance (CL) of risankizumab was 0.31 L/day and terminal elimination half-life ($T_{1/2}$) was 28 days for a typical 90 kg patient with psoriasis. Following a single 300 mg subcutaneous injection in healthy Caucasian subjects, risankizumab mean $T_{1/2}$ was approximately 29 days.

Special Populations and Conditions

Pediatrics

The pharmacokinetics of risankizumab in pediatric patients has not been evaluated.

Geriatrics

Of the 2234 patients with plaque psoriasis exposed to SKYRIZI, a total of 243 were 65 years or older, and 24 patients were 75 years or older. No overall differences in risankizumab exposure, safety and effectiveness were observed between older and younger patients who received SKYRIZI.

Sex

The clearance of risankizumab was not significantly influenced by gender in adult patients with plaque psoriasis.

Ethnic origin

No clinically meaningful differences in risankizumab exposure were found in Chinese or Japanese compared to Caucasian in a clinical pharmacokinetic study in healthy subjects. The number of patients from the Asian region is limited; however, the data from subgroup analyses by region are consistent with the overall results in pivotal clinical studies.

Renal and Hepatic Insufficiency

No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of risankizumab.

As an IgG1 monoclonal antibody, risankizumab is likely eliminated via intracellular catabolism and is not expected to undergo metabolism via hepatic cytochrome P450 enzymes or renal elimination.

Obesity

Risankizumab clearance and volume of distribution increase as body weight increases. Data from a limited number of patients indicate that high body weight (>130 kg) may result in reduced efficacy.

10. STORAGE, STABILITY AND DISPOSAL

Temperature:

Store in a refrigerator between 2 to 8 °C (36 to 46 °F). Do not freeze.

Light:

Keep the pre-filled syringes in the outer carton in order to protect from light.

Others:

Keep out of reach and sight of children.

11. SPECIAL HANDLING INSTRUCTIONS

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

PART II: SCIENTIFIC INFORMATION

12. PHARMACEUTICAL INFORMATION

Proper name:	Risankizumab
Chemical name:	Not applicable. Risankizumab is an immunoglobulin.
Molecular formula and molecular mass:	Based on the amino acid sequence, the molecular formula of the disulfide bonded risankizumab molecule without post-translational modifications is C ₆₄₇₆ H ₉₉₉₂ N ₁₇₂₀ O ₂₀₁₆ S ₄₄ . The predicted molecular weight of aglycosylated risankizumab is approximately 146 kDa.
Structural formula:	Risankizumab is a recombinant humanized IgG1 kappa immunoglobulin comprising two heavy chains, and two light chains. The heavy and light chains are covalently linked by a single disulfide bond and the heavy chains are linked to each other by two disulfide bonds. Each heavy chain contains a single N-linked glycosylation site.
Physicochemical properties:	Risankizumab is supplied as a sterile, preservative-free solution for subcutaneous administration. The solution is colourless to slightly yellow and clear to slightly opalescent, with a pH of 6.2. It may contain a few translucent to white product-related particles.

13. CLINICAL TRIALS

13.1. Trial Design and Study Demographics

The efficacy and safety of SKYRIZI (risankizumab injection) was assessed in 2109 adult patients with moderate to severe plaque psoriasis in four multicenter, randomized, double-blind studies (ULTIMMA-1, ULTIMMA-2, IMMSTANCE, and IMMVENT). Enrolled patients were 18 years of age and older with plaque psoriasis who had a body surface area (BSA) involvement of $\geq 10\%$, a static Physician Global Assessment (sPGA) score of ≥ 3 (moderate psoriasis) on a 5-point severity scale, a Psoriasis Area and Severity Index (PASI) score ≥ 12 , and who were candidates for systemic therapy or phototherapy. Patients with guttate, erythrodermic, or pustular psoriasis were excluded from the studies.

ULTIMMA-1 and ULTIMMA-2 enrolled 997 patients (598 randomized to SKYRIZI 150 mg, 199 to ustekinumab 45 mg [≤ 100 kg body weight] or 90 mg [> 100 kg body weight] and 200 to placebo). Patients received treatment at Week 0, Week 4, and every 12 weeks thereafter.

IMMSTANCE enrolled 507 patients (407 randomized to SKYRIZI 150 mg and 100 to placebo). Patients received treatment at Week 0, Week 4 and every 12 weeks thereafter. Patients who were originally on SKYRIZI and had a sPGA response of clear or almost clear (0/1) at Week 28 were re-randomized to continue SKYRIZI every 12 weeks or have treatment withdrawn.

IMMVENT enrolled 605 patients (301 randomized to SKYRIZI and 304 to adalimumab). Patients randomized to SKYRIZI received 150 mg of treatment at Week 0, Week 4 and every 12 weeks thereafter. Patients randomized to adalimumab received 80 mg at Week 0, 40 mg at Week 1 and 40 mg every other week through Week 15. Starting at Week 16, patients who were receiving adalimumab continued or switched treatment based on response:

- $< \text{PASI } 50$ were switched to SKYRIZI
- $\text{PASI } 50$ to $< \text{PASI } 90$ were re-randomized to either continue adalimumab or switch to SKYRIZI
- $\text{PASI } 90$ continued to receive adalimumab

In all four Phase 3 studies, randomization was stratified by weight (≤ 100 kg versus > 100 kg) and by prior exposure to tumor necrosis factor (TNF) antagonists (0 versus ≥ 1).

In ULTIMMA-1 and ULTIMMA-2, the co-primary endpoints were the proportions of patients who achieved PASI 90 and sPGA of 0/1 at Week 16, comparing SKYRIZI to placebo. In IMMSTANCE, the co-primary endpoints at Week 16 were the proportions of patients who achieved PASI 90 and sPGA of 0/1, comparing SKYRIZI to placebo. In IMMVENT, the co-primary endpoints at Week 16 were the proportions of patients who achieved PASI 90 and sPGA of 0/1, comparing SKYRIZI to adalimumab.

Other endpoints included the proportion of patients who achieved PASI 75, PASI 100, and sPGA clear (0). Patient-reported outcomes were assessed based on the Dermatology Life Quality Index (DLQI) and Psoriasis Symptom Scale (PSS).

Patient demographics (**Table 2**) and baseline disease characteristics were generally balanced across treatment groups and studies. The majority of patients who were randomized to SKYRIZI were male (69.5%) and white (78.1%). Overall, patients had a median baseline PASI score of 17.8 and a median BSA of 20.0%. Baseline sPGA score was severe in 19.3% of patients. A total of 9.8% of study patients had a history of diagnosed psoriatic arthritis.

Across all studies, 38.1% of patients had received prior phototherapy, 48.3% had received prior non-biologic systemic therapy, and 42.1% had received prior biologic therapy for the treatment of psoriasis. Of the patients who had received prior biologic therapy, 23.7% had received at least one anti-tumor necrosis factor (TNF) alpha agent.

Table 2. Summary of Patient Demographics for Clinical Trials in Plaque Psoriasis

Study #	Trial Design	Dosage, Route of Administration, and Schedule ^a	Number of Study Patients	Mean Age (Range) Years	Sex n (%)
ULTIMMA-1 (M16-008/ 1311.3)	Phase 3, randomized, PBO and active-controlled, DB, double dummy, parallel study	RZB 150 mg SC Wks 0, 4, then q12w starting at Wk 16; UST 45 mg SC (\leq 100 kg) or 90 mg SC ($>$ 100 kg) Wks 0, 4, then q12w starting at Wk 16; PBO SC Wks 0, 4, then RZB 150 mg q12w starting at Wk 16	RZB: 304 UST: 100 PBO: 102	48.1 (19 – 85)	Female 145 (28.7) Male 361 (71.3)
ULTIMMA-2 (M15-995/ 1311.28)	Phase 3, randomized, PBO and active-controlled, DB, double dummy, parallel study	RZB 150 mg SC Wks 0, 4, then q12w starting at Wk 16; UST 45 mg SC (\leq 100 kg) or 90 mg SC ($>$ 100 kg) Wks 0, 4, then q12w starting at Wk 16; PBO SC Wks 0, 4, then RZB 150 mg q12w starting at Wk 16	RZB: 294 UST: 99 PBO: 98	46.7 (19 – 76)	Female 155 (31.6) Male 336 (68.4)
IMMHANCE (M15-992/ 1311.4)	Phase 3, randomized, DB, PBO-controlled study with re-randomization at Wk 28 to RZB or PBO based on response	RZB 150 mg SC Wks 0, 4, then q12w starting at Wk 16; PBO SC Wks 0, 4, then RZB q12w starting at Wk 16	RZB: 407 PBO: 100	49.2 (19 – 80)	Female 151 (29.8) Male 356 (70.2)

Study #	Trial Design	Dosage, Route of Administration, and Schedule ^a	Number of Study Patients	Mean Age (Range) Years	Sex n (%)
IMMVENT (M16-010/1311.30)	Phase 3, randomized, active-controlled, DB, double dummy, parallel study with re-randomization at Wk 16 to RZB or ADA based on response to ADA	RZB 150 mg SC Wks 0, 4, then q12w starting at Wk 16; ADA 80 mg SC Wk 0, 40 mg SC Wk 1, then 40 mg SC q2w	RZB: 301 ADA: 304	46.2 (18 – 81)	Female 183 (30.2) Male 422 (69.8)

DB = double blind; SC = subcutaneous; PBO = placebo; RZB = risankizumab; UST = ustekinumab; ADA = adalimumab; q12w = every 12 weeks; q2w = every 2 weeks; wk = week

^a Detailed information about dosage, route of administration and duration of these clinical trials are included above in this section.

13.2. Study Results

ULTIMMA-1 and ULTIMMA-2

The results of ULTIMMA-1 and ULTIMMA-2 are presented in **Table 3** and **Table 4**.

In ULTIMMA-1 and ULTIMMA-2, SKYRIZI demonstrated superiority to placebo for the co-primary endpoints of PASI 90 and sPGA of 0/1 (clear or almost clear) at Week 16 (**Table 3**).

Table 3. Co-Primary Endpoint Results at Week 16 (NRI^a) in Adults with Plaque Psoriasis in ULTIMMA-1 and ULTIMMA-2

	ULTIMMA-1 ^b			ULTIMMA-2 ^b		
	SKYRIZI N = 304 n (%)	Placebo N = 102 n (%)	Treatment Difference % (95% CI)	SKYRIZI N = 294 n (%)	Placebo N = 98 n (%)	Treatment Difference % (95% CI)
sPGA of 0/1	267 (87.8)	8 (7.8)	79.9 (73.5, 86.3) ^c	246 (83.7)	5 (5.1)	78.5 (72.4, 84.5) ^c
PASI 90	229 (75.3)	5 (4.9)	70.3 (64.0, 76.7) ^c	220 (74.8)	2 (2.0)	72.5 (66.8, 78.2) ^c

^a Non-responder imputation (NRI) was used to impute missing data

^b Treatment differences, 95% CIs and p-values were based on the Cochran-Mantel-Haenszel test stratified by weight (≤ 100 kg versus > 100 kg) and prior TNF exposure (0 versus ≥ 1)

^c $p < 0.001$

Table 4. Secondary Endpoint Results (NRI^a) in Adults with Plaque Psoriasis in ULTIMMA-1 and ULTIMMA-2

	ULTIMMA-1 ^b			ULTIMMA-2 ^b		
	SKYRIZI N=304 n (%)	Ustekinumab N=100 n (%)	Placebo N=102 n (%)	SKYRIZI N=294 n (%)	Ustekinumab N=99 n (%)	Placebo N=98 n (%)
sPGA of 0/1						
Week 16	267 (87.8)	63 (63.0)	*	246 (83.7)	61 (61.6)	*
Difference vs Ustekinumab % (95% CI)	25.1 (15.2, 35.0)			22.3 (12.0, 32.5)		
sPGA of 0						
Week 16	112 (36.8)	14 (14.0)	2 (2.0)	150 (51.0)	25 (25.3)	3 (3.1)
Difference vs Ustekinumab % (95% CI)	22.9 (14.3, 31.6)			26.3 (16.1, 36.4)		
Difference vs Placebo % (95% CI)	34.7 (28.6, 40.8)			47.5 (40.9, 54.2)		
Week 52	175 (57.6)	21 (21.0)	NA ^c	175 (59.5)	30 (30.3)	NA ^c
Difference vs Ustekinumab % (95% CI)	36.5 (27.0, 45.9)			29.5 (18.9, 40.1)		
PASI 90						
Week 16	229 (75.3)	42 (42.0)	*	220 (74.8)	47 (47.5)	*
Difference vs Ustekinumab % (95% CI)	33.5 (22.7, 44.3)			27.6 (16.7, 38.5)		
Week 52	249 (81.9)	44 (44.0)	NA ^c	237 (80.6)	50 (50.5)	NA ^c
Difference vs Ustekinumab % (95% CI)	38.3 (27.9, 48.6)			30.2 (19.6, 40.9)		
PASI 100						
Week 16	109 (35.9)	12 (12.0)	0 (0.0)	149 (50.7)	24 (24.2)	2 (2.0)
Difference vs Ustekinumab % (95% CI)	23.8 (15.5, 32.1)			27.0 (17.0, 37.0)		

	ULTIMMA-1 ^b			ULTIMMA-2 ^b		
	SKYRIZI N=304 n (%)	Ustekinumab N=100 n (%)	Placebo N=102 n (%)	SKYRIZI N=294 n (%)	Ustekinumab N=99 n (%)	Placebo N=98 n (%)
Difference vs Placebo % (95% CI)	35.5 (30.0, 41.0)			48.2 (41.9, 54.6)		
Week 52	171 (56.3)	21 (21.0)	NA ^c	175 (59.5)	30 (30.3)	NA ^c
Difference vs Ustekinumab % (95% CI)	35.1 (25.7, 44.6)			29.5 (18.9, 40.1)		

* sPGA of 0/1 and PASI 90 versus placebo at Week 16 were co-primary endpoints in **Table 3**.

^a Non-responder imputation (NRI) was used to impute missing data

^b Treatment differences and 95% CIs (for SKYRIZI vs Ustekinumab and for SKYRIZI vs Placebo) were based on the Cochran-Mantel-Haenszel test stratified by weight (≤ 100 kg versus > 100 kg) and prior TNF exposure (0 versus ≥ 1). Type I error rate for the multiple endpoints was controlled using a pre-defined hierarchical testing procedure.

^c NA = Not Applicable as comparisons to placebo were not possible at Week 52.

IMMHANCE

The results of the study are presented below.

Table 5. Efficacy Results at Week 16 (NRI^a) in Adults with Plaque Psoriasis in IMMHANCE

	SKYRIZI (N = 407) n (%)	Placebo (N = 100) n (%)	Treatment Difference vs Placebo % (95% CI) ^b
Primary Endpoints			
sPGA of 0/1	340 (83.5)	7 (7.0)	76.5 (70.4, 82.5) ^c
PASI 90	298 (73.2)	2 (2.0)	70.8 (65.7, 76.0) ^c
Secondary Endpoints			
sPGA of 0	189 (46.4)	1 (1.0)	44.8 (39.5, 50.0)
PASI 75	361 (88.7)	8 (8.0)	80.6 (74.5, 86.6)
PASI 100	192 (47.2)	1 (1.0)	45.5 (40.3, 50.8)

^a Non-responder imputation (NRI) was used to impute missing data

^b Treatment differences, 95% CIs and p-values were based on the Cochran-Mantel-Haenszel test stratified by weight (≤ 100 kg versus > 100 kg) and prior TNF exposure (0 versus ≥ 1). Type I error rate for the multiple endpoints was controlled using a pre-defined hierarchical testing procedure.

^c p < 0.001

IMMVENT

The results of the study are presented below.

Table 6. Efficacy Results at Week 16 (NRI^a) in Adults with Plaque Psoriasis in IMMVENT

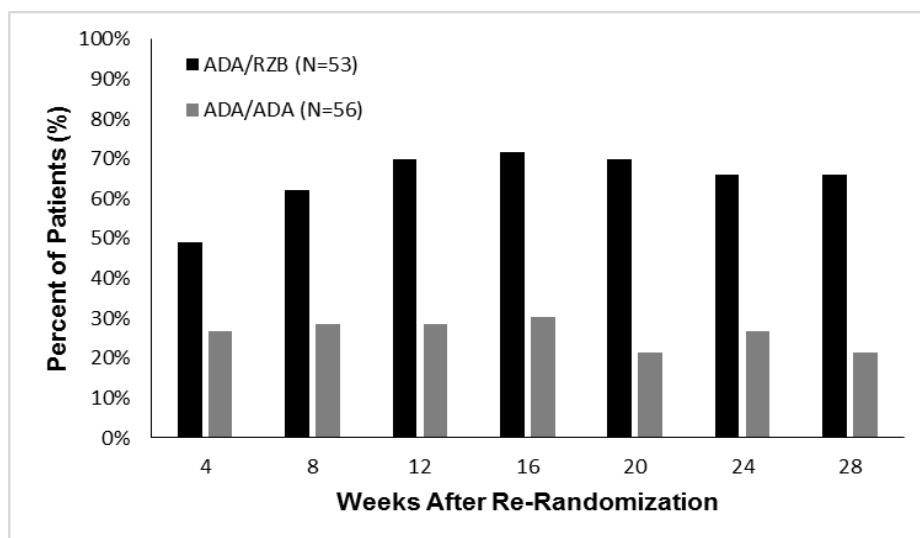
	SKYRIZI (N = 301) n (%)	Adalimumab (N = 304) n (%)	Treatment Difference vs Adalimumab % (95% CI)^b
Primary Endpoints			
sPGA of 0/1	252 (83.7)	183 (60.2)	23.3 (16.6, 30.1) ^c
PASI 90	218 (72.4)	144 (47.4)	24.9 (17.5, 32.4) ^c
Secondary Endpoints			
PASI 75	273 (90.7)	218 (71.7)	18.9 (13.0, 24.9)
PASI 100	120 (39.9)	70 (23.0)	16.7 (9.5, 23.9)

^a Non-responder imputation (NRI) was used to impute missing data

^b Treatment differences, 95% CIs and p-values were based on the Cochran-Mantel-Haenszel test stratified by weight (≤ 100 kg versus > 100 kg) and prior TNF exposure (0 versus ≥ 1). Type I error rate for the multiple endpoints was controlled using a pre-defined hierarchical testing procedure.

^c $p < 0.001$

Among the patients who had PASI 50 to $<$ PASI 90 with adalimumab at Week 16 and were re-randomized, 66.0% (35/53) and 39.6% (21/53) of patients re-randomized to SKYRIZI achieved PASI 90 and PASI 100, respectively, compared with 21.4% (12/56) and 7.1% (4/56) who continued to receive adalimumab at Week 44.



ADA/ADA: Patients randomized to adalimumab and continued adalimumab
 ADA/RZB: Patients randomized to adalimumab and switched to SKYRIZI
 $p < 0.05$ at Week 4 and $p < 0.001$ at each time point beginning at Week 8
 RZB = risankizumab; ADA = adalimumab

Figure 1. Proportion of Patients Achieving of PASI 90 After Re-randomization in IMMVENT

Maintenance and Durability of Response

Among re-randomized patients with sPGA of 0/1 at Week 28 in the IMMCHANGE study, 87.4% (97/111) maintained response with continued treatment compared to 61.3% (138/225) with withdrawal (placebo) at Week 52.

Quality of Life/Patient-Reported Outcomes

In ULTIMMA-1 and ULTIMMA-2, the percentage of patients with Dermatology Life Quality Index (DLQI) of 0/1 (no impact on health-related quality of life) at Week 16 were 65.8% and 66.7%, respectively, in the SKYRIZI groups, 7.8% and 4.1%, respectively, in the placebo groups, and 43.0% and 46.5%, respectively, in the ustekinumab groups.

In ULTIMMA-1 and ULTIMMA-2, psoriasis symptoms of itch, pain, redness, and burning were assessed with the Psoriasis Symptom Scale (PSS). In ULTIMMA-1 and ULTIMMA-2, 29.3% and 31.3% of patients, respectively, in the SKYRIZI groups, and 2.0% and 0% of patients, respectively, in the placebo groups, reported a PSS total score of 0 at Week 16.

13.3. Comparative Bioavailability Studies

Not applicable.

14. MICROBIOLOGY

Not applicable.

15. NON-CLINICAL TOXICOLOGY

General Toxicology

In a 26-week repeat-dose toxicity study in cynomolgus monkeys, risankizumab was well-tolerated at weekly doses up to 50 mg/kg. There were no risankizumab-related adverse effects observed, including on cardiovascular, respiratory, and nervous system functions. At the no-observed-adverse-effect level (NOAEL) of 50 mg/kg once weekly, the AUC was approximately 69-fold higher than the AUC for psoriasis patients following the first two 150 mg doses at Weeks 0 and 4 (622 µg•day/mL).

Carcinogenicity

Carcinogenicity studies have not been conducted with risankizumab.

Genotoxicity

Genotoxicity studies have not been conducted with risankizumab.

Reproductive and Developmental Toxicology

In an enhanced pre- and post-natal development toxicity study, pregnant cynomolgus monkeys (21, 22, and 21 in the 0, 5 and 50 mg/kg groups, respectively) were administered weekly subcutaneous doses of risankizumab from the beginning of organogenesis to parturition. Neonatal deaths occurred in the offspring of 1 of 18 control monkeys, 2 of 17 low-dose monkeys, and 3 of 15 high-dose monkeys (AUC_{ss} values were 13- and 99-fold greater, respectively, than the human exposure levels). These neonatal deaths were attributed to maternal neglect, trauma, and/or early or late delivery, although, a drug-related effect could not be ruled out. An increase in the fetal loss rate (spontaneous abortions, including stillbirths) was also observed at both dose levels. While the incidence rate for fetal loss in each dose group was within the historical control range for the testing facility, a drug-related effect could not be ruled out. The clinical significance of these findings is unknown. No risankizumab-related adverse effects, including any effects on neurobehavioural or immunological development, were observed in surviving infants from birth through 6 months of age.

In the infants, mean serum concentrations increased in a dose-dependent manner and were approximately 20 to 90% of the respective maternal concentrations. Following delivery, most maternal animals and all infants from the risankizumab-administered groups had measurable serum concentrations of risankizumab up to 91 days postpartum. Serum concentrations were below detectable levels at 180 days postpartum in all infants and in all but one maternal animal.

No dedicated fertility studies have been conducted in animals however, in the 26-week repeat-dose toxicity study, histopathology of reproductive organs from female cynomolgus monkeys did not show any relevant adverse finding. In addition, in a separate 26-week repeat dose study

conducted in sexually mature male cynomolgus monkeys, no adverse effects on male fertility-related parameters were observed at a dose of 50 mg/kg (98-fold greater than the human exposure level). Specifically, there were no risankizumab-related adverse effects on testicular volume, semen analysis (total sperm count, sperm concentration, sperm motility, and sperm morphology), serum testosterone concentration, reproductive organ weights, or histopathological findings in reproductive organs.

16. SUPPORTING PRODUCT MONOGRAPHS

Not applicable.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PART III: PATIENT MEDICATION INFORMATION

SKYRIZI™

risankizumab injection

75 mg in 0.83 mL sterile solution (90 mg/mL) subcutaneous injection

Read this carefully before you start taking SKYRIZI 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 SKYRIZI.

What is SKYRIZI used for?

SKYRIZI is a prescription medicine used to treat adults with moderate to severe plaque psoriasis, an inflammatory condition affecting the skin and nails. Plaque psoriasis can cause raised, thick, red and scaly patches (“psoriatic lesions”) that can appear anywhere on your body.

How does SKYRIZI work?

SKYRIZI contains the active substance risankizumab. This medicine works by stopping a protein in the body called IL-23, which causes inflammation. It also improves skin clearance and reduces symptoms of psoriasis such as burning, itching, pain, and redness.

What are the ingredients in SKYRIZI?

Medicinal ingredients: risankizumab

Non-medicinal ingredients: disodium succinate hexahydrate, polysorbate 20, sorbitol, succinic acid, and water for injection

SKYRIZI comes in the following dosage forms:

Pre-filled syringe with 75 mg of risankizumab in 0.83 mL of solution for injection (90 mg/mL).

SKYRIZI is a clear and colourless to slightly yellow liquid in a pre-filled syringe with needle guard. Each carton contains 2 pre-filled syringes.

Do not use SKYRIZI if:

- You are allergic to risankizumab or any of the other ingredients of this medicine. See **What are the ingredients in SKYRIZI?**

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

- you currently have an infection or if you have an infection that keeps coming back. SKYRIZI may lower your ability to fight infections and may increase your risk of infections.
- you have tuberculosis (TB) or have been in close contact with someone with TB.
- you have recently received or plan to receive an immunization (vaccine). You should not be given certain types of vaccines (called 'live vaccines') while using SKYRIZI.

Talk to your healthcare professional right away if you have any of the symptoms of serious infection:

- fever, flu-like symptoms, night sweats
- feeling tired or short of breath
- cough
- blood in your phlegm (mucus)
- warm, red or painful skin, sores on your body different from your psoriasis, or a painful skin rash with blisters
- muscle aches
- weight loss

Talk to your healthcare professional right away if you have any of the signs or symptoms of an allergic reaction, including:

- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps

Other warnings you should know about:

SKYRIZI is not approved for children and adolescents under 18 years of age. This is because it has not been studied in this age group.

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known if SKYRIZI can harm your unborn baby. If you are a woman of childbearing potential, use adequate contraception while using SKYRIZI and for at least 20 weeks after the last SKYRIZI dose. Talk to your doctor about your contraception options.

If you are breastfeeding or are planning to breastfeed, talk to your doctor before using this medicine. It is not known if SKYRIZI passes into breast milk. You and your doctor should decide if you will breastfeed while using SKYRIZI.

Tell your healthcare professional about all the medicines you are using, have recently used or might use, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take SKYRIZI:

Always use this medicine exactly as your doctor, pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure how to use this medicine.

SKYRIZI is given as 2 injections under your skin (called “subcutaneous injections”).

You and your doctor, pharmacist or nurse will decide if you should inject SKYRIZI yourself. Do not inject yourself with this medicine unless you have been trained by your doctor, pharmacist or nurse. A caregiver may also give your injections after training. The AbbVie Care patient assistance program is also available to you if you require assistance with injections should you prefer nurse-administered injections.

For a more comfortable injection: Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **15 to 30 minutes** before injecting.

Read the “**Instructions for Use**” before injecting SKYRIZI yourself.

Usual Dose:

The dose is 150 mg given as two 75 mg injections.

	How much?	When?
1st dose	150 mg (two 75 mg injections)	When your doctor tells you
2nd dose	150 mg (two 75 mg injections)	4 weeks after 1 st dose
Further doses	150 mg (two 75 mg injections)	Every 12 weeks starting after 2 nd dose

Do not stop using SKYRIZI without talking to your doctor first. If you stop treatment, your symptoms may come back.

Overdose:

If you have used more SKYRIZI than you should or the dose has been given sooner than prescribed, talk to your doctor.

If you think you have taken too much SKYRIZI, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forgot to use SKYRIZI, inject a dose as soon as you remember. Then, take your next dose at your regular scheduled time. Talk to your doctor if you are not sure what to do.

What are possible side effects from using SKYRIZI?

These are not all the possible side effects you may feel when taking SKYRIZI. If you experience any side effects not listed here, contact your doctor. Your doctor will decide if you can keep using SKYRIZI.

Tell your doctor, pharmacist or nurse if you get any of the following side effects:

Very common: may affect more than 1 in 10 people

- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people

- feeling tired
- fungal skin infection
- injection site reactions
- headache
- itching
- burning when you urinate or urinating more often than normal

Uncommon: may affect up to 1 in 100 people

- small raised red bumps on the skin

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Uncommon			
Serious Infections: Fever, flu-like symptoms, night sweats, cough, blood in your phlegm (mucus), warm, red or painful skin, muscle aches, weight loss		√	√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your doctor, pharmacist or nurse.

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 (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) 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:

Keep this medicine out of reach and sight of children.

Do not use this medicine after the expiration date which is stated on the syringe label and outer carton after 'EXP'.

Store in a refrigerator between 2 to 8 °C (36 to 46 °F). Do not freeze. Do not use if SKYRIZI has been frozen.

Keep the pre-filled syringes in the original carton in order to protect from light.

The liquid should look clear to slightly yellow. The liquid may contain tiny white or clear particles. Do not use if liquid is cloudy or contains flakes or large particles.

This medicine is for single use only. Ask your doctor, pharmacist or nurse how to throw away used syringes safely.

If you want more information about SKYRIZI:

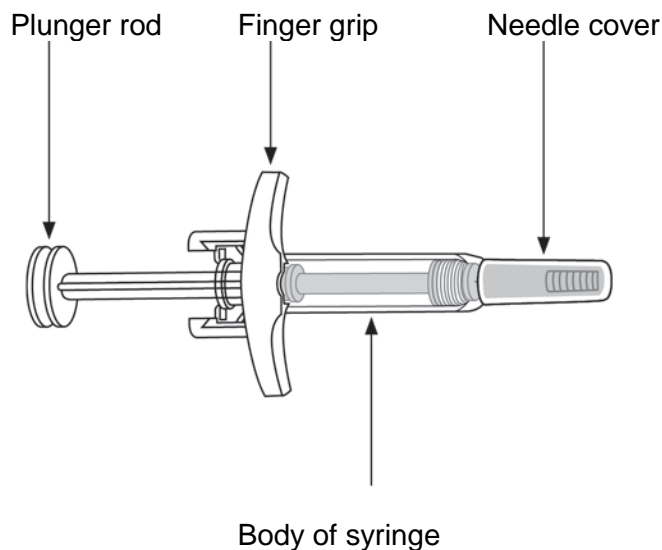
- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<http://hc-sc.gc.ca/index-eng.php>); the manufacturer's website (www.abbvie.ca), or by calling 1-888-704-8271.

This leaflet was prepared by AbbVie Corporation.

Last Revised: April 17, 2019

Instructions for Use
SKYRIZI™
(risankizumab injection)
Pre-filled syringe

Please read complete instructions before using SKYRIZI.



Important information to know before you inject SKYRIZI

- If your doctor decides that you or a caregiver may be able to give your injections at home, you and your caregiver should receive training on how to inject SKYRIZI before giving an injection. Injections should be given in the thighs or abdomen. Caregivers can also give SKYRIZI in the upper outer arm. Talk to your doctor, pharmacist or nurse if you need help. The AbbVie Care patient assistance program is also available to you if you require assistance with injections should you prefer nurse-administered injections.
- Mark the dates on your calendar so you know when to next use SKYRIZI.
- Keep SKYRIZI in the original carton to protect from light until it is time to use it.
- **Do not** inject if the liquid is cloudy or contains flakes or large particles. The liquid should look clear to slightly yellow and may contain tiny white or clear particles.
- **Do not** use if the expiry date (EXP) has passed.
- **Do not** use if the liquid has been frozen (even if thawed).
- **Do not** use if the syringe has been dropped or damaged.
- **Do not** use if the syringe tray cover is broken or missing. Return this medicine to the pharmacy.
- **Do not** remove the needle cover until just before the injection.

For a more comfortable injection: Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **15 to 30 minutes** before injecting.

- **Do not** remove the syringes from the carton until ready to inject.
- **Do not** warm SKYRIZI in any other way. For example, **do not** warm it in a microwave or in hot water.

Storage Information

Store in refrigerator between 2 to 8 °C (36 to 46 °F). Do not freeze. Keep SKYRIZI out of reach and sight of children. Keep SKYRIZI pre-filled syringe in the original carton to protect from light.

Follow the steps below each time you use SKYRIZI

Prepare for Injection

STEP 1



You will need these supplies:

- 2 pre-filled syringes

Not provided in the SKYRIZI carton:

- 2 alcohol pads
- 2 cotton balls or gauze pads
- Special disposal container.

Place these items on a clean, flat surface.

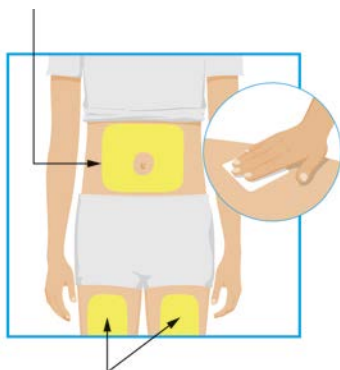
Wash and dry your hands.

Start with one syringe for the first injection.

For a full dose, 2 injections are required, one after the other.

STEP 2

Areas to inject



Areas to inject

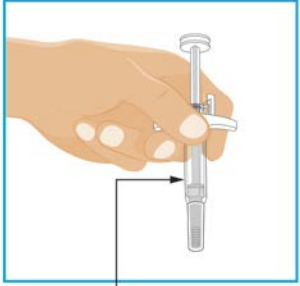
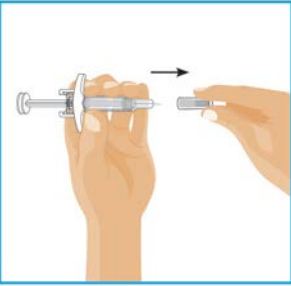
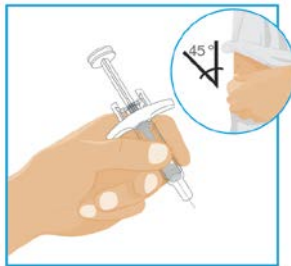
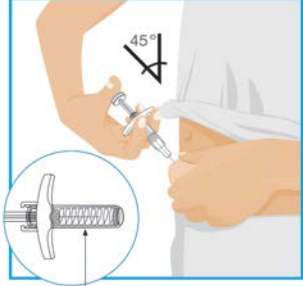
Choose from these 3 areas to inject:

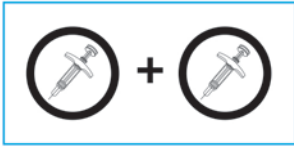
- front of left thigh or right thigh
- belly (abdomen) at least 5 cm (2 inches) from the belly button (navel)

For the second syringe, inject at least 3 cm (1 inch) away from the first injection. **Do not** inject into the same place.

Before each injection, wipe where you will inject in a circular motion with an alcohol pad.

- **Do not** inject through clothes.
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, or has stretch marks.
- **Do not** inject into areas affected by psoriasis.

<p>STEP 3</p>  <p>Check liquid</p>	<p>Hold the syringe with covered needle pointing down, as shown.</p> <p>Check the liquid in the syringe.</p> <ul style="list-style-type: none"> • It is normal to see bubbles in the window. • The liquid should look clear to slightly yellow and may contain tiny white or clear particles. • Do not use if the liquid is cloudy or contains flakes or large particles.
<p>STEP 4</p> 	<p>Removing the needle cover:</p> <ul style="list-style-type: none"> • Hold the syringe in one hand. • With the other hand, gently pull the needle cover straight off. • You may see a drop of liquid at the end of the needle. This is normal. • Throw away the needle cover. • Do not touch the needle with your fingers or let the needle touch anything.
<p>Inject SKYRIZI</p>	
<p>STEP 5</p> 	<p>Hold the body of the syringe in one hand between the thumb and index finger, like you would a pencil.</p> <p>Gently pinch the area of cleaned skin with your other hand and hold it firmly.</p> <p>Insert the needle all the way into the skin at about a 45-degree angle using a quick, short movement. Keep the syringe steady at the same angle.</p>
<p>STEP 6</p>  <p>Needle guard</p>	<p>Slowly push the plunger all the way in until all of the liquid is injected.</p> <p>Pull the needle out of the skin while keeping the syringe at the same angle.</p> <p>Slowly take your thumb off the plunger. The needle will then be covered by the needle guard.</p> <ul style="list-style-type: none"> • The needle guard will not activate unless all the liquid is injected. • Speak to your doctor, pharmacist or nurse if you think you have not given a full dose. <p>Press a cotton ball or gauze pad where you have injected and hold for 10 seconds.</p> <p>Do not rub the skin where you have injected. You may have slight bleeding from where you injected. This is normal.</p>

STEP 7

For a full dose, two injections are needed, one after the other.

- Repeat Steps 2 through 6 with the second syringe.
- Inject the second syringe immediately after the first injection.

After your Injection**STEP 8**

Throw away used syringes in a special disposal container.

- **Do not** throw away used syringes in the household waste.
- Your doctor, pharmacist or nurse will tell you how to return the full special disposal container.

Need Help?

Call your doctor to talk about any questions you may have. For questions or concerns visit the manufacturer's website (www.abbvie.ca) or call 1-888-704-8271.

This leaflet was prepared by AbbVie Corporation.

Last Revised: April 17, 2019