

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SKYRIZI safely and effectively. See full prescribing information for SKYRIZI.

SKYRIZI™ (risankizumab-rzaa) injection, for subcutaneous use  
Initial U.S. Approval: 2019

### INDICATIONS AND USAGE

SKYRIZI is an interleukin-23 antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. (1)

### DOSAGE AND ADMINISTRATION

- 150 mg (two 75 mg injections) administered by subcutaneous injection at Week 0, Week 4 and every 12 weeks thereafter. (2.1)

### DOSAGE FORMS AND STRENGTHS

- Injection: 75 mg/0.83 mL in each single-dose prefilled syringe. (3)

### CONTRAINDICATIONS

- None (4)

### WARNINGS AND PRECAUTIONS

- Infections: SKYRIZI may increase the risk of infection. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If such an infection develops, do not administer SKYRIZI until the infection resolves. (5.1)
- Tuberculosis (TB): Evaluate for TB prior to initiating treatment with SKYRIZI. (5.1)

### ADVERSE REACTIONS

Most common adverse reactions ( $\geq 1\%$ ) are upper respiratory infections, headache, fatigue, injection site reactions, and tinea infections. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AbbVie Inc. at 1-800-633-9110 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

Avoid use of live vaccines in patients treated with SKYRIZI. (7.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 8/2019

## FULL PRESCRIBING INFORMATION: CONTENTS\*

### 1 INDICATIONS AND USAGE

### 2 DOSAGE AND ADMINISTRATION

- 2.1 Dosage
- 2.2 Tuberculosis Assessment Prior to Initiation of SKYRIZI
- 2.3 Important Administration Instructions
- 2.4 Preparation for Use of SKYRIZI Prefilled Syringes

### 3 DOSAGE FORMS AND STRENGTHS

### 4 CONTRAINDICATIONS

### 5 WARNINGS AND PRECAUTIONS

- 5.1 Infections
- 5.2 Pre-treatment Evaluation for Tuberculosis
- 5.3 Immunizations

### 6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Immunogenicity

### 7 DRUG INTERACTIONS

- 7.1 Live Vaccinations

### 8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy

### 8.2 Lactation

### 8.4 Pediatric Use

### 8.5 Geriatric Use

### 10 OVERDOSAGE

### 11 DESCRIPTION

### 12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

### 13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

### 14 CLINICAL STUDIES

### 16 HOW SUPPLIED/STORAGE AND HANDLING

- 16.1 How Supplied
- 16.2 Storage and Handling

### 17 PATIENT COUNSELING INFORMATION

\*Sections or subsections omitted from the full prescribing information are not listed.

# FULL PRESCRIBING INFORMATION

## 1 INDICATIONS AND USAGE

SKYRIZI™ is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Dosage

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

### 2.2 Tuberculosis Assessment Prior to Initiation of SKYRIZI

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with SKYRIZI [*see Warnings and Precautions (5.1)*].

### 2.3 Important Administration Instructions

Administer SKYRIZI subcutaneously. Inject two separate 75 mg single-dose prefilled syringes for the full 150 mg dose. Discard prefilled syringes after use. Do not reuse.

For each dose, administer the injections at different anatomic locations (such as thighs or abdomen), and not into areas where the skin is tender, bruised, erythematous, indurated or affected by psoriasis. Administration of SKYRIZI in the upper, outer arm may only be performed by a healthcare professional or caregiver.

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

SKYRIZI is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject SKYRIZI after training in subcutaneous injection technique. Provide proper training to patients and/or caregivers on the subcutaneous injection technique of SKYRIZI. Instruct the patient that two separate 75 mg single-dose injections are required to achieve the 150 mg dose.

The SKYRIZI “Instructions for Use” contains more detailed instructions on the preparation and administration of SKYRIZI [*see Instructions for Use*]. Instruct the patient to read the Instructions for Use before administration.

### 2.4 Preparation for Use of SKYRIZI Prefilled Syringes

Before injecting, patients may remove the carton from the refrigerator and allow to reach room temperature out of direct sunlight (15 to 30 minutes) without removing the prefilled syringes from the carton.

Visually inspect SKYRIZI for particulate matter and discoloration prior to administration. SKYRIZI is a colorless to slightly yellow and clear to slightly opalescent solution. It may contain a few translucent to white particles. Do not use if the solution contains large particles or is cloudy or discolored.

### **3 DOSAGE FORMS AND STRENGTHS**

Injection: 75 mg/0.83 mL solution in each single-dose prefilled syringe. SKYRIZI is a colorless to slightly yellow and clear to slightly opalescent solution.

### **4 CONTRAINDICATIONS**

None.

### **5 WARNINGS AND PRECAUTIONS**

#### **5.1 Infections**

SKYRIZI may increase the risk of infections. In clinical studies, infections occurred in 22.1% of the SKYRIZI group compared to 14.7% of the placebo group through 16 weeks of treatment. Upper respiratory tract infections and tinea infections occurred more frequently in the SKYRIZI group than in the placebo group. Subjects with known chronic or acute infections were not enrolled in clinical studies [*see Adverse Reactions (6.1)*].

The rate of serious infections for the SKYRIZI group and the placebo group was  $\leq 0.4\%$ . Treatment with SKYRIZI should not be initiated in 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, consider the risks and benefits prior to prescribing SKYRIZI. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy, monitor the patient closely and do not administer SKYRIZI until the infection resolves.

#### **5.2 Pre-treatment Evaluation for Tuberculosis**

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with SKYRIZI. Across the Phase 3 psoriasis clinical studies, of the 72 subjects with latent TB who were concurrently treated with SKYRIZI and appropriate TB prophylaxis during the studies, none developed active TB during the mean follow-up of 61 weeks on SKYRIZI. Two subjects taking isoniazid for treatment of latent TB discontinued treatment due to liver injury. Of the 31 subjects from the IMMSTANCE study with latent TB who did not receive prophylaxis during the study, none developed active TB during the mean follow-up of 55 weeks on 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. Monitor patients for signs and symptoms of active TB during and after SKYRIZI treatment. Do not administer SKYRIZI to patients with active TB.

### 5.3 Immunizations

Prior to initiating therapy with SKYRIZI, consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with SKYRIZI. No data are available on the response to live or inactive vaccines.

## 6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of labeling:

- Infections [see *Warnings and Precautions (5.1)*]

### 6.1 Clinical Trials Experience

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

A total of 2234 subjects were treated with SKYRIZI in clinical development studies in plaque psoriasis. Of these, 1208 subjects 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 subjects were evaluated in the SKYRIZI 150 mg group.

Table 1 summarizes the adverse drug 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 Drug Reactions Occurring in  $\geq$  1% of Subjects on SKYRIZI through Week 16**

Adverse Drug Reactions	SKYRIZI N = 1306 n (%)	Placebo N = 300 n (%)
Upper respiratory infections <sup>a</sup>	170 (13.0)	29 (9.7)
Headache <sup>b</sup>	46 (3.5)	6 (2.0)
Fatigue <sup>c</sup>	33 (2.5)	3 (1.0)
Injection site reactions <sup>d</sup>	19 (1.5)	3 (1.0)
Tinea infections <sup>e</sup>	14 (1.1)	1 (0.3)

<sup>a</sup> Includes: respiratory tract infection (viral, bacterial or unspecified), sinusitis (including acute), rhinitis, nasopharyngitis, pharyngitis (including viral), tonsillitis  
<sup>b</sup> Includes: headache, tension headache, sinus headache, cervicogenic headache  
<sup>c</sup> Includes: fatigue, asthenia  
<sup>d</sup> Includes: injection site bruising, erythema, extravasation, hematoma, hemorrhage, infection, inflammation, irritation, pain, pruritus, reaction, swelling, warmth  
<sup>e</sup> Includes: tinea pedis, tinea cruris, body tinea, tinea versicolor, tinea manuum, tinea infection

Adverse drug reactions that occurred in < 1% but > 0.1% of subjects in the SKYRIZI group and at a higher rate than in the placebo group through Week 16 were folliculitis and urticaria.

### Specific Adverse Drug Reactions

#### *Infections*

In the first 16 weeks, infections occurred in 22.1% of the SKYRIZI group (90.8 events per 100 subject-years) compared to 14.7% of the placebo group (56.5 events per 100 subject-years) and did not lead to discontinuation of SKYRIZI. The rates of serious infections for the SKYRIZI group and the placebo group were  $\leq 0.4\%$ . Serious infections in the SKYRIZI group included cellulitis, osteomyelitis, sepsis and herpes zoster. In ULTIMMA-1 and ULTIMMA-2, through Week 52, the rate of infections (73.9 events per 100 subject-years) was similar to the rate observed during the first 16 weeks of treatment.

#### Safety through Week 52

Through Week 52, no new adverse reactions were identified and the rates of the adverse reactions were similar to those observed during the first 16 weeks of treatment. During this period, serious infections that led to study discontinuation included pneumonia.

## **6.2 Immunogenicity**

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other products, including other risankizumab products, may be misleading.

By Week 52, approximately 24% (263/1079) of subjects treated with SKYRIZI at the recommended dose developed antibodies to risankizumab-rzaa. Of the subjects who developed antibodies to risankizumab-rzaa, approximately 57% (14% of all subjects treated with SKYRIZI) had antibodies that were classified as neutralizing. Higher antibody titers in approximately 1% of subjects treated with SKYRIZI were associated with lower risankizumab-rzaa concentrations and reduced clinical response.

## **7 DRUG INTERACTIONS**

### **7.1 Live Vaccinations**

Avoid use of live vaccines in patients treated with SKYRIZI [*see Warnings and Precautions (5.2)*].

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Risk Summary

Limited available data with SKYRIZI use in pregnant women are insufficient to evaluate a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcome. Human IgG is known to cross the placental barrier; therefore, SKYRIZI may be transmitted from the mother to the developing fetus.

In an enhanced pre- and post-natal developmental toxicity study, pregnant cynomolgus monkeys were administered subcutaneous doses of 5 and 50 mg/kg risankizumab-rzaa once weekly during the period of organogenesis up to parturition. At the 50 mg/kg dose [20 times the maximum recommended human dose (MRHD); 2.5 mg/kg based on administration of a 150 mg dose to a 60 kg individual], increased fetal/infant loss was noted in pregnant monkeys (*see Data*). No risankizumab-rzaa-related effects on functional or immunological development were observed in infant monkeys from birth through 6 months of age. The clinical significance of these findings for humans is unknown.

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

## Data

### *Animal Data*

An enhanced pre- and post-natal developmental toxicity study was conducted in cynomolgus monkeys. Pregnant cynomolgus monkeys were administered weekly subcutaneous doses of risankizumab-rzaa of 5 or 50 mg/kg from gestation day 20 to parturition and the cynomolgus monkeys (mother and infants) were monitored for 6 months after delivery. No maternal toxicity was noted in this study. There were no treatment-related effects on growth and development, malformations, developmental immunotoxicology or neurobehavioral development. However, a dose-dependent increase in fetal/infant loss was noted in the risankizumab-rzaa-treated groups (32% and 43% in the 5 mg/kg and 50 mg/kg groups, respectively) compared to the vehicle control group (19%). The increased fetal/infant loss in the 50 mg/kg group was considered to be related to risankizumab-rzaa treatment. The no observed adverse effect level (NOAEL) for maternal toxicity was identified as 50 mg/kg (20 times the MRHD, based on mg/kg comparison) and the NOAEL for developmental toxicity was identified as 5 mg/kg (2 times the MRHD, based on mg/kg comparison). In the infants, mean serum concentrations increased in a dose-dependent manner and were approximately 17-86% of the respective maternal concentrations. Following delivery, most adult female cynomolgus monkeys and all infants from the risankizumab-rzaa-treated groups had measurable serum concentrations of risankizumab-rzaa up to 91 days postpartum. Serum concentrations were below detectable levels at 180 days postpartum.

## **8.2 Lactation**

### Risk Summary

There are no data on the presence of risankizumab-rzaa in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SKYRIZI and any potential adverse effects on the breastfed infant from SKYRIZI or from the underlying maternal condition.

## **8.4 Pediatric Use**

The safety and efficacy of SKYRIZI in pediatric patients less than 18 years of age have not yet been established.

## **8.5 Geriatric Use**

Of the 2234 subjects with plaque psoriasis exposed to SKYRIZI, 243 subjects were 65 years or older and 24 subjects were 75 years or older. No overall differences in risankizumab-rzaa exposure, safety or effectiveness were observed between older and younger subjects who received SKYRIZI. However, the number of subjects aged 65 years and older was not sufficient to determine whether they respond differently from younger subjects.

## **10 OVERDOSAGE**

In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and administer appropriate symptomatic treatment immediately.

## **11 DESCRIPTION**

Risankizumab-rzaa, an interleukin-23 antagonist, is a humanized immunoglobulin G1 (IgG1) monoclonal antibody. Risankizumab-rzaa is produced by recombinant DNA technology in Chinese hamster ovary cells.

SKYRIZI (risankizumab-rzaa) injection is a sterile, preservative-free, colorless to slightly yellow, and clear to slightly opalescent solution for subcutaneous use.

Each prefilled syringe delivers 0.83 mL containing 75 mg risankizumab-rzaa, disodium succinate hexahydrate (0.88 mg), polysorbate 20 (0.17 mg), sorbitol (34 mg), succinic acid (0.049 mg), and Water for Injection, USP.

## **12 CLINICAL PHARMACOLOGY**

### **12.1 Mechanism of Action**

Risankizumab-rzaa is a humanized immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds to the p19 subunit of human interleukin 23 (IL-23) cytokine and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses.

Risankizumab-rzaa inhibits the release of pro-inflammatory cytokines and chemokines.

### **12.2 Pharmacodynamics**

No formal pharmacodynamics studies have been conducted with risankizumab-rzaa.

### **12.3 Pharmacokinetics**

Risankizumab-rzaa plasma concentrations increased dose-proportionally from 90 to 180 mg and from 18 to 300 mg (0.6 to 1.2 and 0.12 to 2.0 times the approved recommended dosage)

following subcutaneous administration in subjects with plaque psoriasis and healthy volunteers, respectively. Steady-state concentrations were achieved by Week 16 following subcutaneous administration of risankizumab-rzaa at Weeks 0, 4, and every 12 weeks thereafter. At the 150 mg dose, the estimated steady-state peak concentration ( $C_{max}$ ) and trough concentration ( $C_{trough}$ ) were approximately 12 mcg/mL and 2 mcg/mL, respectively.

### Absorption

The absolute bioavailability of risankizumab-rzaa was estimated to be 89% following subcutaneous injection.  $C_{max}$  was reached by 3-14 days.

### Distribution

The estimated steady-state volume of distribution (inter-subject CV%) was 11.2 L (34%) in subjects with plaque psoriasis.

### Elimination

The estimated systemic clearance (inter-subject CV%) was 0.31 L/day (24%) and terminal elimination half-life was approximately 28 days in subjects with plaque psoriasis.

### Metabolism

The metabolic pathway of risankizumab-rzaa has not been characterized. As a humanized IgG1 monoclonal antibody, risankizumab-rzaa is expected to be degraded into small peptides and amino acids via catabolic pathways in a manner similar to endogenous IgG.

### Specific Populations

No clinically significant differences in the pharmacokinetics of risankizumab-rzaa were observed based on age ( $\geq 18$  years). No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of risankizumab-rzaa.

### *Body Weight*

Risankizumab-rzaa clearance and volume of distribution increase and plasma concentrations decrease as body weight increases; however, no dose adjustment is recommended based on body weight.

### Drug Interaction Studies

#### *Cytochrome P450 Substrates*

No clinically significant changes in exposure of caffeine (CYP1A2 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate), or midazolam (CYP3A substrate) were observed when used concomitantly with risankizumab-rzaa 150 mg administered subcutaneously at Weeks 0, 4, 8 and 12 (more frequent than the approved recommended dosing frequency) in subjects with plaque psoriasis.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Carcinogenicity and mutagenicity studies have not been conducted with SKYRIZI.



No effects on male fertility parameters were observed in sexually mature male cynomolgus monkeys subcutaneously treated with 50 mg/kg risankizumab-rzaa (at 20 times the clinical exposure at the MRHD, based on mg/kg comparison) once weekly for 26 weeks.

## 14 CLINICAL STUDIES

Four multicenter, randomized, double-blind studies [ULTIMMA-1 (NCT02684370), ULTIMMA-2 (NCT02684357), IMMSTANCE (NCT02672852), and IMMVENT (NCT02694523)] enrolled 2109 subjects 18 years of age and older with moderate to severe plaque psoriasis who had a body surface area (BSA) involvement of  $\geq 10\%$ , a static Physician's Global Assessment (sPGA) score of  $\geq 3$  ("moderate") in the overall assessment (plaque thickness/induration, erythema, and scaling) of psoriasis on a severity scale of 0 to 4, and a Psoriasis Area and Severity Index (PASI) score  $\geq 12$ .

Overall, subjects had a median baseline PASI score of 17.8 and a median BSA of 20.0%. Baseline sPGA score was 4 ("severe") in 19% of subjects. A total of 10% of study subjects had a history of diagnosed psoriatic arthritis.

Across all studies, 38% of subjects had received prior phototherapy, 48% had received prior non-biologic systemic therapy, and 42% had received prior biologic therapy for the treatment of psoriasis.

### ULTIMMA-1 and ULTIMMA-2

In ULTIMMA-1 and ULTIMMA-2, 997 subjects were enrolled (including 598 subjects randomized to the SKYRIZI 150 mg group, 200 subjects randomized to the placebo group, and 199 to the biologic active control group). Subjects received treatment at Weeks 0, 4, and every 12 weeks thereafter.

Both studies assessed the responses at Week 16 compared to placebo for the two co-primary endpoints:

- the proportion of subjects who achieved an sPGA score of 0 ("clear") or 1 ("almost clear")
- the proportion of subjects who achieved at least a 90% reduction from baseline PASI (PASI 90)

Secondary endpoints included the proportion of subjects who achieved PASI 100, sPGA 0, and PSS 0 at Week 16.

The results are presented in Table 2.

**Table 2. Efficacy Results at Week 16 in Adults with Plaque Psoriasis in ULTIMMA-1 and ULTIMMA-2**

	ULTIMMA-1		ULTIMMA-2	
	SKYRIZI (N=304)	Placebo (N=102)	SKYRIZI (N=294)	Placebo (N=98)
	n (%)	n (%)	n (%)	n (%)

<b>sPGA 0 or 1 ("clear or almost clear")<sup>a</sup></b>	267 (88)	8 (8)	246 (84)	5 (5)
<b>PASI 90<sup>a</sup></b>	229 (75)	5 (5)	220 (75)	2 (2)
<b>sPGA 0 ("clear")</b>	112 (37)	2 (2)	150 (51)	3 (3)
<b>PASI 100</b>	109 (36)	0 (0)	149 (51)	2 (2)
<sup>a</sup> Co-primary endpoints				

Examination of age, gender, race, body weight, baseline PASI score and previous treatment with systemic or biologic agents did not identify differences in response to SKYRIZI among these subgroups at Week 16.

In ULTIMMA-1 and ULTIMMA-2 at Week 52, subjects receiving SKYRIZI achieved sPGA 0 (58% and 60%, respectively), PASI 90 (82% and 81%, respectively), and PASI 100 (56% and 60%, respectively).

#### Patient Reported Outcomes

Improvements in signs and symptoms related to pain, redness, itching and burning at Week 16 compared to placebo were observed in both studies as assessed by the Psoriasis Symptom Scale (PSS). In ULTIMMA-1 and ULTIMMA-2, about 30% of the subjects who received SKYRIZI achieved PSS 0 ("none") at Week 16 compared to 1% of the subjects who received placebo.

#### IMMHANCE

IMMHANCE enrolled 507 subjects (407 randomized to SKYRIZI 150 mg and 100 to placebo). Subjects received treatment at Weeks 0, 4, and every 12 weeks thereafter.

At Week 16, SKYRIZI was superior to placebo on the co-primary endpoints of sPGA 0 or 1 (84% SKYRIZI and 7% placebo) and PASI 90 (73% SKYRIZI and 2% placebo). The respective response rates for SKYRIZI and placebo at Week 16 were: sPGA 0 (46% SKYRIZI and 1% placebo); PASI 100 (47% SKYRIZI and 1% placebo); and PASI 75 (89% SKYRIZI and 8% placebo).

#### Maintenance and Durability of Response

In ULTIMMA-1 and ULTIMMA-2, among the subjects who received SKYRIZI and had PASI 100 at Week 16, 80% (206/258) of the subjects who continued on SKYRIZI had PASI 100 at Week 52. For PASI 90 responders at Week 16, 88% (398/450) of the subjects had PASI 90 at Week 52.

In IMMHANCE, subjects who were originally on SKYRIZI and had sPGA 0 or 1 at Week 28 were re-randomized to continue SKYRIZI every 12 weeks or withdrawal of therapy. At Week 52, 87% (97/111) of the subjects re-randomized to continue treatment with SKYRIZI had sPGA 0 or 1 compared to 61% (138/225) who were re-randomized to withdrawal of SKYRIZI.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

SKYRIZI (risankizumab-rzaa) injection is a sterile, preservative-free, colorless to slightly yellow and clear to slightly opalescent solution. The product is supplied in a 1 mL glass syringe with a fixed 29 gauge ½ inch needle with needle guard.

- NDC 0074-2042-02: one carton containing two prefilled syringes and two alcohol pads

### 16.2 Storage and Handling

- Store in a refrigerator at 2°C to 8°C (36°F to 46° F).
- Do not freeze.
- Do not shake.
- Keep the prefilled syringes in the original carton to protect from light.
- Not made with natural rubber latex.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide and Instructions for Use) before starting SKYRIZI therapy and to reread the Medication Guide each time the prescription is renewed. Advise patients of the potential benefits and risks of SKYRIZI.

### Infections

Inform patients that SKYRIZI may lower the ability of their immune system to fight infections. Instruct patients of the importance of communicating any history of infections to the healthcare provider and contacting their healthcare provider if they develop any symptoms of an infection [*see Warnings and Precautions (5.1)*].

### Administration Instruction

Instruct patients or caregivers to perform the first self-injected dose under the supervision and guidance of a qualified healthcare professional for training in preparation and administration of SKYRIZI, including choosing anatomical sites for administration, and proper subcutaneous injection technique [*see Instructions for Use*].

Instruct patients or caregivers to administer two 75 mg single-dose syringes to achieve the 150 mg dose of SKYRIZI [*see Instructions for Use*].

Instruct patients or caregivers in the technique of needle and syringe disposal [*see Instructions for Use*].

Manufactured by:  
AbbVie Inc.  
North Chicago, IL 60064, USA

US License Number 1889  
SKYRIZI™ is a trademark of AbbVie Biotechnology Ltd.  
© 2019 AbbVie Inc.  
20059638 08/2019

**Medication Guide**  
**SKYRIZI™ (sky-RIZZ-ee)**  
**(risankizumab-rzaa)**  
**injection, for subcutaneous use**

**What is the most important information I should know about SKYRIZI?**

**SKYRIZI may cause serious side effects, including:**

**Infections.** SKYRIZI may lower the ability of your immune system to fight infections and may increase your risk of infections. Your healthcare provider should check you for infections and tuberculosis (TB) before starting treatment with SKYRIZI and may treat you for TB before you begin treatment with SKYRIZI if you have a history of TB or have active TB. Your healthcare provider should watch you closely for signs and symptoms of TB during and after treatment with SKYRIZI. Tell your healthcare provider right away if you have an infection or have symptoms of an infection, including:

- |                                |                                 |                                       |
|--------------------------------|---------------------------------|---------------------------------------|
| ◦ fever, sweats, or chills     | ◦ muscle aches                  | ◦ weight loss                         |
| ◦ cough                        | ◦ warm, red, or painful skin    | ◦ diarrhea or stomach pain            |
| ◦ shortness of breath          | ◦ sores on your body            | ◦ burning when you urinate            |
| ◦ blood in your mucus (phlegm) | ◦ different from your psoriasis | ◦ or urinating more often than normal |

See **“What are the possible side effects of SKYRIZI?”** for more information about side effects.

**What is SKYRIZI?**

SKYRIZI is a prescription medicine used to treat adults with moderate to severe plaque psoriasis who may benefit from taking injections or pills (systemic therapy) or treatment using ultraviolet or UV light (phototherapy).

It is not known if SKYRIZI is safe and effective in children under 18 years of age.

**Before using SKYRIZI, tell your healthcare provider about all of your medical conditions, including if you:**

- have any of the conditions or symptoms listed in the section **“What is the most important information I should know about SKYRIZI?”**
- have an infection that does not go away or that keeps coming back.
- have TB or have been in close contact with someone with TB.
- have recently received or are scheduled to receive an immunization (vaccine). You should avoid receiving live vaccines during treatment with SKYRIZI.
- are pregnant or plan to become pregnant. It is not known if SKYRIZI can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if SKYRIZI passes into your breast milk.

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements.

**How should I use SKYRIZI?**

See the detailed **“Instructions for Use”** that comes with SKYRIZI for information on how to prepare and inject a dose of SKYRIZI, and how to properly throw away (dispose of) used SKYRIZI prefilled syringes.

- Use SKYRIZI exactly as your healthcare provider tells you to use it.

- If you miss your SKYRIZI dose, inject a dose as soon as you remember. Then, take your next dose at your regular scheduled time. Call your healthcare provider if you are not sure what to do.
- If you inject more SKYRIZI than prescribed, call your healthcare provider right away.

**What are the possible side effects of SKYRIZI?**

**SKYRIZI may cause serious side effects. See “What is the most important information I should know about SKYRIZI?”**

**The most common side effects of SKYRIZI include:**

- upper respiratory infections
- feeling tired
- fungal skin infection
- injection site reactions
- headache

These are not all of the possible side effects of SKYRIZI. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**How should I store SKYRIZI?**

- Store SKYRIZI in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Do not freeze SKYRIZI.
- Do not shake SKYRIZI.
- Keep SKYRIZI in the original carton to protect it from light.
- SKYRIZI is not made with natural rubber latex.

**Keep SKYRIZI and all medicines out of the reach of children.****General information about the safe and effective use of SKYRIZI**

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

**What are the ingredients in SKYRIZI?**

**Active ingredient:** risankizumab-rzaa

**Inactive ingredients:** disodium succinate hexahydrate, polysorbate 20, sorbitol, succinic acid, and Water for Injection, USP.

Manufactured by: AbbVie Inc., North Chicago, IL 60064, U.S.A.

US License Number 1889

SKYRIZI™ is a trademark of AbbVie Biotechnology Ltd.

© 2019 AbbVie Inc.

For more information, call 1-866-SKYRIZI (1-866-759-7494) or go to [www.SKYRIZI.com](http://www.SKYRIZI.com).

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised: 08/2019

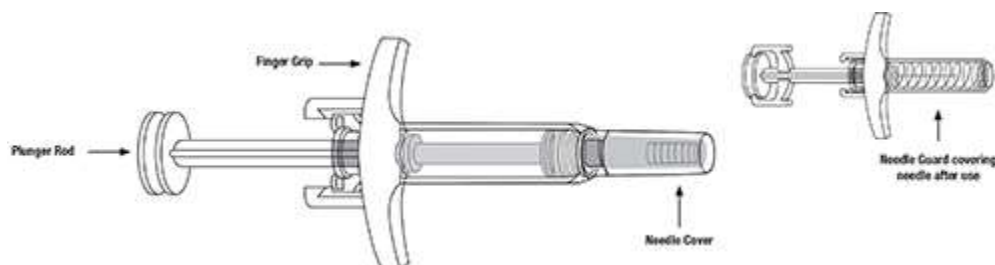
20059638

**Instructions for Use**  
**SKYRIZI™** (sky-RIZZ-ee)  
(risankizumab-rzaa)  
injection, for subcutaneous use

**Read Before First Use**

Refer to the **Medication Guide** for product information.

**SKYRIZI Single-Dose Prefilled Syringe**



**IMPORTANT INFORMATION:**

- Keep SKYRIZI in the original carton to protect from light until time to use.
- The liquid should look clear to slightly yellow and may contain tiny white or clear particles.
- **DO NOT** use SKYRIZI if the liquid is **cloudy** or contains **flakes** or **large particles**.
- **DO NOT** use SKYRIZI if the **expiration date (EXP:)** shown on the carton and prefilled syringe has passed.
- **DO NOT** use SKYRIZI if the liquid has been **frozen** (even if thawed).
- **DO NOT** shake the syringe.
- **DO NOT** use SKYRIZI if the syringe has been **dropped or damaged**.
- **DO NOT** use SKYRIZI if carton perforations are **broken**. **Return product to the pharmacy.**
- **DO NOT** remove the needle cover until right before giving the injections.

**Keep SKYRIZI and all medicines out of the reach of children.**

**Please Read Complete Instructions For Use Before Using SKYRIZI Syringe**

**BEFORE INJECTING:**

- **Receive** training on how to inject SKYRIZI before giving injections. Call your healthcare provider or **(866) SKYRIZI** or **(866) 759-7494** if you need help.
- **Mark your calendar** ahead of time to remember when to take SKYRIZI.

- **Leave** the carton at room temperature and out of direct sunlight for **15 to 30 minutes** to warm.
  - **DO NOT** remove the syringes from the carton while allowing SKYRIZI to reach room temperature.
  - **DO NOT** warm SKYRIZI in any other way (for example, **DO NOT** warm it in a microwave or in hot water).

**IMPORTANT INFORMATION:**

- The liquid should look clear to slightly yellow and may contain tiny white or clear particles.
- **DO NOT** use SKYRIZI if the liquid is **cloudy** or contains **flakes** or **large particles**.
- **DO NOT** use SKYRIZI if the **expiration date (EXP:)** shown on the carton and prefilled syringe has passed.
- **DO NOT** use SKYRIZI if the syringe has been **dropped or damaged**.
- **DO NOT** use SKYRIZI if carton perforations are **broken**. **Return product to the pharmacy.**

**STORAGE INFORMATION:**

- Store SKYRIZI in your refrigerator between **36° F to 46° F** (2° to 8°C).
- Keep SKYRIZI in the original carton to protect from light until time to use.
- **DO NOT** use if liquid has been frozen (even if thawed).

**Keep SKYRIZI and all medicines out of the reach of children.**

Call your healthcare provider or **(866) SKYRIZI** or **(866) 759-7494** if you need help or do not know how to proceed.

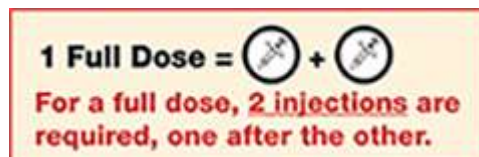


**Gather** the supplies for the injections and place the following on a clean, flat surface:

- **2 prefilled syringes** and **2 alcohol swabs (included)**
- **2 cotton balls** or gauze pads (not included)
- **FDA-cleared sharps disposal container** (not included)

**Wash and dry** your hands.

**Start with one prefilled syringe for first injection.**

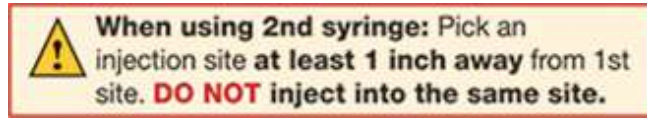






**Pick** from the 3 injectable areas:

- Front of **left thigh** or **right thigh**
- Your **abdomen** (belly) at least 2 inches from your navel (belly button)



**Wipe** the injection site in a circular motion with the alcohol swab (before **both injections**)

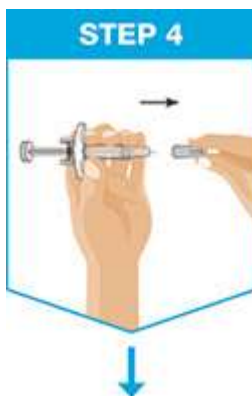
- **DO NOT** touch or blow on the injection site after it is cleaned. Allow the skin to dry before injecting.
- **DO NOT** inject through clothes.
- **DO NOT** inject into skin that is sore, bruised, red, hard, scarred, or has stretch marks, or into areas affected by psoriasis.



**Hold** the prefilled syringe with covered needle facing down, as shown.

**Check** the liquid in the prefilled syringe.

- It is normal to see one or more bubbles in the window.
- The liquid should look clear to slightly yellow and may contain tiny white or clear particles.
- **DO NOT** use the prefilled syringe if liquid is **cloudy** or contains **flakes** or **large particles**.



**Remove** the needle cover.

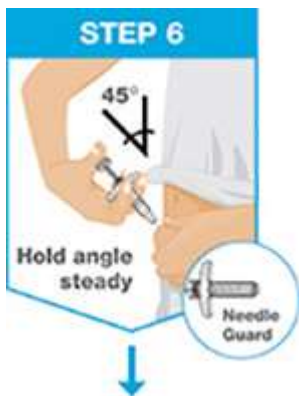
- Hold the syringe in one hand.
- With the other hand, gently pull the needle cover straight off.
- You may see a drop of liquid at the end of the needle. This is normal.
- Throw away the needle cover.
- **DO NOT** touch the needle with your fingers or let the needle touch anything.



**Hold** the body of the prefilled syringe in one hand between the thumb and index fingers.

**Gently pinch** the area of cleaned skin with your other hand and hold it firmly.

**Insert** the needle into the skin at about a **45-degree angle** using a quick, short movement. Hold angle steady.



**Slowly push** the plunger rod all the way in until all of the liquid is injected, and the syringe is empty.

**Pull** the needle out of the skin while keeping the syringe at the same angle.

**Release** the plunger rod and allow the prefilled syringe to move up until the entire needle is covered by the needle guard.

**The prefilled syringe needle guard will not activate unless all the liquid has been injected.**

- **Press** a cotton ball or gauze pad over the injection site and hold for 10 seconds.
- **DO NOT** rub the injection site. You may have slight bleeding. This is normal.



**Repeat Steps 2 through 6** with the 2nd prefilled syringe for a **full dose**.

- Use the 2nd prefilled syringe right after using the 1st syringe.



**Put your used prefilled syringes in a FDA-cleared sharps disposal container right away after use.**

- **DO NOT** throw away (dispose of) used prefilled syringes in the household trash.

**For more information, see “USED SKYRIZI PREFILLED SYRINGE DISPOSAL” section.**

## Questions About Using the SKYRIZI Syringe

**Q. What if I have not received in-person training from a healthcare professional?**

A. Call your healthcare provider or **(866) SKYRIZI** or **(866) 759-7494** if you need help.

**Q. What should I do with both used prefilled syringes after my injections?**

A. Throw away (dispose of) both used prefilled syringes in a sharps disposal container and not your household trash.

You can sign up to receive sharps containers for SKYRIZI syringe disposal at no additional cost by going to **www.SKYRIZI.com** or calling **(866) SKYRIZI** or **(866) 759-7494**.

**Q. How do I know when the injection is complete?**

A. The injection is complete when the prefilled syringe is empty, the plunger rod is pushed all the way in, and the syringe needle guard is activated.

## USED SKYRIZI PREFILLED SYRINGE DISPOSAL

**If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:**

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes.

For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: [www.fda.gov/safesharpsdisposal](http://www.fda.gov/safesharpsdisposal).

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

Manufactured by: AbbVie Inc., North Chicago, IL 60064, U.S.A.

US License Number 1889

SKYRIZI™ is a trademark of AbbVie Biotechnology Ltd.

© 2019 AbbVie Inc.

20059637

Revised: 08/2019