PDL DRUG REVIEW

Proprietary Name: Skyrizi®
Common Name: risankizumab-rzaa
PDL Category: Anti-Inflammatories, Non-NSAID

Comparable Products	Preferred Drug List Status
Cosentyx	Preferred with Conditions
Siliq	Non-Preferred with Conditions
Stelara	Non-Preferred with Conditions
Taltz	Non-Preferred with Conditions

Summary

Pharmacology/Usage: Risankizumab-rzaa, the active ingredient of Skyrizi®, is a humanized immunoglobulin G1 (IgG1) monoclonal antibody produced using recombinant DNA technology. It selectively binds to the p19 subunit of human interleukin 23 (IL-23) cytokine and inhibits its interaction with the IL-23 receptor (an IL-23 antagonist). 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.

Indication: For the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

There is no pregnancy category for this medication; however, the risk summary indicates limited available data with use in pregnant women are not sufficient to evaluate a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human IgG is known to cross the placental barrier; thus, Skyrizi® may be transmitted from the mother to the developing fetus. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Single-dose prefilled syringe for injection, solution: 75mg/0.83ml. Before injection, remove from the refrigerator and allow to reach room temperature out of direct sunlight (15-30 minutes) without removing the prefilled syringes from the carton.

Recommended Dosage: Prior to starting treatment, assess the patient for tuberculosis infection.

For subcutaneous (SC) use. Inject 150mg (two 75mg injections) SC at week 0, week 4, and every 12 weeks thereafter. For each dose, administer 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 in the upper, outer arm may only be performed by a healthcare professional or caregiver. While Skyrizi® is intended for use under the guidance and supervision of a healthcare professional, patients may self-inject after proper training.

Drug Interactions: Avoid use of live vaccines in patients treated with Skyrizi®.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Skyrizi®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the*

same as or that the active drug was less than placebo. The most frequently reported adverse events included upper respiratory infections (3.3%), headache (1.5%), fatigue (1.5%), injection site reactions (0.5%), and tinea infections (0.8%).

Skyrizi® may increase the risk of infections. In clinical trials, infections occurred in 22.1% of the Skyrizi® group as 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. 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 before Skyrizi® use.

Assess patients for tuberculosis (TB) infection before starting treatment with Skyrizi®. In the phase 3 studies, of the 72 patients 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®. Of the 31 subjects from one 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 starting 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.

Prior to starting Skyrizi® treatment, consider completion of all age appropriate immunizations per 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.

Contraindications: There are currently no contraindications listed with this product.

Manufacturer: AbbVie

Analysis: The safety and efficacy of Skyrizi® were assessed in 4 multicenter, randomized, double-blind studies (ULTIMMA-1, ULTIMMA-2, IMMHANCE, and IMMVENT) that included adult subjects ≥18 years of age with moderate to severe plaque psoriasis who had a body surface area (BSA) involvement of ≥10%, a static Physician's Global Assessment (sPGA) score of ≥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 ≥12. Overall, patients had a median baseline PASI score of 17.8 and a median BSA of 20%. Baseline sPGA score was 4 (severe) in 19% of subjects, and 10% of subjects had a history of diagnosed psoriatic arthritis. Furthermore, across all studies, 38% had received prior phototherapy, 48% had received prior non-biologic systemic therapy, and 42% had received prior biologic therapy for the treatment of psoriasis.

In the ULTIMMA-1 and ULTIMMA-2 studies, subjects (N=997) were enrolled and received treatment at weeks 0, 4, and every 12 weeks thereafter. There was a biologic active control group in these studies, but the prescribing information did not include the data on the active control group. Both studies assessed the responses at week 16 for the primary endpoints. The co-primary endpoints in the studies included the proportion of subjects who achieved an sPGA score of 0 (clear) to 1 (almost clear) and the proportion who achieved at least a 90% reduction from baseline PASI (PASI 90). Secondary endpoints include the proportion who achieved PASI 100 and sPGA 0. Results can be seen in the table below, which was adapted from the prescribing information.

	ULTIMMA-1		ULTIMMA-2	
	Skyrizi® (N=304)	Placebo (N=102)	Skyrizi® (N=294)	Placebo (N=98)
sPGA 0 or 1	267 (88%)	8 (8%)	246 (84%)	5 (5%)
PASI 90	229 (75%)	5 (5%)	220 (75%)	2 (2%)
sPGA 0	112 (37%)	2 (2%)	150 (51%)	3 (3%)

	ULTIMMA-1		ULTIMMA-2	
	Skyrizi® (N=304)	Placebo (N=102)	Skyrizi® (N=294)	Placebo (N=98)
PASI 100	109 (36%)	0 (0%)	149 (51%)	2 (2%)

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).

Improvements in signs and symptoms related to pain, redness, itching, and burning at week 16 compared to placebo were seen 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 placebo group.

The IMMHANCE study included subjects (N=507) randomized to Skyrizi® or placebo. At week 16, Skyrizi® was superior to placebo on the co-primary endpoints of sPGA 0 or 1 and PASI 90. Results of these and other assessed response rates can be seen in the table below.

	IMMHANCE at week 16	
	Skyrizi® (N=407)	Placebo (N=100)
sPGA 0 or 1	84%	7%
PASI 90	73%	2%
sPGA 0	46%	1%
PASI 100	47%	1%
PASI 75	89%	8%

In ULTIMMA-1 and ULTIMMA-2, among the subjects who received Skyrizi® and had PASI 100 at week 16, 80% (N=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% (N=97/111) of the subjects re-randomized to continue treatment with Skyrizi® had sPGA 0 or 1 compared to 61% (N=138/225) who were re-randomized to withdrawal of Skyrizi®.

Information on the IMMVENT study was not found in the prescribing information.

Place in Therapy: Skyrizi® is a subcutaneous injection indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. Skyrizi® was found to be more effective as compared with placebo in clinical trials.

Per the full-text study of ULTIMMA-1 and ULTIMMA-2 by Gordon et al[2], the active-control was ustekinumab. In the ULTIMMA-1 study, 42 (42%) receiving ustekinumab achieved PASI 90. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$ vs placebo and ustekinumab). In addition, 63 (63%) receiving ustekinumab achieved sPGA 0 or 1. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$ vs placebo and ustekinumab). In the ULTIMMA-2 study, 47 (47.5%) of the ustekinumab group achieved PASI 90. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$ vs placebo and ustekinumab). In addition, 61 (61.6%) receiving ustekinumab achieved sPGA 0 or 1. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$).

While a full text article is not available via PubMed as of yet, clinicaltrials.gov does include a study comparing Skyrizi® with adalimumab (Humira®) and while some results were posted on May 27, 2019, the manufacturer requests written notice before further disclosure at this time.

There is some evidence at this time from a phase 3 study that suggests Skyrizi® is more effective than ustekinumab for the treatment of plaque psoriasis; however, there is no evidence to support that Skyrizi® is safer or more effective than other preferred, more cost-effective medications, although the data comparing Skyrizi® to adalimumab is available in preliminary format. It is therefore recommended that Skyrizi® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1]Skyrizi [package insert]. North Chicago, IL: AbbVie Inc; 2019.
[2] Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (ULTIMMA-1 and ULTIMMA-2): results from the two double-blind, randomized, placebo-controlled and ustekinumab-controlled phase 3 trials. *Lancet.* 2018; 392(10148): 650-661.