Skyrizi (risankizumab-rzaa) **for Crohn Disease**

FIRST LOOK: NEW INDICATION

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Introduction

- **Brand name:** Skyrizi
- **Generic name:** Risankizumab-rzaa
- **Pharmacologic class:** Interleukin-23 antagonist
- **Strengths and Formulations:** 75mg/0.83mL, 150mg/mL, 360mg/2.4mL; soln for SC inj; 600mg/10mL; soln for IV infusion after dilution; preservative-free
- **Manufacturer:** AbbVie
- **How supplied:** Single-dose prefilled syringe (75mg/0.83mL)—2 (w. supplies); Single-dose prefilled pen or syringe (150mg/mL)—1 (w. supplies); Single-dose prefilled cartridge (360mg/2.4mL)—1 (kit w. on-body injector); Single-dose vial (600mg/10mL)—1
- **Legal Classification:** Rx

New Indication

- Treatment of **moderately to severely active Crohn disease** in adults.

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Other Approved Indication(s)

- Treatment of **moderate to severe plaque psoriasis** in adults who are candidates for systemic therapy or phototherapy.
- Treatment of **active psoriatic arthritis** in adults.

Mechanism of Action

- **Risankizumab-rzaa** is a humanized IgG1 monoclonal antibody that selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor.
- **Risankizumab-rzaa** inhibits the release of pro-inflammatory cytokines and chemokines.

Clinical Trials: Crohn Disease

- Approval was based on 2 multicenter, randomized, double-blind, placebo-controlled phase 3 induction studies (**CD-1**; ClinicalTrials.gov Identifier: [NCT03105128], **CD-2**; [NCT03104413]), and one phase 3 maintenance study (**CD-3**; ClinicalTrials.gov Identifier: [NCT03105102]).

Clinical Trials: Crohn Disease

- **CD-1** and **CD-2** Induction Studies
  - Included adults with moderately to severely active Crohn disease, defined as a Crohn Disease Activity Index (CDAI) of 220 to 450 and Simple Endoscopic Score for Crohn disease (SES-CD) ≥6 (or ≥4 for isolated ileal disease).
  - At baseline, median CDAI was 307 (range, 76-634) and 307 (range, 72-651), and median SES-CD was 12 (range, 4-45) and 13 (range, 4-40), in CD-1 and CD-2, respectively.
  - Patients were randomly assigned to receive Skyrizi 600mg, Skyrizi 1200mg, or placebo as an intravenous (IV) infusion at week 0, week 4, and week 8.

Clinical Trials: Crohn Disease

- **CD-1** and **CD-2** Induction Studies
  - The coprimary endpoints were **clinical remission** (measured by CDAI) and **endoscopic response** (defined as a decrease in SES-CD of >50% from the baseline or a decrease of at least 2 points for patients with a baseline score of 4 and isolated ileal disease, based on central reading) at week 12.
  - Secondary endpoints included **clinical response** (defined as a reduction of CDAI ≥100 points from baseline) and **endoscopic remission** (defined as SES-CD ≤4 and at least a 2-point reduction from baseline, with no individual subscore greater than 1, based on central reading).

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Clinical Trials: Crohn Disease

In **CD-1** and **CD-2**, a greater proportion of patients treated with Skyrizi 600mg met the following efficacy endpoints at week 12 vs placebo (all *P* <.001).

	Study CD-1			Study CD-2		
	Skyrizi 600mg (n=336)	**Placebo (n=175)**	**Treatment Difference (95% CI)**	**Skyrizi 600mg (n=191)**	**Placebo (n=187)**	**Treatment Difference (95% CI)**
Clinical Remission	45%	25%	21% (12-29)	42%	20%	22% (13-31)
Endoscopic Response	40%	12%	28% (21-35)	29%	11%	18% (10-25)
Clinical Response	60%	37%	23% (14-32)	60%	30%	29% (20-39)
Endoscopic Remission	24%	9%	15% (9-21)	19%	4%	15% (9-21)

Clinical Trials: Crohn Disease

- Additional **CD-1** and **CD-2** Findings
  - The **onset of clinical response** and **clinical remission** based on CDAI occurred as early as week 4 in a greater proportion of patients treated with the Skyrizi 600mg induction regimen vs placebo.
  - Reductions in **stool frequency** and **abdominal pain** were observed in a greater proportion of patients treated with the Skyrizi 600mg induction regimen vs placebo.

- The **Skyrizi 1200mg dosage** did not demonstrate additional treatment benefit over the 600mg dosage and is not a recommended regimen.

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Clinical Trials: Crohn Disease

- **CD-3** Maintenance Study
  - Included a total of 247 patients who achieved clinical response in studies CD-1 and CD-2, defined as a reduction in CDAI of at least 100 points from baseline after 12 weeks of induction treatment.
  - Patients were randomly assigned to receive Skyrizi 360mg subcutaneously at week 12, then every 8 weeks thereafter for up to an additional 52 weeks.
  - The coprimary endpoints were **clinical remission** and **endoscopic response** at week 52.

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Clinical Trials: Crohn Disease

- CD-3 Maintenance Study Results
  - **Clinical remission** was observed in 57% of patients treated with Skyrizi 360mg at week 52 compared with 46% of those who received placebo (treatment difference, 14%; 95% CI, 3-26; *P* <.05).
  - **Endoscopic response** was observed in 48% of patients treated with Skyrizi 360mg at week 52 compared with 22% of those who received placebo (treatment difference, 31%; 95% CI, 21-41; *P* <.05).
  - **Endoscopic remission** was observed in 41% of patients treated with Skyrizi 360mg at week 52 compared with 13% of those who received placebo; however, this endpoint was not statistically significant.

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Clinical Trials: Crohn Disease

- Immunogenicity
  - Approximately 3.4% (2/58) patients treated with Skyrizi for Crohn disease at the recommended induction and maintenance dosage developed antibodies to risankizumab-rzaa by week 64.
  - None of the patients who developed antibodies to risankizumab-rzaa had antibodies that were classified as neutralizing.

Dosage & Administration: Crohn Disease

- **Prior to initiating treatment** for Crohn disease, perform the following evaluations:
  - Obtain liver enzymes and bilirubin levels.
  - Evaluate patients for tuberculosis infection.
  - Complete all age-appropriate vaccinations by current immunization guidelines.

Dosage & Administration: Crohn Disease

- ≥18yrs old (**Induction Regimen**):
  - 600mg by intravenous (IV) infusion over a period of at least 1 hour at week 0, week 4, and week 8.
  - Complete the infusion within 8 hours of dilution.
  - Do not administer diluted solution in the same IV line with other medicinal products.
- ≥18yrs old (**Maintenance Regimen**):
  - 360mg using on-body injector to administer prefilled cartridge subcutaneously on thigh or abdomen at week 12, and every 8 weeks thereafter.
  - Do not inject into areas where the skin is tender, bruised, erythematous, indurated or affected by any lesions.

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Considerations for Specific Populations

- **Pregnancy:** Insufficient data to evaluate a drug-associated risk for major birth defects, miscarriage or other adverse maternal or fetal outcomes.
- **Nursing mothers**: No data on the presence of risankizumab-rzaa in human milk, the effects on the breastfed infant, or the effects on milk production.
- **Pediatric**: Not established in pediatric patients.
- **Geriatric:** Number of patients 65 years of age and older in clinical studies was not sufficient to determine whether they respond differently from younger patients.

Contraindications

- History of serious hypersensitivity reaction to risankizumab-rzaa or any of the excipients.
  - Serious hypersensitivity reactions, including anaphylaxis, have been reported with the use of Skyrizi.

Warnings and Precautions

- Discontinue if serious hypersensitivity reactions (eg, anaphylaxis) occur and initiate appropriate therapy immediately.
- May increase risk of infections.
- Do not initiate Skyrizi in patients with any clinically important active infection until the infection resolves or is adequately treated.
- Chronic or history of recurrent infection: consider the risks and benefits prior to initiation.
- If an infection develops or is not responding to standard therapy, monitor closely and discontinue Skyrizi until resolves.

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Warnings and Precautions

- Evaluate for TB infection prior to initiation.
- History of latent or active TB (without confirmed adequate treatment); consider anti-TB therapy prior to initiation.
- Monitor for signs/symptoms of active TB during and after therapy.
- Do not initiate in patients with active TB.
- Hepatotoxicity in treatment of Crohn disease:
  - Evaluate liver enzymes and bilirubin at baseline and during induction at least up to 12 weeks of treatment.
  - Interrupt therapy if drug-induced liver injury is suspected.
  - Consider other treatment options in patients with evidence of liver cirrhosis.

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Interactions

- Avoid use of live vaccines
  - Medications that interact with the immune system may increase the risk of infection following administration of live vaccines.
  - Complete all age-appropriate vaccination according to guidelines prior to initiating therapy with Skyrizi.
  - No data available on response to live or inactive vaccines.

Adverse Reactions

- **Plaque psoriasis and psoriatic arthritis: Most common (≥1%):**
  - Upper respiratory tract infections, headache, fatigue, injection site reactions, tinea infections.
- **Crohn disease: Most common (>3%):**
  - *Induction*: upper respiratory tract infections, headache, arthralgia.
  - *Maintenance*: arthralgia, injection site reactions, abdominal pain, anemia, pyrexia, back pain, arthropathy, urinary tract infection.

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Product Monograph

- For more information view the product monograph available at:

https://www.empr.com/drug/skyrizi/