Risankizumab-rzaa (SKYRIZI) in Ulcerative Colitis
Criteria for Use
February 2025
VA Pharmacy Benefits Management Services and National Formulary Committee

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

Exclusion Criteria

If ANY of the following are selected, the patient will NOT meet criteria for risankizumab-rzaa.

- ☐ Uncontrolled, active, severe infection, including evidence of *C. difficile* and undrained abscess (however, risankizumab-rzaa may be started / restarted once the infection treatment has been initiated).
- ☐ Untreated latent or active tuberculosis infection.
- ☐ Hepatitis B surface antigen (HBsAg)-positive and not on antiviral prophylaxis.^1 Risankizumab-rzaa may be initiated after starting antiviral prophylaxis.
- ☐ Untreated HIV infection. Treated, well-controlled, asymptomatic HIV-positive patients can be treated with risankizumab-rzaa.
- ☐ Concomitant live or live-attenuated vaccines or administration of inactivated, live, or live-attenuated vaccines less than 2 weeks before initiation of risankizumab-rzaa.^2
- ☐ Liver cirrhosis unless the prescriber deems that the potential benefits outweigh the risks.

Inclusion Criteria

All the following criteria must be selected to meet criteria.

- ☐ Current or prior moderate to severe **ulcerative colitis (UC)** confirmed by endoscopy or imaging
- ☐ Prescribed and monitored by a VA/VA Community Care gastroenterologist / hepatologist or locally designated expert
- ☐ Completed tuberculosis (TB) test using tuberculin skin test or interferon-gamma release assay [IGRA]
- ☐ Completed hepatitis B screening (at minimum, HBsAg, total antibody-to-hepatitis-B-core-antigen (anti-HBc) and antibody to hepatitis B surface antigen [anti-HBs])
- ☐ Current or past completion of hepatitis C screening. (Risankizumab-rzaa may be initiated while waiting for test results.)
- ☐ Obtained liver panel including bilirubin

Additional Inclusion Criteria

ONE of the following criteria must be selected to meet criteria.

- ☐ **Tumor necrosis factor inhibitor (TNFi)** is medically inadvisable. Infliximab / biosimilar is the preferred TNFi in UC.
- ☐ Primary nonresponse, inadequate partial response, or loss of response^3 after 12 weeks of **one TNFi** in the presence of adequate TNFi levels (mechanistic failure).
- ☐ Loss of response^3 to a **TNFI** (**infliximab / biosimilar** is the preferred TNFi in UC) despite therapeutic drug monitoring (TDM)-based optimized dosing to address pharmacokinetic failure.^4

See footnote 5 for sequencing UC drugs.

Additional Inclusion Criteria

Select if applicable.

☐ If HBsAg-negative but anti-HBc-positive: A GI / liver or infectious diseases expert has been consulted for advice on whether to start antiviral prophylaxis or to preemptively monitor for HBV reactivation.

☐ For women who can become pregnant: Counseling provided on potential risks vs benefits of treatment and the use of effective contraception.

Other Justification

☐ _____

Footnotes

1 Antiviral prophylaxis for HBV: Agents with high genetic barrier to resistance such as entecavir or tenofovir should be used.

2 When possible, vaccinations should be updated before the patient initiates risankizumab-rzaa. Unless contraindicated, recombinant zoster (SHINGRIX) vaccine should be completed or at least initiated by the end of the first year of treatment with risankizumab-rzaa, preferably when dosage is low, disease is stable, or at other times when a robust immune response to vaccination can be expected.

3 Loss of response refers to active disease confirmed by endoscopy, imaging, or biochemical assessment.

4 Pharmacokinetic failure resulting in low TNFi levels may be immune-mediated or non–immune-mediated.
If **TNFI levels are undetectable with high antidrug antibody (AdAb) titers** (i.e., immune-mediated pharmacokinetic failure): Consider adding an immunomodulator. If the patient is on adalimumab, a switch to a second TNFi is preferred over a switch to another drug class. If on infliximab, switch to a non-TNFI (one of vedolizumab, tofacitinib, upadacitinib, etrasimod, ozanimod, or risankizumab-rzaa). Infliximab / biosimilar is the preferred TNFi. A trial of just one TNFi may be sufficient (prefer not switching infliximab to adalimumab, which has lower efficacy in UC).
If **TNFI levels are undetectable with low AdAb titers** (i.e., also immune-mediated pharmacokinetic failure), optimize dosing (i.e., shorten dosing interval, increase dose, or both; add a conventional immunomodulator if not already started).
If **trough TNFI levels are subtherapeutic with low or high AdAb titers**, optimal management is uncertain.
If **TNFI trough levels are subtherapeutic with no AdAbs** (i.e., non–immune-mediated pharmacokinetic failure due to rapid drug clearance), shorten the TNFI dosing intervals, increase the dose, or both.

5 **<u>Sequencing UC Drugs (1L = First-line, 2L = Second-line, etc.)</u>**
1L: Infliximab (preferred) or adalimumab (less effective alternative)
2L / 3L: Vedolizumab, tofacitinib, upadacitinib, etrasimod, ozanimod, or risankizumab-rzaa (one drug should be risankizumab-rzaa as 2L or 3L drug)
4L: Mirikizumab-mrkz, guselkumab, or ustekinumab

Supplemental Information

This supplemental information is provided to assist in adjudication of requests for risankizumab-rzaa in UC.

Section	Criterion	Issues for Consideration
Inclusion Criteria	Completed tuberculosis (TB) test using tuberculin skin test or interferon-gamma release assay [IGRA].	Routine retesting is not required for prescription renewals. Retesting in high-risk patients should be considered.
	Completed hepatitis B screening (at minimum, HBsAg, total anti-HBc and antibody to hepatitis B surface antigen [anti-HBs]).	Routine retesting is not required for prescription renewals. Retesting in high-risk patients should be considered. Anti-HBs may help to identify patients who require initial or booster vaccination (anti-HBs titers >= 10 IU/L are generally considered protective) or HBsAg-negative patients without past vaccination who have occult HBV from past infection (anti-HBs positive and lost anti-HBc).
	Current or past completion of hepatitis C screening. (Risankizumab-rzaa may be initiated while waiting for test results.)	Routine retesting is not required for prescription renewals. Retesting in high-risk patients should be considered.
Additional Inclusion Criteria	Infliximab / biosimilar is the preferred TNFI in UC.	Other options for UC in TNFI-naïve patients are adalimumab and golimumab. Adalimumab is less preferred than vedolizumab and tofacitinib in TNFi-exposed UC patients.
Additional Inclusion Criteria	If HBsAg-negative but antibody-to-hepatitis-B-core-antigen (anti-HBc)-positive, a gastroenterologist / hepatologist or infectious diseases expert has been consulted for advice on whether to start antiviral prophylaxis or to preemptively monitor for HBV reactivation.	In patients who are HBsAg-negative but **anti-HBc-positive**, the presence of antibody to hepatitis B surface antigen (anti-HBs) does not guarantee protection against HBV reactivation, and the available evidence is insufficient to support the use of anti-HBs titers in deciding whether to give antiviral prophylaxis. Management depends on the patient's risk of HBV reactivation. [Reddy K, et al. American Gastroenterological Association Institute Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Drug Therapy. Gastroenterology. 2015;148(1):215–219. doi: https://doi.org/10.1053/j.gastro.2014.10.039 Ekpanyapong S, Reddy KR. Hepatitis B Virus Reactivation: What Is the Issue, and How Should It Be Managed? Clin Liver Dis. 2020 Aug;24(3):317-333. doi: 10.1016/j.cld.2020.04.002.]

Prepared: February 2025.

Contact: Francine Goodman, PharmD, BCPS, National Program Manager, VA Pharmacy Benefits Management Services – Formulary Management (12PBM)