Skyrizi® (Risankizumab-Rzaa)

Policy Number: CS2023D00116D
Effective Date: October 1, 2023

Instructions for Use

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Related Policies
None

Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Indiana	Refer to the state's Medicaid clinical policy
Kansas	Refer to the state's Medicaid clinical policy
Louisiana	Refer to the state's Medicaid clinical policy
North Carolina	None
Ohio	Skyrizi® (Risankizumab-Rzaa) (for Ohio Only)
Pennsylvania	Refer to the state's Medicaid clinical policy
Washington	Refer to the state's Medicaid clinical policy

Coverage Rationale

This policy refers to Skyrizi (risankizumab-rzaa) injection for intravenous use. Skyrizi (risankizumab-rzaa) for self-administered subcutaneous injection is obtained under the pharmacy benefit.

Crohn's Disease (CD)

Skyrizi is medically necessary for the treatment of Crohn's disease (CD) when all of the following criteria are met:

- Diagnosis of moderately to severely active Crohn's disease; **and**
- **One** of the following:
  - History of failure to **one** of the following conventional therapies at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
    - Corticosteroids (e.g., prednisone, methylprednisolone, budesonide)
    - 6-mercaptopurine (Purinethol)
    - Azathioprine (Imuran)
    - Methotrexate (Rheumatrex, Trexall)

or

- Patient has been previously treated with a biologic DMARD FDA-approved for the treatment of Crohn's disease [e.g., adalimumab, Stelara (ustekinumab), Cimzia (certolizumab pegol)]

and

- History of failure, contraindication or intolerance to **two** biologic DMARDs FDA-approved for the treatment of Crohn's disease (document drug, date, and duration of trial); **and**
- Skyrizi is to be administered as three intravenous induction doses; **and**
- Skyrizi induction dosing is in accordance with the United States Food and Drug Administration (FDA) labeled dosing for CD; **and**
- Patient is not receiving Skyrizi in combination with either of the following:
  - Biologic DMARD [e.g., Cimzia (certolizumab), Humira (adalimumab), Stelara (ustekinumab)]
  - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Rinvoq (upadacitinib)]

and

- Prescribed by or in consultation with a gastroenterologist; **and**
- Authorization will be issued for 3 induction doses

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J2327	Injection, risankizumab-rzaa, intravenous, 1 mg

Diagnosis Code	Description
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication

Diagnosis Code	Description
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications

Background

Skyrizi 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. Skyrizi inhibits the release of pro-inflammatory cytokines and chemokines.

Clinical Evidence

Proven

Crohn's Disease

ADVANCE and MOTIVATE were randomized, double-masked, placebo-controlled, phase 3 induction studies. Eligible patients aged 16–80 years with moderately to severely active Crohn's disease, previously showing intolerance or inadequate response to one or more approved biologics or conventional therapy (ADVANCE) or to biologics (MOTIVATE), were randomly assigned to receive a single dose of intravenous risankizumab (600 mg or 1,200 mg) or placebo (2:2:1 in ADVANCE, 1:1:1 in MOTIVATE) at weeks 0, 4, and 8. We used interactive response technology for random assignment, with stratification by number of previous failed biologics, corticosteroid use at baseline, and Simple Endoscopic Score for Crohn's disease (SES-CD). All patients and study personnel (excluding pharmacists who prepared intravenous solutions) were masked to treatment allocation throughout the study. Coprimary endpoints were clinical remission [defined by Crohn's disease activity index (CDAI) or patient-reported outcome criteria (average daily stool frequency and abdominal pain score)] and endoscopic response at week 12. The intention-to-treat population (all eligible patients who received at least one dose of study drug in the 12-week induction period) was analyzed for efficacy outcomes. Safety was assessed in all patients who received at least one dose of study drug.

Participants were enrolled between May 10, 2017, and Aug. 24, 2020, (ADVANCE trial), and Dec. 18, 2017 and Sept. 9, 2020, (MOTIVATE trial). In ADVANCE, 931 patients were assigned to either risankizumab 600 mg (n = 373), risankizumab 1,200 mg (n = 372), or placebo (n = 186). In MOTIVATE, 618 patients were assigned to risankizumab 600 mg (n = 206), risankizumab 1,200 mg (n = 205), or placebo (n = 207). The primary analysis population comprised 850 participants in ADVANCE and 569 participants in MOTIVATE. All coprimary endpoints at week 12 were met in both trials with both doses of risankizumab (p values ≤ 0·0001). In ADVANCE, CDAI clinical remission rate was 45% (adjusted difference 21%, 95% CI 12–29; 152/336) with risankizumab 600 mg and 42% (17%, 8–25; 141/339) with risankizumab 1,200 mg versus 25% (43/175) with placebo; stool frequency and abdominal pain score clinical remission rate was 43% (22%, 14–30; 146/336) with risankizumab 600 mg and 41% (19%, 11–27; 139/339) with risankizumab 1,200 mg versus 22% (38/175) with placebo; and endoscopic response rate was 40% (28%, 21–35; 135/336) with risankizumab 600 mg and 32% (20%, 14–27; 109/339) with risankizumab 1,200 mg versus 12% (21/175) with placebo. In MOTIVATE, CDAI clinical remission rate was 42% (22%, 13–31; 80/191) with risankizumab 600 mg and 40% (21%, 12–29; 77/191) with risankizumab 1,200 mg versus 20% (37/187) with placebo; stool frequency and abdominal pain score clinical remission rate was 35% (15%, 6–24; 66/191) with risankizumab 600 mg and 40% (20%, 12–29; 76/191) with risankizumab 1,200 mg versus 19% (36/187) with placebo; and endoscopic response rate was 29% (18%, 10–25; 55/191) with risankizumab 600 mg and 34% (23%, 15–31; 65/191) with risankizumab 1,200 mg versus 11% (21/187) with placebo. The overall incidence of treatment-emergent adverse events was similar among the treatment groups in both trials. Three deaths occurred during induction [two in the placebo group (ADVANCE) and one in the risankizumab 1,200 mg group (MOTIVATE)]. The death in the risankizumab-treated patient was deemed unrelated to the study drug.

Risankizumab was effective and well tolerated as induction therapy in patients with moderately to severely active Crohn's disease.

FORTIFY is a phase 3, multicenter, randomized, double-blind, placebo-controlled, maintenance withdrawal study across 273 clinical centers in 44 countries across North and South America, Europe, Oceania, Africa, and the Asia-Pacific region that enrolled participants with clinical response to risankizumab in the ADVANCE or MOTIVATE induction studies. Patients in ADVANCE or MOTIVATE were aged 16–80 years with moderately to severely active Crohn's disease. Patients in the FORTIFY sub-study 1 were randomly assigned again (1:1:1) to receive either subcutaneous risankizumab 180 mg, subcutaneous risankizumab 360 mg, or withdrawal from risankizumab to receive subcutaneous placebo [herein referred to as withdrawal (subcutaneous placebo)]. Treatment was given every 8 weeks. Patients were stratified by induction dose, post-induction endoscopic response, and clinical remission status. Patients, investigators, and study personnel were masked to treatment assignments. Week 52 co-primary endpoints were clinical remission [Crohn's disease activity index (CDAI) in the U.S. protocol, or stool frequency and abdominal pain score in the non-U.S. protocol] and endoscopic response in patients who received at least one dose of study drug during the 52-week maintenance period. Safety was assessed in patients receiving at least one dose of study medication.

712 patients were initially assessed and, between April 9, 2018, and April 24, 2020, 542 patients were randomly assigned to either the risankizumab 180 mg group (n = 179), the risankizumab 360 mg group (n = 179), or the placebo group (n = 184). Greater clinical remission and endoscopic response rates were reached with 360 mg risankizumab versus placebo (CDAI clinical remission was reached in 74 (52%) of 141 patients vs. 67 (41%) of 164 patients, adjusted difference 15% (95% CI 5–24); stool frequency and abdominal pain score clinical remission was reached in 73 (52%) of 141 vs. 65 (40%) of 164, adjusted difference 15% (5–25); endoscopic response 66 (47%) of 141 patients vs. 36 (22%) of 164 patients, adjusted difference 28% (19–37). Higher rates of CDAI clinical remission and endoscopic response [but not stool frequency and abdominal pain score clinical remission (p = 0·124)] were also reached with risankizumab 180 mg versus withdrawal [subcutaneous placebo; CDAI clinical remission reached in 87 (55%) of 157 patients, adjusted difference 15% (95% CI 5–24); endoscopic response 74 (47%) of 157, adjusted difference 26% (17–35)]. Results for more stringent endoscopic and composite endpoints and inflammatory biomarkers were consistent with a dose–response relationship. Maintenance treatment was well tolerated. Adverse event rates were similar among groups, and the most frequently reported adverse events in all treatment groups were worsening Crohn's disease, arthralgia, and headache.

Subcutaneous risankizumab is a safe and efficacious treatment for maintenance of remission in patients with moderately to severely active Crohn's disease and offers a new therapeutic option for a broad range of patients by meeting endpoints that might change the future course of disease.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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
- Active psoriatic arthritis in adults
- Moderately to severely active Crohn's disease in adults

References

1. Skyrizi [package insert]. North Chicago, IL: AbbVie Inc.; May 2023.
2. D'Haens G, Panaccione R, Baert F, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. *Lancet*. 2022;399(10340):2015-2030.
3. Ferrante M, Panaccione R, Baert F, et al. Risankizumab as maintenance therapy for moderately to severely active Crohn's disease: results from the multicentre, randomised, double-blind, placebo-controlled, withdrawal phase 3 FORTIFY maintenance trial. *Lancet*. 2022;399(10340):2031-2046.
4. Lichtenstein GR, Loftus EV, Isaacs KL, et al ACG clinical guideline: management of Crohn’s disease in adults. Am J Gastroenterol. 2018; 113:481-517.

Policy History/Revision Information

Date	Summary of Changes
10/01/2023	**Coverage Rationale** • Revised coverage criteria; replaced criterion requiring "the patient has been previously treated with a biologic DMARD FDA-approved for the treatment of Crohn's disease [e.g., *Humira* (adalimumab), Stelara (ustekinumab)]" with "the patient has been previously treated with a biologic DMARD FDA-approved for the treatment of Crohn's disease [e.g., adalimumab, Stelara (ustekinumab), *Cimzia (certolizumab pegol)*]" **Supporting Information** • Updated *References* section to reflect the most current information • Archived previous policy version CS2023D00116C

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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