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Policy Number: 058.001

Title: Coverage Determination Policy for Skyrizi (Risankizumab-Rzaa)

Regions: ☒ Texas ☒ New Mexico

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: Self-Administered Drug Exclusion List: LCA A53127 (sub-cut use)

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Coverage Policy Number: 058.001

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

This policy refers to Skyrizi (risankizumab-rzaa) injection for intravenous use. Skyrizi (risankizumab-rzaa) for self-administered subcutaneous injection is obtained under the member's pharmacy benefit and is excluded from Medicare Part B coverage since it is on the self-administered drug exclusion list (LCA A53127).

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

A. Diagnosis of moderately to severely active Crohn's disease

B. ONE of the following:

   I. 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:

      a. Corticosteroids (e.g., prednisone, methylprednisolone, budesonide)

      b. 6-mercaptopurine (Purinethol)

      c. Azathioprine (Imuran)

      d. Methotrexate (Rheumatrex, Trexall) or

   II. Patient has been previously treated with a targeted immunomodulator FDA-approved for the treatment of Crohn's disease [e.g., adalimumab, Stelara (ustekinumb), Cimzia (certolizumab pegol), Rinvoq (upadacitinib)]

C. Skyrizi is to be administered as three intravenous induction doses

D. Skyrizi induction dosing is in accordance with the United States Food and Drug Administration (FDA) labeled dosing for CD

E. Patient is not receiving Skyrizi in combination with another targeted immunomodulator [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept), adalimumab, Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Stelara (ustekinumab)]

F. Prescribed by or in consultation with a gastroenterologist

G. Authorization will be issued for 3 induction doses

Renewal/Continuation of Therapy Requests

Continuation of therapy for Skyrizi after the first 3 induction doses is by subcutaneous administration only. This policy refers to Skyrizi (risankizumab-rzaa) injection for intravenous use. Skyrizi (risankizumab-rzaa) for self-administered subcutaneous injection is obtained under the member's pharmacy benefit.

FDA Approved Dose and Indication

FDA Approved Indication	Approved Dosing
Crohn's Disease (Moderately to Severely Active)	• **Induction:** 600mg **IV** infusion at week 0,4,8 • **Maintenance (subcutaneous):** 180 mg or 360 mg at week 12 then every 8 weeks
Plaque psoriasis (Moderate to Severe) if eligible for systemic therapy or phototherapy	150 mg (Subcutaneous) at Week 0, Week 4, and every 12 weeks thereafter
Psoriatic arthritis, Active	150 mg (Subcutaneous) at Week 0, Week 4, and every 12 weeks thereafter

General 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 randomised, 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 1200 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 1200 mg (n = 372), or placebo (n = 186). In MOTIVATE, 618 patients were assigned to risankizumab 600 mg (n = 206), risankizumab 1200 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 1200 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 1200 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 1200 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 1200 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 1200 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 1200 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 1200 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, randomised, 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, subcutaneousrisankizumab 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 US protocol, or stool frequency and abdominal pain score in the non-US 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.

HCPCS Code

HCPCS Code	J2327: Injection, risankizumab-rzaa, 1 mg
Available Dosage Form	• 75mg/0.83ml subcut PFS • 150mg/1ml subcut PFS • 180mg/1.2ml subcut prefilled cartridge • 360mg/2.4ml subcut prefilled cartridge • 600mg/10ml (60mg/ml) single-dose vial Intravenous solution
Route of Administration	Intravenous and Subcutaneous

Acronyms

CD = Crohn's Disease

CDAI = Crohn's Disease Activity Index

DMARD = Disease Modifying Antirheumatic Drugs

FDA = Food and Drug Administration

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