risankizumab-rzaa (Skyrizi™) intravenous

Medicare Advantage Medical Policy #MA-144
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Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Per the Self-Administered Drug list as defined by the Medicare Administrative Contractor for the Health Plan, subcutaneous risankizumab-rzaa (Skyrizi™) is eligible for coverage under Part D only and not targeted by this policy.

Crohn's Disease

Based on review of available data, the Health Plan may consider intravenous risankizumab-rzaa (Skyrizi™) for the treatment of patients with Crohn's disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for intravenous risankizumab-rzaa (Skyrizi) will be considered when the following criteria are met:

- Patient has a diagnosis of moderately to severely active Crohn's disease; AND
- Patient is 18 years of age or older; AND
- Patient has a negative tuberculosis (TB) test (e.g., purified protein derivative [PPD], blood test) prior to treatment; AND
- Patient has failed or become intolerant to treatment with traditional immunomodulators (e.g., azathioprine, 6-mercaptopurine) or corticosteroids OR the patient has failed or become intolerant to a tumor necrosis factor (TNF) blocker or another biologic for the treatment of Crohn's disease such as infliximab (Remicade®‡, biosimilars), adalimumab (Humira, biosimilars), or vedolizumab (Entyvio®)‡; AND
- Requested drug is NOT used in combination with other biologic products such as infliximab (Remicade, biosimilars), adalimumab (Humira, biosimilars), or vedolizumab (Entyvio) for the treatment of moderately to severely active Crohn's disease.
- The requested dose will not exceed 600 mg at week 0, week 4, and week 8.

Ulcerative Colitis
Based on review of available data, the Health Plan may consider intravenous risankizumab-rzaa (Skyrizi) for the treatment of patients with ulcerative colitis to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for intravenous risankizumab-rzaa (Skyrizi) will be considered when the following criteria are met:

- Patient has a diagnosis of moderately to severely active ulcerative colitis; AND
- Patient is 18 years of age or older; AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- Patient has failed or become intolerant to treatment with traditional immunomodulators (e.g., azathioprine, 6-mercaptopurine) or corticosteroids; AND
- Requested drug is NOT used in combination with other biologic products such as infliximab (Remicade, biosimilars), adalimumab (Humira, biosimilars), or vedolizumab (Entyvio) for the treatment of moderately to severely active ulcerative colitis.
- The requested dose will not exceed 1,200 mg at weeks 0, week 4, and week 8.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of intravenous risankizumab-rzaa (Skyrizi) when any of the following criteria for their respective disease state listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary****:

- For Crohn's disease:
  - Patient has failed or become intolerant to treatment with traditional immunomodulators (e.g., azathioprine, 6-mercaptopurine) or corticosteroids OR the patient has failed or become intolerant to a TNF blocker or another biologic for the treatment of Crohn's disease such as infliximab (Remicade, biosimilars), adalimumab (Humira, biosimilars), or vedolizumab (Entyvio)
- For ulcerative colitis:
  - Patient has failed or become intolerant to treatment with traditional immunomodulators (e.g., azathioprine, 6-mercaptopurine) or corticosteroids

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of intravenous risankizumab-rzaa (Skyrizi) when the patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary****).

Background/Overview

Skyrizi is an interleukin-23 (IL-23) antagonist indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy, for the treatment of active psoriatic arthritis in adults, for the treatment of moderate to severely active Crohn's disease in adults, and for the treatment of moderately to severely active ulcerative colitis in adults. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Skyrizi therefore inhibits the release of pro-inflammatory cytokines and chemokines. For plaque psoriasis and psoriatic arthritis, Skyrizi is dosed at 150 mg administered subcutaneously at week 0, week 4, and every 12 weeks thereafter. For Crohn's disease, the recommended induction dosing is 600 mg administered by intravenous infusion at week 0, week 4, and week 8. The recommended maintenance dosage for Crohn's disease is 180 mg or 360 mg administered subcutaneously at week 12 and every 8 weeks thereafter. For ulcerative colitis, the recommended induction dosing is 1,200 mg administered by intravenous infusion over a period of at least two hours at week 0, week 4, and week 8, and the recommended maintenance dosing is 180 mg or 360 mg administered by subcutaneous injection at week 12 and every 8 weeks thereafter. The lowest effective dose should be used to maintain therapeutic response for Crohn's disease and ulcerative colitis.

Crohn's Disease

Crohn's disease is a chronic autoimmune disease that can affect any part of the gastrointestinal tract but most commonly occurs in the ileum. As a result of the immune attack, the intestinal wall becomes thick, and deep ulcers may form. In addition to the bowel abnormalities, Crohn's disease can also affect other organs in the body. Typically, first line treatments such as corticosteroids, 6 -MP and azathioprine are used to treat this condition.

Ulcerative Colitis

Ulcerative colitis is a chronic, episodic, inflammatory disease of the large intestine and rectum characterized by bloody diarrhea. This disease usually begins in the rectal area and may eventually extend through the entire large intestine. Repeated episodes of inflammation lead to thickening of the wall of the intestine and rectum with scar tissue. Death of colon tissue or sepsis may occur with severe disease. The goals of treatment are to control the acute attacks, prevent recurrent attacks and promote healing of the colon. Hospitalization is often required for severe attacks. Typically, first line treatments such as corticosteroids, 6-mercaptopurine and azathioprine are used to treat this condition.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Skyrizi was approved in April of 2019 for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. In early 2022, Skyrizi was approved for the treatment of active psoriatic arthritis in adults. In mid-2022, Skyrizi was approved for the treatment of moderately to severely active Crohn's disease. In June of 2024, Skyrizi was approved for the treatment of moderately to severely active ulcerative colitis.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Crohn's Disease

In two 12-week induction studies (CD-1 and CD-2), subjects with moderately to severely active Crohn's disease were randomized to receive Skyrizi 600 mg, Skyrizi 1,200 mg, or placebo as an intravenous infusion at week 0, week 4, and week 8. Moderately to severely active Crohn's disease was defined as a Crohn's Disease Activity Index (CDAI) of 220 to 450 and Simple Endoscopic Score for Crohn's disease (SES-CD) ≥ 6 (or ≥ 4 for isolated ileal disease). Subjects with inadequate response, loss of response, or intolerance to oral aminosalicylates, corticosteroids, immunosuppressants, and/or biologic therapy were enrolled. In CD-1, 58% (491/850) of subjects had failed or were intolerant to treatment with one or more biologic therapies (prior biologic failure). All subjects in CD-2 had prior biologic failure. At baseline, 30% and 34% of patients were receiving corticosteroids, 24% and 23% of patients were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), and 31% and 19% of patients were receiving aminosalicylates in CD-1 and CD-2, respectively. In CD-1 and CD-2, the co-primary endpoints were clinical remission and endoscopic response at week 12. In CD-1, 45% of the Skyrizi treated population achieved clinical remission compared to 25% of the placebo treated population. For endoscopic response, 40% of the Skyrizi treated population achieved this outcome compared to 12% in the placebo group. In CD-2, 42% of the Skyrizi treated population achieved clinical remission compared to 20% of the placebo treated population. For endoscopic response, 29% of the Skyrizi treated population achieved this outcome compared to 11% in the placebo group. Results for CD-1 and CD-2 were both statistically significant. The Skyrizi 1,200 mg dosage did not demonstrate additional treatment benefit over the 600 mg dosage and is not a recommended regimen.

The maintenance study, CD-3, evaluated 382 subjects who achieved clinical response defined as a reduction in CDAI of at least 100 points from baseline after 12 weeks of induction treatment with intravenous Skyrizi in studies CD-1 and CD-2. Subjects were randomized to receive a maintenance regimen of Skyrizi 180 mg or 360 mg or placebo at week 12 and every 8 weeks thereafter for up to an additional 52 weeks. The co-primary endpoints in CD-3 were clinical remission and endoscopic response at week 52. In CD-3, 57% of the Skyrizi 360 mg treated population and 61% of the Skyrizi 180 mg treated population achieved clinical remission compared to 46% of the placebo treated population. For endoscopic response, 48% of the Skyrizi 360 mg treated population and 50% of the Skyrizi 180 mg treated population achieved this outcome compared to 22% in the placebo group. Both of the co-primary endpoints were statistically significant.

Ulcerative Colitis
In a 12 week induction study (UC-1), 966 subjects with moderately to severely active ulcerative colitis were randomized and received Skyrizi 1,200 mg or placebo as an intravenous infusion at week 0, week 4, and week 8. Disease activity was assessed by the modified Mayo score (mMS), a 3-component Mayo score (0-9) which consists of the following subscores (0 to 3 for each subscore): stool frequency (SFS), rectal bleeding (RBS), and findings on centrally read endoscopy score (ES). An ES of 2 was defined by marked erythema, lack of vascular pattern, any friability, and/or erosions; an ES of 3 was defined by spontaneous bleeding and ulceration. Enrolled subjects had a mMS between 5 and 9, with an ES of 2 or 3. Subjects with inadequate response, or intolerance to oral aminosalicylates, corticosteroids, immunomodulators, biologics, Janus Kinase inhibitors (JAKi), and/or sphingosine-1-phospate receptor modulators (S1PRM) were enrolled. At baseline in UC-1, the median mMS was 7; 37% had severely active disease (mMS >7); 69% had an ES of 3. In UC-1, 52% (499/966) of subjects had failed (inadequate response or intolerance) treatment with one or more biologics, JAKi or S1PRM. Of these 499 subjects, 484 (97%) failed biologics and 90 (18%) failed JAK inhibitors. Enrolled subjects were permitted to use a stable dose of oral corticosteroids (up to 20 mg/day prednisone or equivalent), immunomodulators, and aminosalicylates. At baseline, 36% of subjects were receiving corticosteroids, 16% of subjects were receiving immunomodulators (including azathioprine, 6-mercaptopurine, methotrexate), and 73% of subjects were receiving aminosalicylates in UC-1. In UC-1, the primary endpoint was clinical remission defined using the mMS at week 12. In UC-1, 24% of the Skyrizi treated population achieved clinical remission compared to 8% of the placebo treated population. UC-1 was not designed to evaluate the relationship of histologic endoscopic mucosal improvement at week 12 to disease progression and long-term outcomes.

The maintenance study, UC-2, evaluated 547 subjects who received one of three Skyrizi induction regimens, including the 1,200 mg regimen, for 12 weeks in Studies UC-1 or UC-3 and demonstrated clinical response per mMS after 12 weeks. Subjects were randomized to receive a maintenance regimen of subcutaneous (SC) Skyrizi 180 mg or Skyrizi 360 mg or placebo at week 12 and every 8 weeks thereafter for up to an additional 52 weeks. The primary endpoint in UC-2 was clinical remission using mMS at week 52. In UC-2, 41% of the Skyrizi 360 mg treated population and 45% of the Skyrizi 180 mg treated population achieved clinical remission compared to 26% of the placebo treated population.

References

1. Skyrizi [package insert]. AbbVie, Inc. North Chicago, Illinois. May 2025.
2. Skyrizi Drug Evaluation. Express Scripts. Updated May 2019.

Policy History

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09/16/2025 UM Committee review and approval. New policy.

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Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J2327
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or

diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses

coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.