Drug Coverage Policy

Effective Date.....11/01/2024
Coverage Policy Number.....IP0670
Policy Title.....Skyrizi Subcutaneous Prior Authorization Policy

Inflammatory Conditions – Skyrizi Subcutaneous Prior Authorization Policy

- Skyrizi® (risankizumab-rzaa subcutaneous injection – Abbvie)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW

Skyrizi subcutaneous (SC), an interleukin (IL)-23 blocker, is indicated for the following uses:[1]

- **Crohn's disease**, in patients with moderate to severe active disease; AND
- **Plaque psoriasis**, for treatment of adults with moderate to severe disease who are candidates for systemic therapy or phototherapy; AND

- **Psoriatic arthritis**, for treatment of adults with active disease; AND
- **Ulcerative colitis**, in adults with moderate to severe active disease.

Skyrizi is also available in an intravenous (IV) formulation that is indicated only in Crohn's disease and ulcerative colitis, given as an IV infusion at Weeks 0, 4, and 8 for induction, followed by Skyrizi SC once every 8 weeks thereafter for maintenance.[1] Skyrizi SC is available as a 180 mg or 360 mg single-dose prefilled cartridge for use with an on-body injector for use in Crohn's disease and ulcerative colitis. For other conditions, Skyrizi is available as a 150 mg single-dose prefilled pen and as a 75 mg or 150 mg prefilled syringe.

Guidelines

The following guidelines address conditions for which Skyrizi SC is indicated.

- **Crohn's Disease:** Skyrizi is not addressed in current guidelines. The American College of Gastroenterology has guidelines for Crohn's disease (2018).[5] Biologics are a treatment option in patients who have moderate to severe disease despite treatment with another agent (e.g., corticosteroid, thiopurine, methotrexate, or tumor necrosis factor inhibitors [TNFi]). Guidelines from the American Gastroenterological Association (2021) include biologics among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission.[6]
- **Plaque Psoriasis:** Joint guidelines from the American Academy of Dermatology and National Psoriasis Medical Board (2019) for management of psoriasis with biologics have been published.[2] These guidelines list Skyrizi as a monotherapy treatment option for patients with moderate to severe plaque psoriasis. Guidelines from the European Dermatology Forum (2015) recommend biologics (i.e., etanercept, adalimumab, infliximab, Stelara® [ustekinumab SC injection]) as second-line therapy for induction and long-term treatment if phototherapy and conventional systemic agents have failed, are contraindicated, or are not tolerated.[3]
- **Psoriatic Arthritis:** Guidelines from the American College of Rheumatology (2019) recommend tumor necrosis factor inhibitors over other biologics for use in treatment-naïve patients with psoriatic arthritis and in those who were previously treated with an oral therapy.[4]
- **Ulcerative colitis (UC):** Current guidelines do not address the use of Skyrizi for UC. The American Gastroenterological Association (2020) and the American College of Gastroenterology (2019) have clinical practice guidelines on the management of moderate to severe UC and make recommendations for the use of biologics for induction and maintenance of remission in adults.[7,8] Generally TNFis, Entyvio® (vedolizumab intravenous infusion/subcutaneous injection), Stelara® (ustekinumab intravenous infusion/subcutaneous injection), or Xeljanz®/Xeljanz® XR (tofacitinib tablets, tofacitinib extended-release tablets) are recommended for induction treatment of moderate to severe disease (strong recommendations, moderate quality of evidence). The guidelines also recommend that any drug that effectively treats induction should be continued for maintenance.

Medical Necessity Criteria

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Skyrizi SC. Because of the specialized skills required for evaluation and diagnosis of patients treated with Skyrizi SC as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Skyrizi SC to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Skyrizi subcutaneous is considered medically necessary when ONE of the following is met (1, 2, 3, or 4):

FDA-Approved Indications

1. **Crohn's Disease.** Approve Skyrizi Subcutaneous (on-body injector) for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** According to the prescriber, the patient will receive induction dosing with Skyrizi intravenous within 3 months of initiating therapy with Skyrizi subcutaneous; AND
     - **iii.** Patient meets ONE of the following (a, b, c, or d):
       - **a)** Patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
         Note: Examples of corticosteroids are prednisone or methylprednisolone.
       - **b)** Patient has tried one other conventional systemic therapy for Crohn's disease; OR
         Note: Examples of conventional systemic therapy for Crohn's disease include azathioprine, 6-mercaptopurine, or methotrexate. An exception to the requirement for a trial of or contraindication to steroids or a trial of one other conventional systemic agent can be made if the patient has already tried at least one biologic other than the requested medication A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for Crohn's disease. A trial of mesalamine does not count as a systemic agent for Crohn's disease.
       - **c)** Patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; OR
       - **d)** Patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence); AND
     - **iv.** The medication is prescribed by or in consultation with a gastroenterologist.
   - **B)** Patient is Currently Receiving Skyrizi Subcutaneous. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has been established on therapy for at least 6 months; AND
       Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
     - **ii.** Patient meets at least ONE of the following (a or b):
       - **a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Skyrizi); OR
         Note: Examples of objective measures include fecal markers (e.g., fecal lactoferrin, fecal calprotectin), serum markers (e.g., C-reactive protein), imaging studies (magnetic resonance enterography, computed tomography enterography), endoscopic assessment, and/or reduced dose of corticosteroids.
       - **b)** Compared with baseline (prior to initiating Skyrizi), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or blood in stool.

2. **Plaque Psoriasis.** Approve Skyrizi Subcutaneous (pens or syringes) for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets ONE of the following (a or b):

a) Patient has tried at least one traditional systemic agent for psoriasis for at least 3 months, unless intolerant; OR
Note: Examples of traditional systemic agents for psoriasis include methotrexate, cyclosporine, or acitretin tablets. A 3-month trial of psoralen plus ultraviolet A light (PUVA) also counts. An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already had a 3-month trial or previous intolerance to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for psoriasis. A patient who has already tried a biologic for psoriasis is not required to "step back" and try a traditional systemic agent for psoriasis.

b) Patient has a contraindication to methotrexate, as determined by the prescriber; AND

iii. The medication is prescribed by or in consultation with a dermatologist.

B) Patient is Currently Receiving Skyrizi Subcutaneous. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has been established on the requested drug for at least 3 months; AND
Note: A patient who has received < 3 months of therapy or who is restarting therapy with the requested drug is reviewed under criterion A (Initial Therapy).

ii. Patient experienced a beneficial clinical response, defined as improvement from baseline (prior to initiating the requested drug) in at least one of the following: estimated body surface area, erythema, induration/thickness, and/or scale of areas affected by psoriasis; AND

iii. Compared with baseline (prior to receiving the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain, itching, and/or burning.

3. Psoriatic Arthritis. Approve Skyrizi Subcutaneous (pens or syringes) for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):

i. Patient is ≥ 18 years of age; AND

ii. The medication is prescribed by or in consultation with a rheumatologist or a dermatologist.

B) Patient is Currently Receiving Skyrizi Subcutaneous. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Skyrizi is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Skyrizi); OR
Note: Examples of objective measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

b) Compared with baseline (prior to initiating Skyrizi), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; or decreased soft tissue swelling in joints or tendon sheaths.

4. **Ulcerative Colitis.** Approve Skyrizi Subcutaneous (on-body injector) for the duration noted if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
      i. Patient is ≥ 18 years of age; AND
      ii. According to the prescriber, the patient will receive three induction doses with Skyrizi intravenous within 3 months of initiating therapy with Skyrizi subcutaneous; AND
      iii. Patient meets ONE of the following (a or b):
         a) Patient has had a trial of one systemic agent for ulcerative colitis; OR
         Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone, methylprednisolone. A trial of a mesalamine product does not count as a systemic therapy for ulcerative colitis. A trial of one biologic other than the requested drug also counts as a trial of one systemic agent for ulcerative colitis. A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for ulcerative colitis.
         b) Patient meets BOTH of the following [(1) and (2)]:
            (1) Patient has pouchitis; AND
            (2) Patient has tried an antibiotic, probiotic, corticosteroid enema, or mesalamine enema; AND
            Note: Examples of antibiotics include metronidazole and ciprofloxacin. Examples of corticosteroid enemas include hydrocortisone enema.
      iv. The medication is prescribed by or in consultation with a gastroenterologist; OR
   B) Patient is Currently Receiving Skyrizi Subcutaneous. Approve for 1 year if the patient meets BOTH of the following (i and ii):
      i. Patient has been established on the requested drug for at least 6 months; AND
      Note: A patient who has received < 6 months of therapy or who is restarting therapy with the requested drug is reviewed under criterion A (Initial Therapy).
      ii. Patient meets at least ONE of the following (a or b):
         a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
         Note: Examples of assessment for inflammatory response include fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.
         b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or decreased rectal bleeding.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug.** This medication should not be administered in combination with another biologic or with a

targeted synthetic oral small molecule drug used for an inflammatory condition (see Appendix for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.
Note: This does NOT exclude the use of conventional synthetic disease-modifying antirheumatic drug (e.g., methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine) in combination with this medication.

References

1. Skyrizi® subcutaneous injection or intravenous infusion [prescribing information]. North Chicago, IL: AbbVie; June 2024.
2. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
3. Nast A, Gisondi P, Ormerod AD, et al. European S3-Guidelines on the systemic treatment of psoriasis vulgaris – Update 2015 – Short version – EDF in cooperation with EADV and IPC. *J Eur Acad Dermatol Venereol*. 2015;29(12):2277-2294.
4. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2019;71(1):2-29.
5. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol.* 2018;113(4):481-517.
6. Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. *Gastroenterology*. 2021;160(7):2496-2508.
7. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: management of Crohn's Disease in adults. *Am J Gastroenterol.* 2018;113(4):481-517.
8. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	11/01/2024

The policy effective date is in force until updated or retired.

APPENDIX

	Mechanism of Action	Examples of Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC

Simponi®, Simponi Aria® (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	UC
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq® (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: PsA, PsO, UC
		IV formulation: UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA, AA
Litfulo® (ritlecitinib capsules)	Inhibition of JAK pathways	AA
Leqselvi® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	UC

* Not an all-inclusive list of indications. Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.