Effective Date **2/15/2023**
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Coverage Policy Number **IP0247**

Risankizumab Subcutaneous

Table of Contents

Related Coverage Resources

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. 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.

Overview

This policy supports medical necessity review for the following risankizumab subcutaneous products:

- **Skyrizi® Pen** (risankizumab 150mg/mL single-dose prefilled pen)
- **Skyrizi® Prefilled Syringe** (risankizumab single-dose prefilled syringe 150mg/mL and 75mg/0.83mL)
- **Skyrizi® Prefilled Cartridge with Supplied On-Body Injector** (risankizumab 360mg/2.4mL [150mg/mL] and 180mg/1.2mL [150mg/mL] single-dose prefilled cartridge for use with on-body injector)

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

Medical Necessity Criteria

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

1. **Crohn's Disease [On-Body Injector].** Individual meets **ALL** of the following criteria (A, B, C, D, and E):
   A. Individual is 18 years of age or older

B. According to the prescriber, the individual will receive a three-dose induction regimen with intravenous Skyrizi, in accordance with FDA labeled dosing and frequency for Crohn's disease, prior to initiating therapy with subcutaneous Skyrizi
C. Documentation of **ONE** of the following (i, ii, iii, or iv):
    i. Inadequate response corticosteroids, unless contraindicated or intolerant, OR Skyrizi will be taken concurrently with a corticosteroid
    ii. Inadequate response **ONE** conventional systemic therapy, unless contraindicated or intolerant, OR Skyrizi will be taken concurrently with a conventional systemic therapy

        Examples of conventional systemic therapy: azathioprine, 6-mercaptopurine, methotrexate.

    iii. Individual has already tried a biologic for Crohn's disease

        Refer to Appendix for biologics used in Crohn's disease.

    iv. Individual meets **ONE** of the following conditions (a, b, c, d, e, f, g, h, i or j):
        a. Severe disease needing hospitalization
        b. Involvement of the upper GI tract
        c. Smoker
        d. Less than 40 years of age
        e. Stricturing disease
        f. Perianal disease or other enterocutaneous fistula
        g. Extraintestinal manifestations (ankylosing spondylitis, pyoderma gangrenosum, erythema nodosum)
        h. Previous Crohn's disease-related surgery (for example, ileocolonic resection to reduce the chance of Crohn's disease recurrence)
        i. Bowel obstruction
        j. History of abscess or perforation (after healing)

D. The medication is prescribed by, or in consultation with, a gastroenterologist
E. Individual meets the preferred covered alternatives criteria as indicated in the table below [Individual and Family Plan]

2. **Plaque Psoriasis [Pens or Syringes].** Individual meets **ALL** of the following criteria (A, B, C, D, and E):
    A. Individual is 18 years of age or older
    B. Body Surface Area (BSA) of greater than 5%, OR BSA less than 5% and there is and there is involvement of the scalp, face, the palms and soles (i.e., palmoplantar disease), or genitals
    C. Documentation of **ONE** of the following (i or ii):
        i. Inadequate response to **ONE** of the following, unless contraindicated or intolerant (a, b or c):
            a. Topical therapy (for example, topical corticosteroids, topical vitamin D analogs, Tazorac)
            b. Systemic therapy (for example, methotrexate, cyclosporine, Soriatane)
            c. Phototherapy
        ii. Individual has already tried a biologic or targeted synthetic DMARD (tsDMARD) for Plaque Psoriasis

            Refer to Appendix for biologics and tsDMARDs used in Plaque Psoriasis

    D. The medication is prescribed by, or in consultation with, a dermatologist
    E. Individual meets the preferred covered alternatives criteria as indicated in the table below [Individual and Family Plan]

3. **Psoriatic Arthritis [Pens or Syringes].** Individual meets **ALL** of the following (A, B, C, and D):

A. Individual is 18 years of age or older
B. Documentation of **ONE** of the following (i, ii, or iii):

   i. For Non-axial disease, inadequate response to **ONE** disease-modifying anti-rheumatic drug (DMARD), unless contraindicated or intolerant

   ii. For Axial disease, inadequate response to **ONE** disease-modifying anti-rheumatic drug (DMARD), OR a nonsteroidal anti-inflammatory drug (NSAID), unless contraindicated or intolerant

   iii. Individual has already tried a biologic or targeted synthetic DMARD (tsDMARD)

   Refer to Appendix for biologics and tsDMARDs used in Psoriatic Arthritis.

C. Medication is being prescribed by, or in consultation with a rheumatologist or dermatologist
D. Individual meets the preferred covered alternatives criteria as indicated in the tables below [Individual and Family Plan]

Coverage varies across plans and may requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Employer Group - Standard/Performance, Value/Advantage, Legacy, Cigna Total Savings Covered Alternatives	
Condition	**Criteria**
Crohn's Disease - Adult	**Preferred** [requires prior authorization]
Plaque Psoriasis - Adult	
Psoriatic Arthritis - Adult	

Individual and Family Plan Covered Alternatives	
Condition	**Criteria**
Crohn's Disease - Adult	**Preferred** [requires prior authorization]
Plaque Psoriasis - Adult	
Psoriatic Arthritis - Adult	

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.

Reauthorization Criteria

Risankizumab (Skyrizi) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Examples of beneficial response include:
1. **Crohn's Disease**: decreased pain, fatigue, stool frequency, and/or blood in stool; or improvement via fecal markers (e.g., fecal lactoferrin, fecal calprotectin), serum markers (e.g., C-reactive protein), imaging

studies (magnetic resonance enterography [MRE], computed tomography enterography [CTE]), endoscopic assessment, and/or reduced dose of corticosteroids.

2. **Plaque Psoriasis:** decreased pain, itching, and/or burning; or improvement in estimated body surface area, erythema, induration/thickness, and/or scale of areas affected by psoriasis.

3. **Psoriatic Arthritis:** less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants (for example, C-reactive protein); or improvement per standardized measure of disease activity such as the 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).

Authorization Duration

Initial approval duration: up to 12 months.

Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Concurrent Use with other Biologics or with Targeted Synthetic Disease-Modifying Antirheumatic Drugs (tsDMARDs).** Data are lacking evaluating concomitant use of Skyrizi with another biologic or with a targeted synthetic DMARD for an inflammatory condition (see Appendix for examples). Combination therapy with biologics and targeted synthetic DMARDs has a potential for a higher rate of adverse effects and lacks controlled trial data in support of additive efficacy.[4]

   This does NOT exclude the use of methotrexate (a traditional systemic agent used to treat psoriasis) in combination with Skyrizi.

Background

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.
- **Psoriatic arthritis**, for treatment of adults with active disease.

Skyrizi is also available in an intravenous formulation that is indicated only in Crohn's disease, given as an IV infusion at Weeks 0, 4, and 8 for induction, followed by Skyrizi SC once every 8 weeks thereafter for maintenance. Skyrizi SC is available as a 360 mg/2.4mL and 180mg/1.2mL single-dose prefilled cartridge for use with an on-body injector for use in Crohn's disease. 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). 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) have been published for management of psoriasis with biologics.[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]

References

1. Skyrizi® subcutaneous injection or intravenous infusion [prescribing information]. North Chicago, IL: AbbVie; June 2022.
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.

APPENDIX

Table 1. Approved TNFis for Targeted Indications.

	Rheumatology					Dermatology	Gastroenterology	
	RA	**JIA**	**AS**	**nr-axSpA**	**PsA**	**PsO**	**CD**	**UC**
Tumor Necrosis Factor Inhibitors								
Cimzia	√	--	√	√	√	√	√	--
Enbrel	√	√	√	--	√	√	--	--
Humira	√	√	√	--	√	√	√	√
Infliximab Products	√	--	√	--	√	√	√	√
Simponi Subcutaneous	√	--	√	--	√	--	--	√
Simponi Aria	√	√	√	--	√	--	--	--

TNFis – Tumor necrosis factor inhibitor; RA – Rheumatoid arthritis; JIA – Juvenile idiopathic arthritis; AS – Ankylosing spondylitis; nr-axSpA – Non-radiographic spondyloarthritis; PsA – Psoriatic arthritis; PsO – Plaque psoriasis; CD – Crohn's disease; UC – Ulcerative colitis.

Table 2. Approved IL-17, IL-23, and IL-12/23 Blockers for Targeted Indications.

	Rheumatology			Dermatology	Gastroenterology	
	Ankylosing Spondylitis	**nr-axSpA**	**Psoriatic Arthritis**	**Plaque Psoriasis**	**Crohn's Disease**	**Ulcerative Colitis**
Interleukin-17 Blockers						
Cosentyx	√	√	√	√	--	--
Siliq	--	--	--	√	--	--

Taltz	√	√	√	√	--	--
Interleukin-23 Blockers						
Ilumya	--	--	--	√	√	--
Skyrizi Intravenous	--	--	--	--	√#	--
Skyrizi Subcutaneous	--	--	√	√	√^	--
Tremfya	--	--	√	√	--	--
Interleukin-12/23 Blockers						
Stelara Subcutaneous	--	--	√	√	√^	√^
Stelara Intravenous	--	--	--	--	√#	√#

IL – Interleukin; nr-axSpA – Non-radiographic spondyloarthritis; ^ Maintenance dosing only; # Induction dosing only.

Table 3. Approved Oral tsDMARDs for Targeted Indications.

	Rheumatology				Dermatology	Gastro-enterology
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Ankylosing Spondylitis**	**Psoriatic Arthritis**	**Plaque Psoriasis**	**Ulcerative Colitis**
Janus Kinases Inhibitors						
Olumiant	√	--	--	--	--	--
Rinvoq	√	--	√	√	--	√
Xeljanz tablets	√	√#	√	√	--	√
Xeljanz oral solution	--	√#	--	--	--	--
Xeljanz XR	√	--	√	√	--	√
Phosphodiesterase Type 4 Inhibitor						
Otezla	--	--	--	√	√	--
Sphingosine 1-Phosphate Receptor Modulator						
Zeposia	--	--	--	--	--	√

tsDMARDs – Targeted synthetic disease-modifying antirheumatic drugs; # Indicated in polyarticular JIA.

Table 4. Other Approved Biologics for Targeted Indications.

	Rheumatology		
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Psoriatic Arthritis**
Interleukin-6 Blockers			
Actemra Intravenous	√	√^	--
Actemra Subcutaneous	√	√^	--
Kevzara	√	--	--
Interleukin-1 Blocker			
Kineret	√	--	--
T-Cell Costimulation Modulator			
Orencia Intravenous	√	√#	√
Orencia Subcutaneous	√	√#	√
CD20-Directed Cytolytic Antibody			
Rituximab Intravenous Products	√	--	--

^ Indicated in polyarticular and systemic JIA; # Indicated in polyarticular JIA.