Drug and Biologic Coverage Policy

Effective Date 1/1/2024
Next Review Date… 1/1/2025
Coverage Policy Number IP0239

Ustekinumab Subcutaneous

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Related Coverage Resources

Ustekinumab Intravenous - (IP0240)

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 ustekinumab (Stelara®) subcutaneous.

The coverage of ustekinumab (Stelara) intravenous is addressed in a separate coverage policy, refer to the related coverage policy resources section above (*Ustekinumab Intravenous - IP0240*).

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

Medical Necessity Criteria

Ustekinumab (Stelara) subcutaneous is medically necessary when ONE of the following is met:

1. **Crohn's Disease.** Individual meets **ALL** of the following criteria:
   A. 18 years of age or older
   B. According to the prescriber, will receive a single induction dose with Stelara intravenous prior to initiating therapy with Stelara subcutaneous

C. Documentation of **ONE** of the following:
    i. Failure, contraindication or intolerance to a corticosteroid, OR taken concurrently with a corticosteroid
    ii. Failure, contraindication or intolerance to **ONE** conventional systemic therapy, OR taken concurrently with conventional systemic therapy
    iii. Already tried a biologic for Crohn's Disease
    iv. Meets **ONE** of the following:
        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
        g. Other enterocutaneous fistula
        h. Extraintestinal manifestations (ankylosing spondylitis, pyoderma gangrenosum, erythema nodosum)
        i. Previous Crohn's disease-related surgery (for example, ileocolonic resection (to reduce the chance of Crohn's disease recurrence)
        j. Bowel obstruction
        k. History of abscess or perforation (after healing)
D. Medication is being prescribed by, or in consultation with, a gastroenterologist

2. Plaque Psoriasis. Individual meets **ALL** of the following:
A. 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
B. Documentation of **ONE** of the following:
    i. Failure to **ONE** of the following, unless contraindicated or intolerant to **ALL** of the following:
        a. Topical therapy (for example, topical corticosteroids, topical vitamin D analogs, Tazorac)
        b. Systemic therapy (for example, methotrexate, cyclosporine, Soriatane)
        c. Phototherapy
    ii. Already tried a biologic or targeted synthetic DMARD (tsDMARD) for Plaque Psoriasis
C. Medication is prescribed by, or in consultation with, a dermatologist

3. Psoriatic Arthritis. Individual meets **ALL** of the following:
A. 6 years of age or older
B. Documentation of **ONE** of the following:
    i. For Non-axial disease, failure to **ONE** disease-modifying anti-rheumatic drug (DMARD), unless contraindicated or intolerant
    ii. For Axial disease, failure to **ONE** conventional synthetic disease-modifying anti-rheumatic drug (csDMARD), OR a nonsteroidal anti-inflammatory drug (NSAID), unless contraindicated or intolerant to csDMARDs AND NSAIDs
    iii. Already tried a biologic or targeted synthetic DMARD (tsDMARD) for Psoriatic Arthritis
C. Medication is being prescribed by, or in consultation with, a rheumatologist or dermatologist

4. Ulcerative Colitis. Individual meets **ALL** of the following criteria:
A. 18 years of age or older
B. According to the prescriber, will receive a single induction dose with Stelara intravenous prior to initiating therapy with Stelara subcutaneous
C. Documentation of **ONE** of the following:
    i. Failure to **ONE** conventional systemic therapy (for example, aminosalicylates, corticosteroids, immunosuppressants), unless contraindicated or intolerant
    ii. Already tried a biologic or targeted synthetic DMARD (tsDMARD) for Ulcerative Colitis
    iii. Has pouchitis, AND has tried therapy with an antibiotic (for example, metronidazole, ciprofloxacin), corticosteroid enema or suppository, or mesalamine enema or suppository
D. Medication is being prescribed by, or in consultation with, a gastroenterologist

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

Employer Group Plans	
Condition(s)	
Crohn's Disease	**Preferred** [requires prior authorization]
Plaque Psoriasis - Adult	
Plaque Psoriasis - Pediatric/Adolescent	
Psoriatic Arthritis - Adult	
Psoriatic Arthritis - Pediatric/Adolescent	
Ulcerative Colitis	

Individual and Family Plan	
Condition(s)	
Crohn's Disease	**Preferred** [requires prior authorization]
Plaque Psoriasis - Adult	
Plaque Psoriasis - Pediatric/Adolescent	
Psoriatic Arthritis - Adult	
Psoriatic Arthritis - Pediatric/Adolescent	
Ulcerative Colitis	

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

Continuation of ustekinumab (Stelara) subcutaneous is considered medically necessary for ALL covered diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration is up to 12 months.

Reauthorization approval duration is 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. **Ankylosing Spondylitis.** There are other biologic therapies indicated in ankylosing spondylitis (e.g., Cimzia® [certolizumab pegol subcutaneous injection], etanercept, adalimumab, infliximab, Simponi® subcutaneous [golimumab subcutaneous injection], Cosentyx™ [secukinumab subcutaneous injection]). More data are needed to demonstrate efficacy of Stelara in this condition. There is a published proof-of-concept trial evaluating Stelara in ankylosing spondylitis.[7] TOPAS was a prospective, open-label study evaluating Stelara 90 mg at Week 0, 4, and 16 in patients (n = 20) with ankylosing spondylitis. After Week 16, patients were followed through Week 28. Patients who previously failed to respond to tumor necrosis factor (TNF) blockers were excluded, but patients who discontinued a TNF for reasons other than lack of efficacy were allowed to enroll. The primary endpoint was a 40% improvement in disease activity at Week 24 according to the Assessment of SpondyloArthritis International Society (ASAS) criteria (ASAS40). Efficacy analysis was completed in the intent-to-treat population which included all patients who received at least one dose of Stelara. In all, 65% of patients (95% confidence interval [CI]: 41%, 85%; n = 13/20) achieved an ASAS40 response at Week 24. There was at least a 50% improvement of the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) achieved by 55% of patients (95% CI: 32%, 77%; n = 11/20); improvement in other secondary endpoints were also noted. However, enthesitis (measured by MASES [Maastricht AS Entheses Score] and SPARCC [SPondyloArthritis Research Consortium of Canada] enthesitis indices) and the number of swollen joints were not significantly improved at Week 24. There was a significant reduction of active inflammation on magnetic resonance imaging at Week 24 compared with baseline in sacroiliac joints.

2. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (tsDMARD).** Stelara should not be administered in combination with another biologic agent or with a targeted synthetic DMARD used for an inflammatory condition (see Appendix for examples). Combination therapy is generally not recommended due to a potential for a higher rate of adverse effects with combinations and lack of additive efficacy.

   This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Stelara.

Background

OVERVIEW

Stelara subcutaneous, an interleukin-12/23 blocker, is indicated for the following uses:[1]

- **Crohn's disease**, in patients ≥ 18 years of age with moderate to severe active disease.
- **Plaque psoriasis**, in patients ≥ 6 years of age with moderate to severe disease who are candidates for phototherapy or systemic therapy.
- **Psoriatic arthritis**, in patients ≥ 6 years of age with active disease, given alone or in combination with methotrexate.
- **Ulcerative colitis**, in patients ≥ 18 years of age with moderate to severe active disease.

Guidelines

Guidelines for the treatment of inflammatory conditions recommend use of Stelara subcutaneous.

- **Crohn's Disease:** The American College of Gastroenterology has guidelines for Crohn's disease (2018).[2] Stelara is 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 [TNFis]).
- **Plaque Psoriasis:** Guidelines (2019) from the American Academy of Dermatology and National Psoriasis Foundation recommend Stelara as a monotherapy treatment option or in combination with other therapies for adults with moderate to severe disease.[3]
- **Psoriatic Arthritis:** Guidelines from the American College of Rheumatology (2018) recommend Stelara after other agents (e.g., TNFis) have been tried.[4] Stelara may be used in patients who have active disease despite treatment with other agents, particularly in those with concomitant inflammatory bowel disease.[4]

- **Ulcerative Colitis:** Guidelines from the American Gastroenterological Association (2020) recommend Stelara for moderate to severe ulcerative colitis.[6] Stelara is not addressed in the 2019 American College of Gastroenterology guidelines for ulcerative colitis.[5] These guidelines note that the following agents can be used for induction of remission in moderately to severely active disease: Uceris® (budesonide extended-release tablets); oral or intravenous systemic corticosteroids, Entyvio® (vedolizumab intravenous infusion), Xeljanz® (tofacitinib tablets, extended-release tablets), or TNFis (adalimumab, Simponi® subcutaneous, infliximab).

References

1. Stelara® subcutaneous injection [prescribing information]. Horsham, PA: Janssen Biotech; July 2022.
2. 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.
3. 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.
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. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
6. Feuerstein JD, Isaac s KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158:1450-1461.
7. Poddubnyy D, Hermann KG, Callhoff J, et al. Ustekinumab for the treatment of patients with active ankylosing spondylitis: results of a 28-week, prospective, open-label, proof-of-concept study (TOPAS). *Ann Rheum Dis*. 2014;73(5):817-823.

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	√	√	√	--	√	√	--	--
Adalimumab products (Humira, biosimilars)	√	√	√	--	√	√	√	√
Infliximab Products	√	--	√	--	√	√	√	√
Simponi Subcutaneous	√	--	√	--	√	--	--	√
Simponi Aria	√	√	√	--	√	--	--	--

TNFis – Tumor necrosis factor inhibitors; 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**	**nr-axSpA**	**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	--	--	--	--	--	--	√
Tyrosine Kinase 2 Inhibitor							
Sotyktu	--		--	--	--	√	--

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.