Effective Date **1/1/2024**
Next Review Date… **1/1/2025**
Coverage Policy Number **IP0240**

Ustekinumab Intravenous

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Related Coverage Resources

Ustekinumab Subcutaneous - (IP0239)

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®) intravenous.

The coverage of ustekinumab (Stelara) subcutaneous is addressed in a separate coverage policy, refer to the related coverage policy resources section above (*Ustekinumab Subcutaneous - IP0239*).

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

Medical Necessity Criteria

Ustekinumab (Stelara) intravenous is considered 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. Medication will be used as induction therapy

C. Documentation of **ONE** of the following:
    i. Inadequate response, contraindication or intolerance to a corticosteroid, OR taken concurrently with a corticosteroid
    ii. Inadequate response, contraindication or intolerance to **ONE** other conventional systemic therapy, OR taken concurrently with a 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

Dosing for Crohn's Disease. Individual meets **ONE** of the following weight-based dosing regimens:
A. Less than or equal to 55 kg (121 lbs): up to 260 mg as an intravenous infusion
B. Greater than 55 kg but less than or equal to 85 kg (121 lbs to 187 lbs): up to 390 mg as an intravenous infusion
C. Greater than 85 kg (187 lbs): up to 520 mg as an intravenous infusion

2. Ulcerative Colitis. Individual meets **ALL** of the following criteria:
A. 18 years of age or older
B. Medication will be used as induction therapy
C. Documentation of **ONE** of the following:
    i. Inadequate response to **ONE** conventional systemic therapy, 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

Dosing for Ulcerative Colitis. Meets **ONE** of the following weight-based dosing regimens:
A. Less than or equal to 55 kg (121 lbs): up to 260 mg as an intravenous infusion
B. Greater than 55 kg but less than or equal to 85 kg (121 lbs to 187 lbs): up to 390 mg as an intravenous infusion
C. Greater than 85 kg (187 lbs): up to 520 mg as an intravenous infusion

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	
Crohn's Disease	**Preferred** [requires prior authorization]
Ulcerative Colitis	

Individual and Family Plan	
Condition	
Crohn's Disease	**Preferred** [requires prior authorization]
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

Not applicable for continuation beyond initial approval duration.

Authorization Duration

A single intravenous infusion dose of Stelara (IV) up to a maximum dose of 520 mg will be approved.

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 (AS).** There are other biologic therapies indicated in AS. More data are needed to demonstrate efficacy of Stelara in this condition. There is a published proof-of-concept trial evaluating Stelara in AS (TOPAS – Ustekinumab for the treatment Of Individuals with active Ankylosing Spondylitis).[4] TOPAS was a prospective, open-label study evaluating Stelara 90 mg subcutaneous at Week 0, 4, and 16 in individuals (n = 20) with AS. After Week 16, individuals were followed through Week 28. Individuals who previously failed to respond to tumor necrosis factor inhibitor (TNFi) were excluded, but individuals who discontinued a TNFi 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 individuals who received at least one dose of Stelara. In all, 65% of individuals (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 individuals (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 intravenous should not be administered in combination with another biologic or with a targeted synthetic DMARD 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 agents (e.g., methotrexate, 6-mercaptopurine, azathioprine, and sulfasalazine) in combination with Stelara intravenous.

3. **Children or Adolescents less than 18 Years of Age.** Stelara intravenous is indicated in adult individuals ≥ 18 years of age.[1] Efficacy and optimal dosing needs to be identified for the intravenous formulation.

4. **Plaque Psoriasis.** Stelara for subcutaneous injection is indicated for treatment of plaque psoriasis.[1] Appropriate dosing of Stelara intravenous in plaque psoriasis is unclear.

5. **Psoriatic Arthritis.** Stelara for subcutaneous injection is indicated for treatment of psoriatic arthritis.[1] Appropriate dosing of Stelara intravenous in psoriatic arthritis is unclear.

Coding

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3358	Ustekinumab, for intravenous injection, 1 mg

Background

OVERVIEW
Stelara intravenous, a monoclonal antibody against the p40 subunit of the interleukin (IL)-12 and IL-23 cytokines, is indicated in patients ≥ 18 years of age with the following conditions:[1]

- **Crohn's disease**, in patients with moderate to severe active disease; AND
- **Ulcerative colitis**, in patients with moderate to severe active disease.

Dosing and Administration
In Crohn's disease and ulcerative colitis, a single weight-based dose is administered by intravenous infusion. Following induction therapy with the intravenous product, the recommended maintenance is Stelara subcutaneous injection, given as a 90 mg subcutaneous injection administered 8 weeks after the initial intravenous dose, then once every 8 weeks thereafter. [1]

Initial Intravenous Dosage of Stelara[1]

Body Weight of Patient at the time of dosing	Dose	Number of 130 mg/26 mL (5 mg/mL) Stelara vials
55 kg (121 lbs) or less	260 mg	2
more than 55 kg (121 lbs) to 85 kg (187 lbs)	390 mg	3
more than 85 kg (187 lbs)	520 mg	4

Dosage Forms and Strengths[1]
Subcutaneous Injection

- Injection: 45 mg/0.5 mL or 90 mg/mL solution in a single-dose prefilled syringe
- Injection: 45 mg/0.5 mL solution in a single-dose vial

Intravenous Infusion

- Injection: 130 mg/26 mL (5 mg/mL) solution in a single-dose vial

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

- **Crohn's Disease:** The American College of Gastroenterology (ACG) 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). Guidelines from the American Gastroenterological Association (AGA) [2021] include Stelara

among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission.[5]

- **Ulcerative Colitis:** Stelara is not addressed in the 2019 ACG guidelines for ulcerative colitis.[3] Current guidelines for ulcerative colitis from the AGA (2020) include Stelara among the therapies recommended for moderate to severe disease.[4]

References

1. Stelara [prescribing information]. Horsham, PA: Janssen Biotech; December 2020.
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. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
4. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020 Apr158(5):1450-1461.
5. 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	√	√	√	--	√	√	--	--
Humira	√	√	√	--	√	√	√	√
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.