



## PRIOR AUTHORIZATION POLICY

- POLICY:** Inflammatory Conditions – Stelara Intravenous Prior Authorization Policy
- Stelara® (ustekinumab intravenous infusion – Janssen Biotech)

**REVIEW DATE:** 07/24/2024; selected revision 09/11/2024

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## CIGNA NATIONAL FORMULARY COVERAGE:

### OVERVIEW

Stelara intravenous, a monoclonal antibody against the p40 subunit of the interleukin (IL)-12 and IL-23 cytokines, is indicated for the following conditions:<sup>1</sup>

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

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.

### 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).<sup>2</sup> 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.<sup>5</sup>

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

#### **POLICY STATEMENT**

Prior Authorization is recommended for prescription benefit coverage of Stelara intravenous. Because of the specialized skills required for evaluation and diagnosis of patients treated with Stelara intravenous as well as the monitoring required for adverse events and long-term efficacy, approval requires Stelara intravenous to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 30 days, which is an adequate duration for the patient to receive one dose.

- **Stelara® (ustekinumab intravenous infusion – Janssen Biotech)**

**is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

#### **FDA-Approved Indications**

- 1. Crohn's Disease.** Approve a single dose if the patient meets ALL of the following (A, B, C, and D):
  - A)** Patient is  $\geq$  18 years of age; AND
  - B)** The medication will be used as induction therapy; AND
  - C)** Patient meets ONE of the following (i, ii, iii, or iv):
    - i.** Patient has tried or is currently taking a systemic corticosteroid, or a systemic corticosteroid is contraindicated in this patient; OR
    - ii.** 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.
    - iii.** Patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; OR
    - iv.** Patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence); AND
  - D)** The medication is prescribed by or in consultation with a gastroenterologist.
- 2. Ulcerative Colitis.** Approve a single dose if the patient meets ALL of the following (A, B, C, and D):
  - A)** Patient is  $\geq$  18 years of age; AND
  - B)** The medication will be used as induction therapy; AND
  - C)** Patient meets ONE of the following (i or ii):
    - i.** Patient has tried one systemic therapy; OR  
Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or 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 medication 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.

- ii. Patient meets BOTH of the following (a and b):
  - a) Patient has pouchitis; AND
  - b) 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.

- D) The medication is prescribed by or in consultation with a gastroenterologist.

#### CONDITIONS NOT COVERED

- **Stelara® (ustekinumab intravenous infusion – Janssen Biotech)**

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

- 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 Patients with active Ankylosing Spondylitis).<sup>4</sup> TOPAS was a prospective, open-label study evaluating Stelara 90 mg subcutaneous at Week 0, 4, and 16 in patients (n = 20) with AS. After Week 16, patients were followed through Week 28. Patients who previously failed to respond to tumor necrosis factor inhibitor (TNFi) were excluded, but patients 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 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 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 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 DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine) in combination with this medication.
- 3. Plaque Psoriasis.** Stelara for subcutaneous injection is indicated for treatment of plaque psoriasis.<sup>1</sup> Appropriate dosing of Stelara intravenous in plaque psoriasis is unclear.

**4. Psoriatic Arthritis.** Stelara for subcutaneous injection is indicated for treatment of psoriatic arthritis.<sup>1</sup> Appropriate dosing of Stelara intravenous in psoriatic arthritis is unclear.

**REFERENCES**

1. Stelara® intravenous infusion, subcutaneous injection [prescribing information]. Horsham, PA: Janssen Biotech; March 2023.
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.

**HISTORY**

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/28/2022
Annual Revision	<b>Ulcerative Colitis:</b> A note was added that a trial of a mesalamine product does not count as a systemic agent for ulcerative colitis.	07/24/2024
Selected Revision	<b>Conditions Not Covered</b> : Concurrent use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug was changed to as listed (previously oral small molecule drug was listed as Disease-Modifying Antirheumatic Drug).	09/11/2024

**APPENDIX**

	Mechanism of Action	Examples of Indications*
<b>Biologics</b>		
<b>Adalimumab SC Products</b> (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
<b>Cimzia®</b> (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
<b>Etanercept SC Products</b> (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
<b>Infliximab IV Products</b> (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
<b>Zymfentra®</b> (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
<b>Simponi®, Simponi Aria®</b> (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA

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

<b>Xeljanz® XR</b> (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
<b>Zeposia®</b> (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
<b>Velsipity®</b> (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 – Entesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.

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