



**POLICY:** Inflammatory Conditions – Stelara® (ustekinumab intravenous infusion – Janssen Biotech)

**APPROVAL DATE:** 09/11/2019; selected revision 10/23/2019

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## OVERVIEW

Stelara for intravenous (IV) infusion is a human immunoglobulin G (IgG) 1κ monoclonal antibody against the p40 subunit of the interleukin (IL)-12 and IL-23 cytokines.<sup>1</sup> It is indicated for the treatment of patients ≥ 18 years of age with the following conditions:

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

In Crohn's disease and ulcerative colitis, a single weight-based dose is administered by IV infusion. Following induction therapy with the IV product, the recommended maintenance is Stelara for subcutaneous (SC) injection, given as a 90 mg SC injection administered 8 weeks after the initial IV dose, then once every 8 weeks (Q8W) thereafter.

## Disease Overview

The P40 subunit of the IL-12 and IL-23 cytokines are involved in inflammatory and immune responses. Stelara SC binds to the P40 subunit of used by both the IL-12 and IL-23 cytokines. By binding to this location, Stelara SC disrupts IL-12 and -23 mediated signaling and cytokine cascade. The IL-12 and -23 cytokines have been implicated as important contributors to the chronic inflammation that is observed in inflammatory bowel disease (Crohn's disease and ulcerative colitis). By blocking IL-12 and -23, Stelara may control the inflammatory response in patients with these conditions.

## Guidelines

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 TNFi). Stelara is not addressed in the 2019 ACG guidelines for UC. 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, Xeljanz, or TNFis (adalimumab, Simponi SC, infliximab).<sup>3</sup>

## Safety

Stelara has Warnings concerning risks of serious infection and the risk of malignancy.<sup>1</sup> Prior to initiating therapy with Stelara, patients should be evaluated for active tuberculosis (TB) infection. Patients should also be monitored for signs and symptoms of infection during treatment with Stelara, and if a serious infection develops, it should be stopped until the infection resolves.

## POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Stelara IV. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist).

Because of the of the specialized skills required for evaluation and diagnosis of patients treated with infliximab as well as the monitoring required for adverse events and long-term efficacy, initial approval

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requires infliximab 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.

## RECOMMENDED AUTHORIZATION CRITERIA

### FDA-Approved Indications

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**1. Crohn's Disease.** Approve one dose if the patient must meet ALL of the following (A, B, C, and D):

- A) The patient is greater than or equal to 18 years of age; AND
- B) Stelara IV will be used as induction therapy; AND
- C) The patient meets one of the following conditions (i or ii):
  - i. The patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
  - ii. The patient has tried one other agent for Crohn's disease.  
Note: Examples of conventional systemic therapy for Crohn's disease include azathioprine, 6-mercaptopurine, or methotrexate (MTX). A previous trial of a biologic (e.g., Cimzia [certolizumab pegol SC injection], Entyvio [vedolizumab IV infusion], an adalimumab product, or an infliximab product) also counts as a trial of one other agent for Crohn's disease; AND
- D) Stelara IV is prescribed by or in consultation with a gastroenterologist.  
Note: Patients with fistulizing Crohn's disease or Crohn's disease of the ileal pouch must meet the above criteria for Crohn's disease in adults.

**Dosing.** Approve ONE of the following weight-based doses (A, B, or C):

- A) ≤ 55 kg (121 lbs): Approve up to 260 mg as an intravenous infusion.
- B) > 55 kg but ≤ 85 kg (> 121 lbs but ≤ 187 lbs): Approve up to 390 mg as an intravenous infusion.
- C) > 85 kg (> 187 lbs): Approve up to 520 mg as an intravenous infusion.

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**2. Ulcerative Colitis.** Approve a single dose if the patient meets the following criteria (A, B, C, and D):

- A) The patient is 18 years of age or older; AND
- B) Stelara IV will be used as induction therapy; AND
- C) The patient has had a trial of one systemic agent for ulcerative colitis.  
Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a biologic (e.g., an adalimumab product, an infliximab product, Simponi® [golimumab for SC injection], or Entyvio [vedolizumab injection]) also counts as a trial of one systemic agent for UC; AND
- D) The agent is prescribed by or in consultation with a gastroenterologist.

**Dosing.** Approve ONE of the following weight-based doses (A, B, or C):

- A) ≤ 55 kg (121 lbs): Approve up to 260 mg as an intravenous infusion.
- B) > 55 kg but ≤ 85 kg (> 121 lbs but ≤ 187 lbs): Approve up to 390 mg as an intravenous infusion.
- C) > 85 kg (> 187 lbs): Approve up to 520 mg as an intravenous infusion.

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### Conditions Not Recommended for Approval

Stelara IV has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Ankylosing Spondylitis (AS).** There are other biologic therapies indicated in AS (e.g., Cimzia, Enbrel® [etanercept SC injection], Humira, Remicade, Simponi for SC use, Cosentyx® [secukinumab SC injection]). 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>5</sup> TOPAS was a prospective, open-label study evaluating Stelara 90 mg SC 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 TNF blockers were excluded, but patients who discontinued a TNF blocker 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 (ITT) 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 (MRI) at Week 24 compared with baseline in sacroiliac joints.
- 2. Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (DMARD).** Stelara IV 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. Note: This does NOT exclude the use of conventional agents (e.g., MTX, 6-MP, azathioprine, and sulfasalazine) in combination with Stelara IV.
- 3. Children or Adolescents < 18 Years of Age.** Stelara IV is indicated in adult patients ≥ 18 years of age.<sup>1</sup> Efficacy and optimal dosing needs to be identified for the intravenous formulation.
- 4. Plaque Psoriasis.** Stelara for SC injection is indicated for treatment of plaque psoriasis.<sup>1</sup> Appropriate dosing of Stelara IV in plaque psoriasis is unclear.
- 5. Psoriatic Arthritis.** Stelara for SC injection is indicated for treatment of psoriatic arthritis.<sup>1</sup> Appropriate dosing of Stelara IV in psoriatic arthritis is unclear.
- 6.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### REFERENCES

1. Stelara [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; October 2019.
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. 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	Approval Date
New Policy	--	08/29/2018
Annual revision	<b>Crohn’s Disease:</b> Criteria were added to require that the patient is greater than or equal to 18 years of age, and that Stelara IV is being used for Induction Therapy. Previously, these requirements were part of the indication (i.e., previously, approval condition was listed as Crohn’s Disease in an adult, Induction Therapy). For approvals, clarify that 30 days is adequate duration for the patient to receive a single dose. In the dosing section, clarify that the dose is up to the approved dose administered intravenously.	09/11/2019
Selected revision	<b>Ulcerative Colitis:</b> This condition was added to the policy as an FDA-approved use. Criteria approve for one dose if the patient is greater than or equal to 18 years of age and Stelara IV is being used for Induction Therapy, and if the patient has tried one other agent for UC. Criteria also require that Stelara IV is prescribed by or in consultation with a gastroenterologist.	10/23/2019

**APPENDIX**

Brand (generic name)	Mechanism of Action
<b>Adalimumab SC Products</b> (Humira®, biosimilars)	Inhibition of TNF
<b>Cimzia®</b> (certolizumab pegol SC injection)	Inhibition of TNF
<b>Etanercept SC Products</b> (Enbrel®, biosimilars)	Inhibition of TNF
<b>Infliximab IV Products</b> (Remicade®, biosimilars)	Inhibition of TNF
<b>Simponi®, Simponi® Aria™</b> (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF
<b>Actemra®</b> (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6
<b>Kevzara®</b> (sarilumab SC injection)	Inhibition of IL-6
<b>Orencia®</b> (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator
<b>Rituximab IV Products</b> (Rituxan®, biosimilars)	CD20-directed cytolytic antibody
<b>Kineret®</b> (anakinra SC injection)	Inhibition of IL-1
<b>Stelara®</b> (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23
<b>Siliq™</b> (brodalumab SC injection)	Inhibition of IL-17
<b>Cosentyx™</b> (secukinumab SC injection)	Inhibition of IL-17A
<b>Taltz®</b> (ixekizumab SC injection)	Inhibition of IL-17A
<b>Ilumya™</b> (tildrakizumab-asnm SC injection)	Inhibition of IL-23
<b>Skyrizi™</b> (risankizumab-rzza SC injection)	Inhibition of IL-23
<b>Tremfya™</b> (guselkumab SC injection)	Inhibition of IL-23
<b>Entyvio™</b> (vedolizumab IV infusion)	Integrin receptor antagonist
<b>Otezla®</b> (apremilast tablets)	Inhibition of PDE4
<b>Olumiant®</b> (baricitinib tablets)	Inhibition of the JAK pathways
<b>Xeljanz®, Xeljanz XR</b> (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways

SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase.