EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Stelara® (ustekinumab subcutaneous injection – Janssen Biotech)

TAC APPROVAL DATE: 08/29/2018

OVERVIEW

Stelara SC is a human immunoglobulin G (IgG) 1κ monoclonal antibody against the p40 subunit of the interleukin (IL)-12 and IL-23 cytokines.[1] It is indicated for the treatment of patients with one of the following indications:

1. Moderate to severe plaque psoriasis in patients 12 years of age and older who are candidates for phototherapy or systemic therapy;[1-3]
2. Adults with active psoriatic arthritis (PsA) alone or in combination with methotrexate (MTX); [1,4] and
3. Moderate to severe active Crohn's disease, in adults who have failed or were intolerant to immunomodulators or corticosteroids, but never failed a tumor necrosis factor inhibitor (TNFi), or in patients who failed or were intolerant to at least one TNFi.[1]

A weight-based injection is administered by subcutaneous (SC) injection under the supervision of a physician, although with proper training patients may self-inject.

Disease Overview

The P40 subunit of the IL-12 and IL-23 cytokines are involved in inflammatory and immune responses.[1] 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 are thought to play a role in plaque psoriasis and have been implicated as important contributors to the chronic inflammation that is observed in Crohn's disease.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Stelara SC. Because of the specialized skills required for evaluation and diagnosis of patients treated with Stelara as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Stelara SC to be prescribed by or in consultation with a physician who specializes in the condition being treated. When *ESI Standard Inflammatory Conditions – Stelara SC PA Policy* criteria are met, the dose approved is based on the dosing recommended in the Stelara prescribing information or, in cases when the patient was previously taking Stelara SC, are based on previous patient dosing history. All approvals are provided for the duration listed below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Stelara SC is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Crohn's Disease in an Adult.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets the following criteria (i, ii, and iii):
     - **i.** The patient meets one of the following conditions (a or b):
       - **a)** The patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
       - **b)** The patient has tried one conventional systemic therapy for Crohn's disease (e.g., azathioprine, 6-mercaptopurine, or methotrexate [MTX]).
         NOTE: 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 a biologic (e.g., Cimzia® [certolizumab pegol SC injection], Entyvio® [vedolizumab for IV infusion], an adalimumab product [e.g., Humira®], an infliximab product [e.g., Remicade®, Inflectra, Renflexis], or Stelara IV). These patients who have already received a biologic are not required to "step back" and try another agent); AND
     - **ii.** The patient has received a single induction dose with Stelara IV within 2 months of initiating therapy with Stelara SC; AND
     - **iii.** Stelara SC is prescribed by or in consultation with a gastroenterologist.
   - **B)** Patients Currently Receiving Stelara SC. Approve for 3 years if the patient has had a response to Stelara SC (e.g., decrease in symptoms such as diarrhea, pain, and/or bleeding; and/or improvement in erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], complete blood count [CBC], and/or fecal calprotectin [fCal]) as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Stelara.

   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.

   The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).[10] Stelara is recommended in patients who have moderate-to-severe disease and have failed previous treatments with corticosteroids, thioprines, methotrexate, or tumor necrosis factor inhibitor(s). Stelara should also be used for maintenance of Stelara-induced remission.

2. **Plaque Psoriasis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy: Approve for 3 months if the patient meets ALL of the following criteria (i, ii, and iii):
     - **i.** The patient is 12 years of age or older; AND
     - **ii.** The patient meets ONE of the following conditions (a or b):
       - **a)** The patient has tried at least at least one traditional systemic agent for psoriasis (e.g., methotrexate [MTX], cyclosporine, acitretin tablets, or psoralen plus ultraviolet A light [PUVA]) for at least 3 months, unless intolerant.
         NOTE: An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already has a 3-month trial or previous intolerance to at least one biologic (e.g., an adalimumab product [e.g., Humira®], Cimzia [certolizumab pegol SC injection], an etanercept product [e.g., Enbrel®], for SC injection], an infliximab product [e.g., Remicade®, Inflectra, Renflexis], Cosentyx® [secukinumab for SC injection], Ilumya [tildrakizumab-asmn SC injection], Siliq [brodalumab SC injection], Taltz® [ixekizumab for SC injection], or Tremfya

[guselkumab SC injection]). These patients who have already tried a biologic for psoriasis are not required to "step back" and try a traditional systemic agent for psoriasis); OR

b) The patient has a contraindication to methotrexate (MTX), as determined by the prescribing physician; AND

iii. Stelara is prescribed by or in consultation with a dermatologist.

B) Patient is Currently Receiving Stelara SC: Approve for 3 years if the patient has responded, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Stelara.

Guidelines developed by the National Psoriasis Foundation Medical Board (2012) note that Stelara, Humira, and Enbrel are appropriate first-line biologics for treatment of psoriasis.[4] In the professional opinion of specialist physicians reviewing the data, we have adopted the criteria requirements for previous therapy.

3. Psoriatic Arthritis (PsA). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy: Approve for 3 months if Stelara is prescribed by or in consultation with a rheumatologist or a dermatologist.

B) Patient is Currently Receiving Stelara SC: Approve for 3 years if the patient has responded (e.g., 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]), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Stelara.

The European League Against Rheumatism (EULAR) recommendations for treatment of PsA (2015) recommend consideration of an IL-12/23 blocker (e.g., Stelara) or IL-17 blocker (e.g., Cosentyx® [secukinumab SC injection]) in patients with peripheral disease who have had an inadequate response to one conventional synthetic DMARD and when tumor necrosis factor (TNF) blockers are not appropriate.[6] In patients with enthesitis, dactylitis, or axial disease, the initial DMARD recommended is a biologic. In patients who fail to respond to a biologic, switching to another biologic should be considered, including switching between TNF blockers.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Stelara SC 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, Humira, Remicade, Simponi SC, Cosentyx). 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).[7] TOPAS was a prospective, open-label study evaluating Stelara 90 mg 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 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 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).[8] 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 synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Stelara.

3. 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® injection [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; June 2018.
2. Leonardi C, Kimball AB, Papp KA, et al, for the PHOENIX 1 study investigators. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody in patients with psoriasis: 76-weeks results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). *Lancet.* 2008;371:1665-1674.
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- Ruiz Villaverde R, Sánchez Cano D. Successful treatment of type 1 pityriasis rubra pilaris with ustekinumab therapy. *Eur J Dermatol*. 2010;20(5):630-631.
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- Coates LC, Kavanaugh A, Mease PJ, et al. Group for research and assessment of psoriasis and psoriatic arthritis: treatment recommendations for psoriatic arthritis 2015. *Arthritis Rheumatol*. 2016;68(5):1060-1071.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Selected revision	For PsA, add Cosentyx as an example of a medication that may have been tried prior to approval of Stelara. Change duration of previous biologic trial to be 3 months, unless not tolerated (previously was 2 months, unless not tolerated).	02/03/2016
Selected revision	For psoriasis, the criterion that allows an exception for patients with a contraindication to one traditional oral therapy is being adjusted to specify a contraindication to MTX. In addition, the psoriasis criteria concerning previous therapy are being reworded for clarification.	04/06/2016
Annual revision	Remove Crohn's disease and multiple sclerosis from the Conditions Not Recommended for Coverage.	07/27/2016
Selected revision	Add criteria for CD, to approve if the patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated, or if the patient has tried one other agent for CD. The 90-mg dose is approved, if prescribed by or in consultation with a gastroenterologist. Initial approval is for 3 months and continuing therapy with Stelara IV or SC is for 3 years, if there has been a response, as determined by the prescriber.	10/05/2016
Selected revision	Revise CD criteria so that initial approval is for 3 months if induction dose was with Stelara IV (previously approved for 3 years). Examples of response criteria were added for patients currently receiving Stelara SC.	11/30/2016
Selected revision	Remove requirement that a biologic is tried prior to approval of Stelara SC for PsA. Change initial approval for PsA to 3 months (previously was 4 months).	12/14/2016
Selected revision	Clarify criteria to note that patients with CD are directed to a conventional systemic therapy, but patients who have already tried a biologic are not required to "step back". Also clarify that induction with Stelara IV for CD must have been administered within 2 months of initiating therapy with Stelara SC.	04/12/2017
Annual revision	No changes to the criteria.	08/02/2017
Selected revision	For plaque psoriasis, remove "in an adult" from the criteria. Add criteria to approve the single-dose vial of Stelara SC for patients 12 to 17 years of age with plaque psoriasis who weigh < 60 kg and notation that patients ≥ 60 kg and ≤ 100 kg are authorized the 45-mg dose and patients > 100 kg are authorized the 90-mg dose. Revise Conditions not Recommended for Coverage to not cover for patients < 12 years of age (previously was < 18 years of age). In addition, update the list of biologics a patient could have tried prior to Stelara SC to include Siliq and Tremfya. Throughout the policy, update reference to Enbrel and Humira to an etanercept and adalimumab product, respectively with the name of the innovator product as examples of these products.	10/18/2017
Annual revision	**Plaque Psoriasis:** Add Ilumya and Cimzia as biologics that may have been tried prior to Stelara SC. **Conditions Not Recommended for Approval:** Remove exclusion for patients < 12 years of age (addressed in criteria). **Other:** Throughout the policy, remove criteria related to the dose (45 mg vs. 90 mg dose) approved in PA criteria (DQM now in place).	08/29/2018

* For a further summary of criteria changes, refer to respective Therapeutic Assessment Committee (TAC) minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee; PsA – Psoriatic arthritis; DEU – Drug Evaluation Unit; FDA – Food and Drug Administration; DMARD(s) – Disease-modifying antirheumatic drug(s); MTX – Methotrexate; CD – Crohn's disease.

APPENDIX

Brand (generic name)	Mechanism of Action
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF
Enbrel® (etanercept for SC injection)	Inhibition of TNF
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF
Humira® (adalimumab for SC injection)	Inhibition of TNF
Amjevita® (adalimumab-atto for SC injection)	Inhibition of TNF
Cyltezo® (adalimumab-adbm for SC injection)	Inhibition of TNF
Simponi® (golimumab for SC injection)	Inhibition of TNF
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF
Remicade® (infliximab for IV infusion)	Inhibition of TNF
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator
Orencia® (abatacept for SC injection)	T-cell costimulation modulator
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23
Siliq™ (brodalumab SC injection)	Inhibition of IL-17
Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A
Ilumya™ (tildrakizumab-asmn for SC injection)	Inhibition of IL-23
Tremfya™ (guselkumab for SC injection)	Inhibition of IL-23
Otezla® (apremilast tablets)	Inhibition of PDE4
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathway
Xeljanz®, Xeljanz XR (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.