PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Stelara Subcutaneous Prior Authorization Policy
- Stelara® (ustekinumab subcutaneous injection – Janssen Biotech)

REVIEW DATE: 09/01/2021; selected revision 09/22/2021

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 ≥ 18 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.

A weight-based dose is administered by subcutaneous injection under the supervision of a physician or by the patient or a caregiver. For each condition, the pivotal trials for Stelara subcutaneous assessed a response to therapy on or before Month 3.

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).
- **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., tumor necrosis factor inhibitors) 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:** 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 (vedolizuamb intravenous infusion), Xeljanz (tofacitinib tablets, extended-release tablets), or tumor necrosis factor inhibitors (adalimumab, Simponi subcutaneous, infliximab). Guidelines from the American Gastroenterological Association (2020) recommend Stelara for moderate to severe ulcerative colitis.[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Stelara subcutaneous. Because of the specialized skills required for evaluation and diagnosis of patients treated with Stelara subcutaneous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Stelara subcutaenous to be prescribed by or in consultation with a physician who specializes in the condition being

treated. 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 subcutaneous is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Crohn's Disease.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   Note: A patient with fistulizing Crohn's disease or Crohn's disease of the ileal pouch must meet the above criteria for Crohn's disease.
   - **A)** Initial Therapy. Approve for 3 months if the patient meets the following criteria (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets one of the following conditions (a, b, c, or d):
       - **a)** Patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
       - **b)** Patient has tried one 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. Refer to Appendix for examples of biologics used for Crohn's disease. A patient who has already received a biologic is not required to "step back" and try another agent.
       - **c)** Patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; OR
       - **d)** Patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence); AND
     - **iii.** According to the prescriber, the patient will receive a single induction dose with Stelara intravenous within 2 months of initiating therapy with Stelara subcutaneous; AND
     - **iv.** The medication is prescribed by or in consultation with a gastroenterologist.
   - **B)** Patient is Currently Receiving Stelara Subcutaneous. Approve for 3 years if the patient has had a response to Stelara subcutaneous, as determined by the prescriber.
     Note: Examples of a response to therapy include a 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). The patient may not have a full response, but there should have been a recent or past response to Stelara.

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.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient meets ONE of the following conditions (a or b):
       - **a)** Patient has tried at least one traditional systemic agent for psoriasis for at least 3 months, unless intolerant; OR
         Note: Examples of traditional systemic agents used for psoriasis include methotrexate, cyclosporine, acitretin, or psoralen plus ultraviolet A light (PUVA). 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.

Refer to Appendix for examples of biologics used for plaque psoriasis. A patient who has already tried a biologic for psoriasis is not required to "step back" and try a traditional systemic agent for psoriasis.

b) Patient has a contraindication to methotrexate as determined by the prescriber; AND

iii. The medication is prescribed by or in consultation with a dermatologist.

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

3. **Psoriatic Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 3 months if prescribed by or in consultation with a rheumatologist or a dermatologist.
   B) Patient is Currently Receiving Stelara Subcutaneous. Approve for 3 years if the patient has responded, as determined by the prescriber.
   Note: Examples of a response to therapy include 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). The patient may not have a full response, but there should have been a recent or past response to Stelara.

4. **Ulcerative Colitis.** 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 (i, ii, iii, and iv):
   i. Patient is ≥ 18 years of age; AND
   ii. Patient has had a trial of one systemic agent for ulcerative colitis; AND
   Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone, methylprednisolone. A trial of a biologic also counts as a trial of one systemic agent for ulcerative colitis. Refer to Appendix for examples of biologics used for ulcerative colitis.
   iii. According to the prescriber, the patient will receive a single induction dose with Stelara intravenous within 2 months of initiating therapy with Stelara subcutaneous; AND
   iv. The medication is prescribed by or in consultation with a gastroenterologist.
   B) Patient is Currently Receiving Stelara Subcutaneous. Approve for 3 years if the patient has had a response to therapy, as determined by the prescriber.
   Note: Examples of a response to therapy include decreased stool frequency or rectal bleeding.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Stelara subcutaneous is not recommended in the following situations:

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 (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). 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., methotrexate 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; 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. 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

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, HS, PsO, PsA, RA, UC, UV
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA

Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsA, PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	RA
Xeljanz® (tofacitinib tablets, oral solution)	Inhibition of JAK pathways	Tablets: RA, PJIA, PsA, UC
		Oral solution: JIA
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indications (e.g., oncology indications and less common inflammatory conditions are not listed). 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; HS – Hidradenitis suppurativa; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; UV – Uveitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, IL – Interleukin; ^ Off-label use of Kineret in JIA supported in guidelines; DMARDs – Disease-modifying antirheumatic drugs; PDE4 – Phosphodiesterase 4; JAK – Janus kinase.