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UTILIZATION REVIEW MANAGEMENT POLICY

POLICY: Inflammatory Conditions – Stelara Intravenous Utilization Management Medical Policy
- Stelara® (ustekinumab intravenous infusion – Janssen Biotech)

REVIEW DATE: 06/28/2023

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.

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).[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]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Stelara intravenous. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. 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 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Stelara intravenous is recommended in those who meet one of the following:
FDA-Approved Indications

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1. Crohn's Disease. Approve a single dose if the patient meets the following (A, B, C, and D):
A) Patient is ≥ 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.

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 (A, B, C, and D):
A) Patient is ≥ 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 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.

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.

Conditions Not Recommended for Approval

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

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).[4] 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 Disease-Modifying Antirheumatic Drug (DMARD).** 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. Note: This does NOT exclude the use of conventional agents (e.g., methotrexate, 6-mercaptopurine, azathioprine, and sulfasalazine) in combination with Stelara intravenous.

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

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

5. 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; 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
Early Annual Revision	**Ulcerative Colitis:** An exception was added for a patient who has pouchitis and has tried a listed therapy (i.e., an antibiotic, probiotic, corticosteroid enema, or mesalamine enema). A patient who meets this exception is not required to try another therapy prior to Stelara. **Conditions Not Recommended for Coverage:** Children or Adolescents < 18 Years of Age was removed from this section of the policy (not needed since age is addressed for each Condition Recommended for Approval).	06/22/2022
Annual Revision	No criteria changes.	06/28/2023

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
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
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, ERA, 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, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO
		IV formulation: CD
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Sotyktu™ (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
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 rare 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; 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 – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; TYK2 – Tyrosine kinase 2.