

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Ustekinumab Intravenous Products Prior Authorization Policy

- Stelara[®] (ustekinumab intravenous infusion – Janssen Biotech)
- Wezlana[™] (ustekinumab-aaub intravenous infusion – Amgen)

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OVERVIEW

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

- **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 ustekinumab 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 ustekinumab.

- **Crohn's Disease:** The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).² Ustekinumab 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 ustekinumab among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission.⁵
- **Ulcerative Colitis:** Ustekinumab is not addressed in the 2019 ACG guidelines for ulcerative colitis.³ Current guidelines for ulcerative colitis from the AGA (2020) include ustekinumab among the therapies recommended for moderate to severe disease.⁴

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of ustekinumab intravenous. Because of the specialized skills required for evaluation and diagnosis of patients treated with ustekinumab intravenous as well as the monitoring required for adverse events and long-term efficacy, approval requires ustekinumab 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 ustekinumab intravenous is recommended in those who meet one of the following:

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 ≥ 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 ≥ 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 RECOMMENDED FOR APPROVAL

Coverage of ustekinumab 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 ustekinumab in this condition. There is a published proof-of-concept trial evaluating ustekinumab in AS (TOPAS – UsTekinumab for the treatment Of Patients with active Ankylosing Spondylitis).⁴ TOPAS was a prospective, open-label study evaluating ustekinumab 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. The primary endpoint was a 40% improvement in disease activity at Week 24 according to the Assessment of SpondyloArthritis International Society (ASAS) criteria (ASAS40) in the intent-

to-treat population which included all patients who received at least one dose of ustekinumab. 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). 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 generally 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.** Ustekinumab for subcutaneous injection is indicated for treatment of plaque psoriasis.¹ Appropriate dosing of ustekinumab intravenous in plaque psoriasis is unclear.
4. **Psoriatic Arthritis.** Ustekinumab for subcutaneous injection is indicated for treatment of psoriatic arthritis.¹ Appropriate dosing of ustekinumab 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® 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 Apr;158(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.

APPENDIX

* 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 – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.