Medical Drug Clinical Criteria

Subject:	Stelara (ustekinumab)		
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Overview

This document addresses the use of Stelara (ustekinumab), a monoclonal antibody which binds to the p40 protein subunit used by both the interleukin-12 and interleukin-23 (IL-12/23) cytokines disrupting their interaction with receptors and thereby inhibiting the release of proinflammatory cytokines and chemokines. Stelara (ustekinumab) is approved for the treatment of plaque psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis.

Plaque Psoriasis (otherwise known as psoriasis vulgaris): The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) published joint guidelines on the management and treatment of psoriasis with biologics. The guidelines do not include a treatment algorithm or compare biologics to each other or conventional therapy. The guideline notes that patients with mild-moderate disease may be adequately controlled with topical therapy and/or phototherapy while moderate to severe disease may necessitate treatment with a biologic. Biologics approved for psoriasis were studied in a population with 10% or greater BSA involvement. Moderate to severe disease is defined as involvement in > 3% of body surface area (BSA) or involvement in sensitive areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia). Tumor necrosis factor inhibitor (TNFi) biologics, ustekinumab, IL17 inhibitors, and IL23 inhibitors are all recommended as monotherapy treatment options for adult patients with moderate to severe plaque psoriasis. Combination use of TNFi biologics (etanercept, infliximab, adalimumab) and ustekinumab with apremilast is poorly studied and the AAD has given this practice a grade C recommendation based on limited-quality evidence.

Psoriatic Arthritis: The American College of Rheumatology (ACR) guidelines recommend that initial treatment of patients with active severe PsA or concomitant psoriasis should include a TNFi biologic over an oral small molecule (OSM; including methotrexate, sulfasalazine, cyclosporine, leflunomide, and apremilast). For initial therapy, OSMs are preferred over IL-17 and ustekinumab; and may be considered over TNFi biologics in mild to moderate disease without comorbid conditions or in those who prefer oral therapy. Recommendations involving biologics over OSMs as first line therapy are conditional and based on low quality evidence. Evidence cited includes indirect comparisons of placebo-controlled trials, studies with open-label design, and extrapolation from studies in plaque psoriasis. Furthermore, most pivotal trials for TNFi biologics included a study population that were DMARD experienced. Overall, there is a lack of definitive evidence for the safety and efficacy of biologic drugs over conventional therapy for the initial treatment of most patients with psoriatic arthritis. The ACR guidelines also include recommendations for patients whose disease remains active despite treatment with an OSM. Here, TNFi biologics are recommended over other therapies including IL-17 inhibitors, ustekinumab, tofacitinib, and abatacept. When TNFi biologics are not used, IL-17 inhibitors are preferred over ustekinumab; both of which are preferred over tofacitinib and abatacept. For disease that remains active despite TNFi monotherapy, switching to a different TNFi is recommended over other therapies.

Crohn's Disease: According to the American Gastrointestinal Association clinical practice guidelines, evidence supports the use of methotrexate, corticosteroids, TNFi +/- immunomodulator, ustekinumab, or vedolizumab for induction of remission. Among the biologics, infliximab, adalimumab, ustekinumab, or vedolizumab are recommended or suggested over certolizumab for induction of remission. Evidence supports biologic agents, thiopurines, and methotrexate for maintenance of remission. Ustekinumab and vedolizumab are options for individuals with primary nonresponse to initial treatment with TNFi. Adalimumab, ustekinumab, or vedolizumab may be used in cases where an individual previously responded to infliximab and then lost response (secondary nonresponse).

Ulcerative Colitis: The American Gastroenterological Association (AGA) guidelines define moderate to severe UC as those who are dependent on or refractory to corticosteroids, have severe endoscopic disease activity, or are at high risk of colectomy. AGA strongly recommends biologics (TNFi, vedolizumab, or ustekinumab) or tofacitinib over no treatment in induction and maintenance of remission (moderate quality of evidence). For biologic-naïve individuals, Infliximab or vedolizumab are conditionally recommended over adalimumab for induction of remission (moderate quality evidence).

Immune-checkpoint Inhibitor Therapy-Related Toxicity: The National Comprehensive Cancer Network (NCCN) guidelines on Management of Immunotherapy-Related Toxicities provide a 2A recommendation for the use of ustekinumab in mild persistent diarrhea or colitis for positive lactoferrin/calprotectin and for moderate or severe diarrhea or colitis that is refractory to infliximab and/or vedolizumab. There is no high-quality data provided to support this use.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Stelara (ustekinumab)

Initial requests for Stelara (ustekinumab) may be approved for the following:

I. Crohn's disease (CD) when the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe CD; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as systemic corticosteroids or immunosuppressants [such as thiopurines or methotrexate]);

OR

II. Psoriatic arthritis (PsA) when the following criteria are met:
   A. Individual is 6 years of age or older with moderate to severe PsA; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [nonbiologic DMARDs (such as methotrexate, sulfasalazine, cyclosporine or leflunomide)];

OR

III. Plaque psoriasis (Ps) when the following criteria are met:
   A. Individual is 6 years of age or older with chronic moderate to severe (that is, extensive or disabling) plaque Ps with either of the following (AAD 2019):
      1. Plaque Ps involving greater than three percent (3%) body surface area (BSA); **OR**
      2. Plaque Ps involving less than or equal to three percent (3%) BSA involving sensitive areas or areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia); **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to phototherapy or other systemic therapy (such as acitretin, cyclosporine, or methotrexate);

OR

IV. Ulcerative colitis (UC) when the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe UC; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as 5-Aminosalicylic acid products, systemic corticosteroids, or immunosuppressants [such as thiopurines]).

Continuation requests for Stelara (ustekinumab) may be approved if the following criterion is met:

I. There is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Requests for Stelara (ustekinumab) may not be approved for the following:

I. In combination with phototherapy; **OR**
II. In combination with oral or topical JAK inhibitors, apremilast, ozanimod, deucravacitinib, or any of the following biologic immunomodulators: Other TNF antagonists, IL-23 inhibitors, IL-17 inhibitors, IL-6 inhibitors, IL-1 inhibitors, vedolizumab, abatacept, rituximab, or natalizumab; **OR**
III. History of posterior reversible encephalopathy syndrome; **OR**
IV. Tuberculosis, other active serious infections, or a history of recurrent infections; **OR**
V. If initiating therapy, individual has not had a tuberculin skin test (TST) or a Centers for Disease Control (CDC-) and Prevention -recommended equivalent to evaluate for latent tuberculosis (unless switching therapy from another targeted immune modulator and no new risk factors); **OR**
VI. When the above criteria are not met and for all other indications.

Quantity Limits

Stelara (ustekinumab) Quantity Limits

Drug	Limit
Stelara 130 mg/26 mL (5 mg/mL) vial	Body weight 55 kg or less: 2 vials (8 week supply, one time fill) Body weight more than 55kg to 85 kg: 3 vials (8 week supply, one time fill) Body weight more than 85 kg [max limit]: 4 vials (8 week supply, one time fill)
Stelara 45 mg/0.5 mL vial*^	1 vial per 84 days (12 weeks)

Stelara 45 mg/0.5 mL single-use prefilled syringe*†^	1 syringe per 84 days (12 weeks)
Stelara 90 mg/1 mL single-use prefilled syringe#^	1 syringe per 84 days (12 weeks)

Override Criteria

*Initiation of therapy for Plaque Psoriasis (Ps) or Psoriatic Arthritis (PsA) in individuals less than or equal to 100 kg (220 lbs.): May approve 1 (one) additional syringe or vial (45 mg/0.5 mL) in the first 84 days (12 weeks) of treatment.

†Initiation of therapy for PsA in individuals greater than 100 kg (220 lbs.): May approve 1 (one) additional syringe (45 mg/0.5 mL) in the first 84 days (12 weeks) of treatment.

#Initiation of therapy for Ps or concomitant PsA and moderate to severe Ps in individuals greater than 100 kg (220 lbs.): May approve 1 (one) additional syringe (90 mg/1 mL) in the first 84 days (12 weeks) of treatment.

^Maintenance therapy for adult Crohn's Disease (CD) and Ulcerative Colitis (UC): May approve 1 (one) 90 mg syringe or 2 (two) 45 mg vials/syringes every 8 weeks (56 days).

^For CD or UC, may also approve increased dosing, up to 1 (one) 90 mg syringe or 2 (two) 45 mg vials/syringes every 4 weeks if the following criteria are met:

I. Individual has been treated with standard maintenance dosing (i.e. every 8 weeks) for *at least* 2 doses or 16 weeks; **AND**
II. The increased dosing is being prescribed by or in consultation with a gastroenterologist; **AND**
III. Individual initially achieved an adequate response to standard maintenance dosing but has subsequently lost response, as determined by the prescriber; **OR**
IV. Individual partially responded but had an inadequate response to standard maintenance dosing as determined by the prescriber; **AND**
V. Symptoms, if present, are not due to active infections or any other gastrointestinal disorder other than the primary disease; **AND**
VI. Requested dosing does not exceed up to 1 (one) 90 mg syringe or 2 (two) 45 mg vials/syringes every 4 weeks.

Initial approval duration for increased dosing for CD or UC: 16 weeks

^Requests for continued escalated dosing for CD and UC may be approved if the following criteria are met:

I. Requested dosing does not exceed up to 1 (one) 90 mg syringe or 2 (two) 45 mg vials/syringes every 4 weeks; **AND**
II. Individual has subsequently regained response or achieved adequate response following increased dosing, as shown by improvement in signs and symptoms of the disease (including but not limited to reduction in stool frequency/bloody stools, improvement abdominal pain, or endoscopic response); **AND**
III. Individual is not experiencing unacceptable adverse effects from increased dosing; **AND**
IV. Individual will be assessed regularly for dose de-escalation.

Continued approval duration for increased dosing CD or UC: 6 months

^For CD or UC, Increased dosing may not be approved for the following:

I. Individual has had no response to Stelara at standard maintenance dosing (i.e. every 8 weeks); **OR**
II. Individual is requesting dose escalation in absence of signs and symptoms of the disease (for example, requesting based on results of therapeutic drug level or anti-drug antibody testing alone).

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3357	Ustekinumab, for subcutaneous injection, 1 mg [Stelara subcutaneous]
J3358	Ustekinumab, for intravenous injection, 1 mg [Stelara IV]

ICD-10 Diagnosis

K50.00-K50.919	Crohn's disease [regional enteritis]
K51.00-K51.919	Ulcerative colitis
L40.0	Psoriasis vulgaris

L40.1	Generalized pustular psoriasis
L40.2	Acrodermatitis continua
L40.3	Pustulosis palmaris et plantaris
L40.4	Guttate psoriasis
L40.50-L40.59	Arthropathic psoriasis
L40.8	Other psoriasis
L40.9	Psoriasis, unspecified

Document History

Revised: 08/18/2023
Document History:

- 08/18/2023 – Select Review: Clarify may not approve section. Coding Reviewed: No changes.
- 03/08/2023 – Update to quantity limit table/override.
- 11/18/2022 – Annual Review: Update combination exclusion use to include additional agents and specify biologic immunomodulators; include examples of conventional therapy per guidelines; add quantity limit override criteria for increased dosing; wording and formatting updates. Coding Reviewed: No changes.
- 08/19/2022 – Select Review: Update age for psoriatic arthritis based on labeling update; update quantity limit for clarity. Coding Reviewed: No changes.
- 11/19/2021 – Annual Review: Remove prior therapy with biologics to align with other agents; update exclusion list for combination use; update loading dose quantity limit to include weight based limits; clarify tuberculosis testing language; wording and formatting changes for clarity. Coding Reviewed: No changes.
- 11/20/2020 – Annual Review: Add continuation of use section; remove 5-ASA products as examples of conventional therapy for Crohn's disease; add additional examples of combination use for clarity; update tuberculosis testing language. Coding Reviewed: No changes.
- 09/14/2020 – Select Review: Update criteria for expanded psoriasis age indication per label. Coding Reviewed: No changes.
- 11/15/2019 – Annual Review: Add treatment of ulcerative colitis to prior authorization and quantity limit override criteria per FDA label, update definition of moderate psoriasis using BSA based on guidelines; update combination therapy criteria for consistency with other agents; wording and formatting changes. Coding reviewed: Add K51.00-K51.919 for UC.
- 09/23/2019 - Administrative update to add drug specific quantity limit.
- 11/16/2018 – Annual Review: Initial P&T review of Stelara Clinical Guideline. Update clinical criteria to delete "active" disease wording. Update criteria to delete requirement agent is being used "to reduce signs and symptoms, maintain clinical response" etc. Add examples of conventional therapy to approval criteria for clarity. Wording and formatting changes to criteria for consistency. HCPCS and ICD-10 Coding Review: No changes.

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
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10. Centers for Disease Control and Prevention (CDC). Tuberculosis (TB). Available at: https://www.cdc.gov/tb/topic/basics/risk.htm. Last updated: March 18, 2016. Accessed September 29, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.