Clinical Policy: Ustekinumab (Stelara)

Reference Number: IL.ERX.SPA.01
Effective Date: 06.01.21
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Line of Business: Illinois Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Ustekinumab (Stelara®) is a human interleukin-12 (IL-12) and -23 (IL-23) antagonist.

FDA Approved Indication(s)
Stelara is indicated for the treatment of:
- Patients 6 years or older with moderate-to-severe plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy
- Adult patients with active psoriatic arthritis (PsA), alone or in combination with methotrexate
- Adult patients with moderately to severely active Crohn's disease (CD)
- Adult patients with moderately to severely active ulcerative colitis (UC)

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Stelara is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Crohn's Disease (must meet all)**:**
1. Diagnosis of CD;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], MTX) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
   b. Medical justification supports inability to use immunomodulators (*see Appendix E*);
5. Failure of a ≥ 3 consecutive month trial of Cimzia® AND Humira®, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for adalimumab and certolizumab*
6. Dose does not exceed:
   a. Initial dose (IV):
      i. Weight < 55 kg: 260 mg once;
      ii. Weight 55 kg to 85 kg: 390 mg once;
      iii. Weight > 85 kg: 520 mg once;
   b. Maintenance dose (SC): 90 mg 8 weeks after the initial IV dose, followed by maintenance dose of 90 mg every 8 weeks.

Approval duration: 6 months

B. Plaque Psoriasis (must meet all)**:**
1. Diagnosis of moderate-to-severe PsO as evidenced by involvement of one of the following (a or b):
   a. ≥ 3% of total body surface area;

b. Hands, feet, scalp, face, or genital area;
2. Request is for SC formulation;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Age ≥ 6 years;
5. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of cyclosporine at up to maximally indicated doses unless clinically significant adverse effects are experienced or both are contraindicated;
6. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel®, Humira, Cimzia;
   **Prior authorization may be required for Enbrel, Humira, and Cimzia*
7. Dose does not exceed one of the following (*see Appendix G for dose rounding guidelines*) (a or b):
   a. Adult: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (i or ii);
      i. Weight ≤ 100 kg: 45 mg per dose;
      ii. Weight > 100 kg: 90 mg per dose;
   b. Pediatrics: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (i, ii, or iii);
      i. Weight < 60 kg: 0.75 mg/kg per dose;
      ii. Weight 60 kg to 100 kg: 45 mg per dose;
      iii. Weight > 100 kg: 90 mg per dose.

Approval duration: 6 months

C. Psoriatic Arthritis (must meet all)**:**
1. Diagnosis of PsA;
2. Request is for SC formulation;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Age ≥ 18 years;
5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel, Humira, Cimzia, Xeljanz®/Xeljanz® XR;
   **Prior authorization may be required for Enbrel, Humira, Cimzia, and Xeljanz/Xeljanz XR*
6. Dose does not exceed one of the following (a or b):
   a. 45 mg initially and 4 weeks later, followed by maintenance dose of 45 mg every 12 weeks;
   b. Co-existent PsO and weight > 100 kg: 90 mg initially and 4 weeks later, followed by maintenance dose of 90 mg every 12 weeks.

Approval duration: 6 months

D. Ulcerative Colitis (must meet all)**:**
1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Documentation of Mayo Score ≥ 6 (*see Appendix F*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
6. If age ≥ 18 years: Failure of a ≥ 3 consecutive month trial of Humira and Xeljanz/Xeljanz XR, unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for Humira and Xeljanz/Xeljanz XR*
7. Dose does not exceed:
   a. Initial dose (IV):
      i. Weight ≤ 55 kg: 260 mg once;

ii. Weight > 55 kg to 85 kg: 390 mg once;
iii. Weight > 85 kg: 520 mg once;

b. Maintenance dose (SC): 90 mg 8 weeks after the initial IV dose, followed by maintenance dose of 90 mg every 8 weeks.

Approval duration: 6 months

E. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Request is for SC formulation;
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. PsO alone (*see Appendix G for dose rounding guidelines*) (i or ii):
      i. Adults (a or b):
         a) Weight ≤ 100 kg: 45 mg every 12 weeks;
         b) Weight > 100 kg: 90 mg every 12 weeks;
      ii. Pediatrics (a, b, or c):
         a) Weight < 60 kg: 0.75 mg/kg every 12 weeks;
         b) Weight 60 kg to 100 kg: 45 mg every 12 weeks;
         c) Weight > 100 kg: 90 mg every 12 weeks;
   b. PsA (i or ii):
      i. 45 mg every 12 weeks;
      ii. Co-existent PsO and weight > 100 kg: 90 mg every 12 weeks;
   c. CD, UC: 90 mg every 8 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia®, Enbrel®, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz®/Xeljanz® XR, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, and Rituxan Hycela®], selective co-stimulation modulators [Orencia®], or integrin receptor antagonists [Entyvio®] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6-MP: 6-mercaptopurine
CD: Crohn's disease

FDA: Food and Drug Administration
GI: gastrointestinal
IL-12: interleukin-12
IL-23: interleukin-23
MTX: methotrexate
PsO: plaque psoriasis
PsA: psoriatic arthritis
TNF: tumor necrosis factor
UC: ulcerative colitis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan®, Imuran)	**CD** 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
corticosteroids	**CD*** prednisone 40 mg PO QD for 2 weeks or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC®) 6 – 9 mg PO QD **UC** budesonide (Uceris®) 9 mg PO QD	Various
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
6-mercaptopurine (Purixan®)	**CD** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate (Rheumatrex®)	**CD*** 15 – 25 mg/week IM or SC **PsO** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day
Enbrel® (etanercept)	**PsA** 25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
Humira® (adalimumab)	**CD, UC** <u>Initial dose:</u> 160 mg SC on Day 1, then 80 mg SC on Day 15 <u>Maintenance dose:</u> 40 mg SC every other week starting on Day 29 **PsA** 40 mg SC every other week **PsO** <u>Initial dose:</u> 80 mg SC <u>Maintenance dose:</u> 40 mg SC every other week starting one week after initial dose	40 mg every other week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Xeljanz® (tofacitinib)	**PsA, UC** 5 mg PO BID	10 mg/day
Xeljanz XR® (tofacitinib extended-release)	**PsA, UC** 11 mg PO QD	11 mg/day
Cimzia® (certolizumab)	**CD** Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 400 mg SC every 4 weeks **PsA** Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 200 mg SC every other week (or 400 mg SC every 4 weeks) **PsO** 400 mg SC every other week. For some patients (with body weight ≤ 90 kg), a dose of 400 mg SC at 0, 2 and 4 weeks, followed by 200 mg SC every other week may be considered.	CD, PsA: 400 mg every 4 weeks PsO: 400 mg every other week

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): clinically significant hypersensitivity to ustekinumab or any of its excipients
- Boxed warning(s): none reported

Appendix D: General Information
- Definition of failure of MTX or DMARDs:
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in erythrocyte sedimentation rate/C-reactive protein (ESR/CRP) levels
  - Improvements in activities of daily living
- PsA: According to the 2018 American College of Rheumatology and National Psoriasis Foundation guidelines, TNF inhibitors or oral small molecules (e.g., methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilast) are preferred over other biologics (e.g., interleukin-17 inhibitors or interleukin-12/23 inhibitors) for treatment-naïve disease. TNF inhibitors are also generally recommended over oral small molecules as first-line therapy unless disease is not severe, member prefers oral agents, or TNF inhibitor therapy is contraindicated.

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:
  - Inability to induce short-term symptomatic remission with a 3-month trial of systemic glucocorticoids
  - High-risk factors for intestinal complications may include:
    - Initial extensive ileal, ileocolonic, or proximal GI involvement
    - Initial extensive perianal/severe rectal disease
    - Fistulizing disease (e.g., perianal, enterocutaneous, and rectovaginal fistulas)
    - Deep ulcerations
    - Penetrating, stricturing or stenosis disease and/or phenotype
    - Intestinal obstruction or abscess

Appendix F: Mayo Score

- Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician's global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0 – 2	Remission
3 – 5	Mild activity
6 – 10	Moderate activity
>10	Severe activity

- The following may be considered for medical justification supporting inability to use an immunomodulator for ulcerative colitis:
  - Documentation of Mayo Score 6 – 12 indicative of moderate to severe ulcerative colitis.

Appendix G: Dose Rounding Guidelines for PsO

Weight-based Dose Range	Quantity Recommendation
Subcutaneous, Syringe	
≤ 46.99 mg	1 syringe of 45 mg/0.5 mL
47 to 94.49 mg	1 syringe of 90 mg/1 mL
94.5 to 141.49 mg	1 syringe of 45 mg/0.5 mL and 1 syringe of 90 mg/1 mL
Subcutaneous, Vial	
≤ 46.99 mg	1 vial of 45 mg/0.5 mL
47 to 94.49 mg	2 vials of 45 mg/0.5 mL
Intravenous, Vial	
94.5 to 136.49 mg	1 vial of 130 mg/26 mL

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PsO	Weight based dosing SC at weeks 0 and 4, followed by maintenance dose every 12 weeks *Adult:* Weight ≤ 100 kg: 45 mg Weight > 100 kg: 90 mg *Pediatrics (Age 12 years and older):* Weight < 60 kg: 0.75 mg/kg Weight 60 to 100 kg: 45 mg Weight > 100kg: 90 mg	90 mg every 12 weeks
PsA	45 mg SC at weeks 0 and 4, followed by 45 mg every 12 weeks	45 mg every 12 weeks
PsA with co-existent PsO	Weight > 100 kg: 90 mg SC at weeks 0 and 4, followed by 90 mg every 12 weeks	90 mg every 12 weeks

Indication	Dosing Regimen	Maximum Dose
CD, UC	Weight based dosing IV at initial dose, followed by 90 mg SC every 8 weeks Weight ≤ 55 kg: 260 mg Weight 55 kg to 85 kg: 390 mg Weight > 85 kg: 520 mg	90 mg every 8 weeks

VI. Product Availability

- Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/mL
- Single-dose vial for SC injection: 45 mg/0.5 mL
- Single-dose vial for IV infusion: 130 mg/26 mL

VII. References

1. Stelara Prescribing information Horsham, PA: Janssen Biotech Inc; December 2020. Available at: www.stelarainfo.com. Accessed January 13, 2021.
2. Bernell O, Lapidus A, Hellers G. Risk Factors for Surgery and Postoperative Recurrence in Crohn's Disease. *Annals of Surgery*. 2000; 231(1): 38-45.
3. Menter A, Gottlieb A, Feldman SR, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2008;58:826-850.
4. Menter A, Gottlieb A, Feldman, SR, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. *J Am Acad Dermatol.* 2008; 58(5): 826-50.
5. Menter A, Korman, NJ, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. *J Am Acad Dermatol*. 2009;60:643-659.
6. Menter A, Korman NF, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 2009; doi: 10.1016/j.jaad.2009.03.027
7. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis.* 2015;0:1-12. doi:10.1136/annrheumdis-2015-208337
8. Lichtenstein GR, Loftus Jr. EV, Isaacs KI, Regueiro MD, Gerson LB, and Sands BE. ACG clinical guideline: management of Crohn's disease in adults. *Am J Gastroenterol*. 2018; 113:481-517.
9. 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;80:1029-72. doi:10.1016/j.aad.201811.057.
10. Rubin DT,Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384-413.
11. Sands BE, Sandborn WJ, Panaccione, et al. Ustekinumab as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med.* 2019;381:1201-14.
12. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *American College of Rheumatology*. 2019; 71(1):5-32. doi: 10.1002/art.40726.
13. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: https://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.22.21	05.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.