Clinical Policy: Ustekinumab (Stelara)

Reference Number: MDN.CP.PHAR.264
Effective Date: 04.01.22
Last Review Date: 04.22
Line of Business: Meridian IL Medicaid

Coding Implications
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.

It is the policy of health plans affiliated with Centene Corporation® 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 Humira®, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Humira*
6. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V:
      i. Initial dose (IV):
         1) Weight ≤ 55 kg: 260 mg once;

2) Weight > 55 kg to 85 kg: 390 mg once;
3) Weight > 85 kg: 520 mg once;

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

b. If request is for a dose that exceeds 90 mg every 8 weeks, all of the following (i and ii):
i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
ii. Dose dose not exceed 90 mg every 4 or 6 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 or acitretin at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
6. Failure of TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Cimzia®, Enbrel®, Humira®;
   **Prior authorization may be required for Cimzia, Enbrel, and Humira*
7. Request meets one of the following (a or b):
   a. Dose does not exceed one of the following (*see Appendix G for dose rounding guidelines*) (i or ii):
      i. Adult: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (1 or 2);
         1) Weight ≤ 100 kg: 45 mg per dose;
         2) Weight > 100 kg: 90 mg per dose;
      ii. Pediatrics: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (1, 2, or 3);
         1) Weight < 60 kg: 0.75 mg/kg per dose;
         2) Weight 60 kg to 100 kg: 45 mg per dose;
         3) Weight > 100 kg: 90 mg per dose.
   b. If request is for a dose that exceeds 90 mg every 12 weeks, all of the following (i, ii, and iii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;

ii. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel® and Cimzia®;

Dose dose not exceed 90 mg every 8 weeks.
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 TWO of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a and b):
   a. Cimzia®;
   b. Enbrel®;
   c. Humira®;
   d. Xeljanz®/Xeljanz XR®;

   **Prior authorization may be required for Cimzia, Enbrel, Humira, and, Xeljanz/Xeljanz XR*
6. Requests meets one of the following (a or b);
   a. Dose does not exceed one of the following (i or ii):
      i. 45 mg initially and 4 weeks later, followed by maintenance dose of 45 mg every 12 weeks;
      ii. Co-existent PsO and weight > 100 kg: 90 mg initially and 4 weeks later, followed by maintenance dose of 90 mg every 12 weeks.
   b. If request is for a dose that exceeds 45 mg every 12 weeks, there must be documentation that supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;

Dose dose not exceed 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 a 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. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a and b):
   a. Humira®;
   b. Xeljanz/Xeljanz XR®;

   **Prior authorization may be required for Humira and Xeljanz/Xeljanz XR*
7. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V:

i. Initial dose (IV):
   1) Weight ≤ 55 kg: 260 mg once;
   2) Weight > 55 kg to 85 kg: 390 mg once;
   3) Weight > 85 kg: 520 mg once;
ii. Maintenance dose (SC): 90 mg 8 weeks after the initial IV dose, followed by maintenance dose of 90 mg every 8 weeks;

b. If request is for a dose that exceeds 90 mg every 8 weeks, all of the following (i and ii):
   i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
   ii. Dose does not exceed 90 mg every 4 or 6 weeks.

Approval duration: 6 months

E. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Request is for SC formulation;
4. Member meets one of the following (a or b):
   a. If request is for a dose increase, new dose does not exceed one of the following (i, ii, or iii):
      i. PsO alone (*see Appendix G for dose rounding guidelines*) (1 or 2):
         1) Adults (a or b):
            a) Weight ≤ 100 kg: 45 mg every 12 weeks;
            b) Weight > 100 kg: 90 mg every 12 weeks;
         2) 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;
      ii. PsA (1 or 2):
         1) 45 mg every 12 weeks;
         2) Co-existent PsO and weight > 100 kg: 90 mg every 12 weeks;
      iii. CD, UC: 90 mg every 8 weeks;
   b. For CD and UC, if request is for a dose increase and new maintenance dose exceeds the maximum dose and frequency indicated in Section V, all of the following (i, ii and iii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. One of the following (1, 2, 3 or 4):

1) CD: Failure of a trial of ≥ 3 consecutive months of Humira unless contraindicated or clinically significant adverse effects are experienced;
2) UC: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated: Humira, Xeljanz/Xeljanz XR;
3) For PsO: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated: Cimzia, Enbrel/Humira;
4) For PsA: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: Cimzia, Enbrel/Humira, Xeljanz/Xeljanz XR;

iii. Dose does not exceed 90 mg every 4 or 6 weeks.

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

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 policies – CP.PMN.53 for Medicaid 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
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO daily	50 mg/day
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	40 mg every other week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Otezla® (apremilast)	**PsA** Initial dose: Day 1: 10 mg PO QAM Day 2: 10 mg PO QAM and 10 mg PO QPM Day 3: 10 mg PO QAM and 20 mg PO QPM Day 4: 20 mg PO QAM and 20 mg PO QPM Day 5: 20 mg PO QAM and 30 mg PO QPM Maintenance dose: Day 6 and thereafter: 30 mg PO BID	60 mg/day
Simponi® (golimumab)	**UC** Initial dose: 200 mg SC at week 0, then 100 mg SC at week 2 Maintenance dose: 100 mg SC every 4 weeks	100 mg every 4 weeks
Taltz® (ixekizumab)	**PsA** Initial dose: 160 mg (two 80 mg injections) SC at week 0 Maintenance dose: 80 mg SC every 4 weeks **PsO** Initial dose: 160 mg (two 80 mg injections) SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, and 12 Maintenance dose: 80 mg SC every 4 weeks	80 mg every 4 weeks
Xeljanz® (tofacitinib)	**PsA** 5 mg PO BID	**PsA, RA** 10 mg/day
Xeljanz XR® (tofacitinib extended-release)	**PsA** 11 mg PO QD	**PsA,RA** 11 mg/day
Zeposia® (ozanimod)	**UC** Days 1-4: 0.23 mg PO QD Days 5-7: 0.46 mg PO QD	**UC** 0.92 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Day 8 and thereafter: 0.92 mg PO QD	

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

Indication	Dosing Regimen	Maximum Dose
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
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

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13. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at http://www.clinicalpharmacology-ip.com/.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3357	Ustekinumab, for subcutaneous injection,1 mg
J3358	Ustekinumab, for intravenous injection, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created, adapted from CP.PHAR.264	04.01.22	04.22

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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