# Clinical Policy: Ustekinumab (Stelara)

Reference Number: IN.PHAR.264
Effective Date: 08.16
Last Review Date: 08.21
Line of Business: 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. 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*);
2. 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*
3. 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: 12 months**

**B. Plaque Psoriasis** (must meet all)**:**

1. Diagnosis of moderate-to-severe PsO
2. Request is for SC formulation;
3. 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;
4. Failure of a ? 3 consecutive month trial of Taltz®, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Taltz*
5. 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: 12 months**

**C. Psoriatic Arthritis** (must meet all)**:**

1. Request is for SC formulation;
2. Failure of at least two of the following, each used for ? 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: Enbrel®, Otezla®, Simponi®/Simponi Aria®, Taltz, Xeljanz®/Xeljanz XR®;
   **Prior authorization may be required for Enbrel, Otezla, Simponi/Simponi Aria, Taltz, Xeljanz/Xeljanz XR*
3. 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: 12 months**

**D. Ulcerative Colitis** (must meet all)**:**

1. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
2. Failure of a ≥ 3 consecutive month trial of Humira or Simponi®, unless clinically significant adverse effects are experienced or both are contraindicated;

**Prior authorization may be required for Humira and Simponi*

3. 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: 12 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. History of the requested agent within thepast 90 days;
2. Request is for SC formulation;
3. 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 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. 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**<br>25 or 50 mg PO daily | 50 mg/day |
| azathioprine (Azasan®, Imuran) | **CD**<br>1.5 – 2 mg/kg/day PO | 2.5 mg/kg/day |
| corticosteroids | **CD***<br>prednisone 40 mg PO QD for 2 weeks or IV 50 – 100 mg Q6H for 1 week<br><br>budesonide (Entocort EC® ) 6 – 9 mg PO QD<br><br>**UC**<br>budesonide (Uceris® ) 9 mg PO QD | Various |
| cyclosporine (Sandimmune®, Neoral®) | **PsO**<br>2.5 – 4 mg/kg/day PO divided BID | 4 mg/kg/day |
| 6-mercaptopurine (Purixan®) | **CD**<br>50 mg PO QD or 1 – 2 mg/kg/day PO | 2 mg/kg/day |
| methotrexate (Rheumatrex®) | **CD***<br>15 – 25 mg/week IM or SC<br><br>**PsO**<br>10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week | 30 mg/week |
| Pentasa® (mesalamine) | **CD**<br>1,000 mg PO QID | 4 g/day |
| Enbrel® (etanercept) | **PsA**<br>25 mg SC twice weekly or 50 mg SC once weekly | 50 mg/week |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Humira® (adalimumab) | **CD, UC**<br>Initial dose:<br>160 mg SC on Day 1, then 80 mg SC on Day 15<br><br>Maintenance dose:<br>40 mg SC every other week starting on Day 29 | 40 mg every other week |
| Otezla® (apremilast) | **PsA**<br>Initial dose:<br>Day 1: 10 mg PO QAM<br>Day 2: 10 mg PO QAM and 10 mg PO QPM<br>Day 3: 10 mg PO QAM and 20 mg PO QPM<br>Day 4: 20 mg PO QAM and 20 mg PO QPM<br>Day 5: 20 mg PO QAM and 30 mg PO QPM<br><br>Maintenance dose:<br>Day 6 and thereafter: 30 mg PO BID | 60 mg/day |
| Simponi® (golimumab) | **PsA**<br>50 mg SC once monthly | 50 mg/month |
| | **UC**<br>Initial dose:<br>200 mg SC at week 0, then 100 mg SC at week 2<br>Maintenance dose:<br>100 mg SC every 4 weeks | 100 mg every 4 weeks |
| Simponi Aria® (golimumab) | **PsA**<br>Initial dose:<br>2 mg/kg IV at weeks 0 and 4<br>Maintenance dose:<br>2 mg/kg IV every 8 weeks | 2 mg/kg every 8 weeks |
| Taltz® (ixekizumab) | **PsA**<br>Initial dose: 160 mg (two 80 mg injections) SC at week 0<br>Maintenance dose:<br>80 mg SC every 4 weeks<br><br>**PsO**<br>Initial dose: | 80 mg every 4 weeks |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| | 160 mg (two 80 mg injections) SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, and 12<br>Maintenance dose:<br>80 mg SC every 4 weeks | |
| Xeljanz® (tofacitinib) | **PsA**<br>5 mg PO BID | 10 mg/day |
| Xeljanz XR® (tofacitinib extended-release) | **PsA**<br>11 mg PO QD | 11 mg/day |

*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: 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 |

## IV. 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<br><br>*Adult:*<br>Weight < 100 kg: 45 mg<br>Weight > 100 kg: 90 mg<br><br>*Pediatrics (Age 12 years and older):*<br>Weight < 60 kg: 0.75 mg/kg<br>Weight 60 to 100 kg: 45 mg<br>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 |
| CD, UC | Weight based dosing IV at initial dose, followed by 90 mg SC every 8 weeks<br><br>Weight < 55 kg: 260 mg<br>Weight 55 kg to 85 kg: 390 mg<br>Weight > 85 kg: 520 mg | 90 mg every 8 weeks |

## V. 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

## VI. References

1. Stelara Prescribing Information. Horsham, PA: Janssen Biotech; December 2020. Available at: www.stelarainfo.com. Accessed January 13, 2021.
2. 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 |
|---|---|---|
| Created for PA Criteria Alignment with IN Medicaid FFS | 08/21 | OMPP Approved |

**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.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.