Clinical Policy: Ustekinumab (Stelara)

Reference Number: PA.CP.PHAR.264
Effective Date: 01/18
Last Review Date 04/19 Revision Log

Coding Implications

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

FDA Approved Indication
Stelara is indicated for the treatment of:

- Adult and adolescent (12 years or older) patients 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) who have:
  - Failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker; or
  - Failed or were intolerant to treatment with one or more TNF blockers

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness® that Stelara is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of PsO;
2. Request is for SC formulation;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;;
4. Age ≥ 12 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 unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. For age ≥ 18 years, failure of etanercept *(Enbrel® is preferred)* AND adalimumab (*Humira® is preferred*) used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced, or member is currently receiving Stelara;
   **Prior authorization is required for etanercept and adalimumab*
7. Dose does not exceed one of the following (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

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

1. Diagnosis of active 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 etanercept *(Enbrel is preferred)* and adalimumab *(Humira is preferred)*, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced, or member is currently receiving Stelara;
   **Prior authorization is required for etanercept and adalimumab*
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

C. 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 contraindicated or clinically significant adverse effects are experienced;
   b. Medical justification supports inability to use immunomodulators (*see Appendix E*);
5. Failure of a ≥ 3 consecutive month trial of adalimumab *(Humira is preferred)* unless contraindicated or clinically significant adverse effects are experienced, or member is currently receiving Stelara;
   **Prior authorization is required for adalimumab*
6. Dose does not exceed:
   a. Initial dose (IV):
      i. Weight < 55 kg: 260 mg IV once;
      ii. Weight 55 kg to 85 kg: 390 mg IV once;

iii. Weight > 85 kg: 520 mg IV once;

b. Maintenance dose (SC):

i. 90 mg SC 8 weeks after the initial IV dose, then every 8 weeks thereafter.

Approval duration: 6 months

c. **Other diagnoses/indications**

1. Refer to PA.CP.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via PA Health and Wellness benefit or member has previously met initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy
3. Request is for SC formulation;
1. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):

a. PsO alone (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: 90 mg every 8 weeks.

Approval duration: 12 months

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

1. Currently receiving medication via PA Health and Wellness benefit benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to PA.CP.PMN.53

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

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	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** <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	40 mg every other week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	PsO Initial dose: 80 mg SC Maintenance dose: 40 mg SC every other week starting one week after initial dose	

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: 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

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 *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 in adults	• 45 mg SC at 0 and 4 weeks, followed by 45 mg every 12 weeks	45 mg every 12 weeks
PsA in adults with co-existent mod/severe PsO	SC: • >100 kg: 90 mg SC at 0 and 4 weeks, followed by 90 mg every 12 weeks	>100 kg: 90 mg every 12 weeks
CD in adults	• ≤ 55 kg: 260 mg IV initially, followed by 90 mg SC 8 weeks after initial IV dose, then every 8 weeks thereafter • 55 kg to 85 kg: 390 mg IV initially, followed by 90 mg SC 8 weeks after initial IV dose, then every 8 weeks thereafter • >85 kg: 520 mg IV initially, followed by 90 mg SC 8 weeks after initial IV dose, then every 8 weeks thereafter	90 mg every 8 weeks

V. Product Availability

- Subcutaneous Injection:
  - Injection: 45 mg/0.5mL or 90 mg/mL in a single-dose prefilled syringe
  - Injection: 45 mb/0.5mL in a single-dose vial
- Intravenous Infusion: 130 mg/26mL (5 mg/mL) solution in a single-dose vial

VI. References

1. Stelara Prescribing Information. Horsham, PA: Janssen Biotech; June 2018. Available at: www.stelarainfo.com. Accessed February 26, 2019.

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10. 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

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	Injection, ustekinumab, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: removed specific diagnosis requirements for PsO and CD, added rheumatologist as prescriber specialty requirement for PsO, removed trial and failure of phototherapy and topical therapy for PsO,		

Reviews, Revisions, and Approvals	Date	Approval Date
modified trial and failure to require use of methotrexate or alternative DMARD and Enbrel and Humira for PsO, modified max dosing requirements per package insert, removed TB testing for all indications; references reviewed and updated.	02.27.18	
2Q 2019 annual review: modified prescriber specialist from GI specialist to gastroenterologist for CD; removed trial and failure requirement of conventional DMARDs (e.g., MTX)/NSAIDs for PsA per ACR/NPF 2018 guidelines; removed redirection to Humira for PsO for members < 18 years old; references reviewed and updated.	04.17.19	