Clinical Policy: Ustekinumab (Stelara)

Reference Number: ERX.SPA.01
Effective Date: 04.01.17
Last Review Date: 11.17 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 and -23 antagonist.

FDA Approved Indication(s)
Stelara is indicated:

- For the treatment of adult patients with moderate-to-severe plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy
- For the treatment of adult patients with active psoriatic arthritis (PsA), alone or in combination with methotrexate
- For the treatment of 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 health plans affiliated with Envolve Pharmacy Solutions™ that Stelara is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of moderate-to-severe PsO;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a trial of methotrexate (MTX) at up to a dose of 15-20 mg/week used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX, failure of a trial of cyclosporine or acitretin unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of etanercept (*Enbrel is preferred*) AND adalimumab (*Humira is preferred*), each trialed for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
6. Dose does not exceed:
   a. Weight ≤ 100 kg: 45 mg SC initially and 4 weeks later, followed by 45 mg SC every 12 weeks thereafter;
   b. Weight > 100 kg: 90 mg SC initially and 4 weeks later, followed by 90 mg SC every 12 weeks thereafter.

Approval duration: 6 months

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

1. Diagnosis of active PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):

a. Failure of a trial of MTX for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
b. If intolerance or contraindication to MTX, failure of a trial of leflunomide, sulfasalazine, or cyclosporine used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;

5. Failure of etanercept (*Enbrel is preferred*) AND adalimumab (*Humira is preferred*), each trialed for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
6. Dose does not exceed 45 mg SC initially and 4 weeks later, followed by 45 mg SC every 12 weeks thereafter (90 mg SC initially, at 4 weeks, and every 12 weeks thereafter for members with co-existent moderate-to-severe psoriasis).

Approval duration: 6 months

C. Crohn's Disease (must meet all)**:**

1. Diagnosis of moderate-to-severe CD;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Failure of a trial of thiopurines (6-mercaptopurine or azathiopurine) or MTX used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of a trial of adalimumab (*Humira is preferred*) for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for adalimumab*
6. Dose does not exceed:
   a. Initial (IV):
      i. Weight up to 55 kg: 260 mg as a single dose;
      ii. Weight ≥ 55 kg to 85 kg: 390 mg as a single dose;
      iii. Weight > 85 kg: 520 mg as a single dose;
   b. Maintenance (SC): 90 mg every 8 weeks.

Approval duration: 6 months

D. 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 (e.g., labs, sign/symptom reduction, no significant toxicity);
3. If request is for a dose increase, new dose does not exceed:
   a. PsO: 45 mg (if weight ≤ 100 kg) or 90 mg (if weight > 100 kg) SC every 12 weeks;
   b. PsA: 45 mg SC every 12 weeks (90 mg every 12 weeks if co-existent psoriasis);
   c. CD: 90 mg SC 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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: Crohn's disease
FDA: Food and Drug Administration
MTX: methotrexate
PsO: plaque psoriasis
PsA: psoriatic arthritis
TNF: tumor necrosis factor

Appendix B: General Information

- Serious infections were seen in clinical studies with concurrent use of Kineret and another TNF-blocking agent, Enbrel, with no added benefit compared to Enbrel alone. Because of the nature of the adverse reactions with this combination therapy, similar toxicities may also result from combination of anakinra and other TNF blocking agents.
- Per prescribing information, Xeljanz should not be used in combination with biologic DMARDs [such as Kineret] or potent immunosuppressants such as azathioprine and cyclosporine. As stated in the black box warning, patients treated with Xeljanz are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as MTX or corticosteroids.
- Stelara is for subcutaneous administration and is intended for use under the guidance and supervision of a physician. After proper training in subcutaneous injection technique, a patient may self inject with Stelara if a physician determines that it is appropriate. Patients should be instructed to follow the directions provided in the Medication Guide.
- In the PHOENIX 2 trial, dosing intensification of Stelara to every 8 weeks did not result in greater efficacy compared with continuing treatment every 12 weeks.

Appendix C: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Imuran®)	**CD** 100-250 mg PO daily	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	Varies
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5-4 mg/kg/day PO divided BID **PsA** 2.5-3 mg/kg/day	4 mg/kg/day
mercaptopurine (Purinethol®)	**CD** 75-125 mg PO daily	1.5 mg/kg/day
methotrexate (Rheumatrex®)	**PsO** 10-25 mg/week, IM, IV or PO **PsA** 7.5 to 15 mg/week PO	30 mg/week
sulfasalazine (Azulfidine®)	**PsA** 2,000 mg/day PO	5 g/day
leflunomide (Arava®)	**PsA** 100 mg/day PO loading dose for 3 days followed by 20 mg/day PO	100 mg/day
Pentasa® (mesalamine)	**CD** 1000 mg PO QID	4000 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO daily	50 mg/day
adalimumab (Humira®, Amjevita®)*	**PsA** 40 mg SC every other week **Adult CD** Initial dose (Day 1): 160 mg SC Second dose two weeks later (Day 15): 80 mg SC Two weeks later (Day 29): Begin a maintenance dose of 40 mg SC every other week **Pediatric CD** *17 kg (37 lbs) to < 40 kg (88 lbs):* Initial dose (Day 1): 80 mg SC Second dose two weeks later (Day 15): 40 mg SC Two weeks later (Day 29): Begin a maintenance dose of 20 mg SC every other week *≥ 40 kg (88 lbs):* Initial dose (Day 1): 160 mg SC Second dose two weeks later (Day 15): 80 mg SC Two weeks later (Day 29): Begin a maintenance dose of 40 mg SC every other week **PsO** 80 mg SC initial dose, followed by 40 mg SC every other week starting one week after initial dose	**Adults** 40 mg SC every other week for PsA, CD, and PsO . **Adolescents** Crohn's disease ≥ 40 kg: 40 mg SC every other week. 17 kg to < 40 kg: 20 mg SC every other week. **Children** Crohn's disease ≥ 6 years and ≥ 40 kg: 40 mg SC every other week. ≥ 6 years and ≥ 17 kg to < 40 kg: 20 mg SC every other week. < 6 years: Safety and efficacy have not been established.
etanercept (Enbrel®, Erelzi®)*	**PsA** 25 mg SC twice weekly or 50 mg SC once weekly **PsO** 50 mg SC twice weekly for 3 months followed by 50 mg SC once weekly	50 mg twice weekly

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.
**Requires PA*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PsO	*Weight ≤ 100 kg*: 45 mg SC initially and 4 weeks later, followed by 45 mg SC every 12 weeks thereafter *Weight > 100 kg*: 90 mg SC initially and 4 weeks later, followed by 90 mg SC every 12 weeks thereafter	45 mg every 12 weeks if weight ≤ 100 kg, 90 mg every 12 weeks if weight > 100 kg
PsA	45 mg SC initially and 4 weeks later, followed by 45 mg SC every 12 weeks thereafter (90 mg SC initially, at 4 weeks, and every 12 weeks thereafter for patients with co-existent moderate to severe plaque psoriasis)	45 mg every 12 weeks (90 mg every 12 weeks if co-existent Ps)

Indication	Dosing Regimen	Maximum Dose
CD	Initial (IV) *Weight up to 55 kg*: 260 mg as a single dose *Weight ≥ 55 kg to 85 kg*: 390 mg as a single dose *Weight > 85 kg*: 520 mg as a single dose Maintenance (SC) 90 mg every 8 weeks	Initial: weight based single dose Maintenance: 90 mg every 8 weeks

VI. Product Availability

- Single-dose prefilled syringe for SC injection: 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; September 2016. Available at: https://www.stelarainfo.com/pdf/prescribinginformation.pdf. Accessed September 18, 2017.
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3. Lichtenstein G, Hanauer S, Sandborn W, et al. Management of Crohn`s Disease in Adults. Am J Gastroenterol 2009;104:465-483.
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 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008;58:826-850.
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6. 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.
7. 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. 10.1016/j.jaad.2009.03.027
8. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed September 18, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.16	02.17
4Q17 Annual Review -Added trial of leflunomide, sulfasalazine, or cyclosporine for PsA if contraindicated to MTX and trial of thiopurines or MTX for Crohn's per 3Q17 TCRs -Added age requirements per PI and safety guidance -PsO, PsA, CD: added "or in consultation with" specialist	09.30.17	11.17

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.