Clinical Policy: Ustekinumab (Stelara®)

Reference Number: QCP.PHAR.007
Date of Last Revision:

Coding Implications
Revision Log

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

Description
Ustekinumab (Stelara®) is an immunosuppressive drug.

Policy/Criteria
I. Initial Approval Criteria
A. Crohn's Disease (must meet all):
1. Diagnosis of CD;
2. Request is for IV: Stelara
3. Prescribed by or in consultation with a gastroenterologist;
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], methotrexate [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. age ≥ 18 years;
6. Member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
7. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

B. Plaque Psoriasis (must meet all):
1. Diagnosis of PsO and PsO is moderate-to-severe as evidenced by involvement of one of the following (i or ii):
    i. ≥ 3% of total body surface area;
    ii. Hands, feet, scalp, face, or genital area;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 6 years;
4. Member meets one of the following (a or b):
    a. Member has moderate-to-severe disease, and one of the following (i, ii, or iii):
        i. Failure of a ≥ 3 consecutive months trial of methotrexate (MTX) at up to maximally indicated doses;
        ii. Member has intolerance or contraindication to MTX (see Appendix D), and failure of a ≥ 3 consecutive months trial of cyclosporine or acitretin at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;

iii. Member has intolerance or contraindication to MTX, cyclosporine, and acitretin, and failure of phototherapy, unless contraindicated or clinically significant adverse effects are experienced;

5. For Stelara: If request is through the pharmacy benefit for 45 mg/0.5 mL vial formulation, member must use Stelara pre-filled syringe;
6. member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
7. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

C. Psoriatic Arthritis (must meet all):

1. Diagnosis of PsA;
2. Request is for Stelara
3. Age ≥ 6 years;
4. For Stelara: If request is through the pharmacy benefit for 45 mg/0.5 mL vial formulation, member must use Stelara pre-filled syringe;
5. Member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
6. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

D. Ulcerative Colitis (must meet all):

1. Diagnosis of UC;
2. Request is for Stelara
3. Prescribed by or in consultation with a gastroenterologist;
4. Documentation of a Mayo Score ≥ 6 (see Appendix F);
5. : Age ≥ 18 years
6. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
7. For Stelara: If request is through the pharmacy benefit for 45 mg/0.5 mL vial formulation, member must use Stelara pre-filled syringe;
8. Member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors(see Section III: Diagnoses/Indications for which coverage is NOT authorized);
9. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

II. Continued Therapy

All Other Indications in Section I (must meet all):

1. Member currently receiving medication via Centene benefit or member has previously met initial approval criteria;

2. Member is responding positively to therapy;
3. Member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
4. If request is for a dose increase, new dose does not exceed maximum dose indicated in Section V.

Approval duration: 12 months

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 – HIM.PA.154 for health insurance marketplace or evidence of coverage documents;
B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs) or potent immunosuppressants, including but not limited to any tumor necrosis factor (TNF) antagonists [e.g., Cimzia®, Enbrel®, Humira® and its biosimilars, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [e.g., 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® (IL23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Xeljanz®/Xeljanz® XR, Cibinqo™, Olumiant™, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, Rituxan Hycela®], selective co-stimulation modulators [Orencia®], and integrin receptor antagonists [Entyvio®] because of the additive immunosuppression, increased risk of neutropenia, as well as increased risk of serious infections

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: Crohn's disease
DMARDs: disease-modifying antirheumatic drugs
JAK: Janus kinase
MTX: methotrexate
NSAIDs: non-steroidal anti inflammatory drugs
PsO: plaque psoriasis
PsA: psoriatic arthritiss
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 QD	50 mg/day
azathioprine (Azasan®, Imuran®)	**CD*** 1.5 – 2 mg/kg/day PO	3 mg/kg/day
corticosteroids - Oral: e.g., prednisone, budesonide -Medium to very high potency topical: e.g., desoximetasone 0.05%, fluocinolone acetonide 0.025%, mometasone 0.1% cream, triamcinolone acetonide 0.1%, augmented betamethasone dipropionate 0.05%, clobetasol propionate 0.05% cream, ointment, gel, or solution, halobetasol propionate 0.05% cream, ointment	**CD*** Adult: -prednisone 40 mg – 60 mg PO QD for 1 to 2 weeks, then taper daily dose by 5 mg weekly until 20 mg PO QD, and then continue with 2.5 – 5 mg decrements weekly or IV 50 – 100 mg Q6H for 1 week - budesonide (Entocort EC□) 6 – 9 mg PO QD Pediatric: -Prednisone 1 to 2 mg/kg/day PO QD **UC** Adult: -Prednisone 40 mg – 60 mg PO QD, then taper dose by 5 to 10 mg/week -budesonide (Uceris□) 9 mg PO QD Pediatric: -Prednisone 1 to 2 mg/kg/day 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 0.75 – 1.5 mg/kg/day PO	1.5 mg/kg/day

methotrexate (Trexall®, Otrexup™, Rasuvo®, RediTrex®, Xatmep™, Rheumatrex®)	**CD*** 15 – 25 mg/week IM or SC **PsO** 10 to 25 mg/week IM, SC or 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
tacrolimus (Prograf®)	**CD*** 0.27 mg/kg/day PO in divided doses or 0.15 – 0.29 mg/kg/day PO	N/A
biologic DMARDs (e.g., Humira, Enbrel, Cosentyx, Remicade, Simponi Aria, Otezla, Xeljanz/Xeljanz XR, Kevzara)	See Section V. Dosing and Administration	See Section V. Dosing and Administration

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

Contraindications: Clinically significant hypersensitivity to ustekinumab or any of its excipients
BBW: None

Appendix D: General Information

- Definition of failure of MTX or DMARDs
  - Failure of a trial of conventional 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.
- Ulcerative Colitis:
  - For Ulcerative Colitis maintenance therapy, failure is defined as having two or more exacerbations requiring steroid therapy
- Ulcerative colitis: there is insufficient evidence to support the off-label weekly dosing of adalimumab for the treatment of moderate-to-severe UC. It is the position of Centene Corporation® that the off-label weekly dosing of adalimumab for the treatment of moderate-to-severe UC is investigational and not medically necessary at this time.

- The evidence from the post hoc study of the adalimumab pivotal trial suggests further studies are needed to confirm the benefit of weekly adalimumab dosing for the treatment of UC in patients with inadequate or loss of therapeutic response to treatment with adalimumab every other week. No large, randomized or prospective studies have been published to support the efficacy of the higher frequency of dosing, while national and international treatment guidelines also do not strongly support dose escalation of adalimumab for UC. The current market consensus is that weekly dosing of adalimumab is not medically necessary due to lack of evidence to support its benefit

- TNF blockers:
  - Etanercept (Enbrel®), adalimumab (Humira®) and its biosimilars, infliximab (Remicade®) and its biosimilars (Avsola™, Renflexis™, Inflectra®), certolizumab pegol (Cimzia®), and golimumab (Simponi®, Simponi Aria®).

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for CD:
  - 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
  - For TNF-inhibitors, high risk factors for postoperative recurrence may include:
    - Less than 10 years duration between time of diagnosis and surgery
    - Disease location in the ileum and colon
    - Perianal fistula
    - Prior history of surgical resection
    - Use of corticosteroids prior to surgery

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

Appendix G: Dose Rounding Guidelines for Weight-Based Doses

Stelara for PsO

Weight-based Dose Range	Quantity Recommendation
Subcutaneous, Vial	
≤ 46.99 mg	1 vial of 45 mg/0.5 mL
47 to 94.49 mg	2 vial of 45 mg/0.5 mL

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ustekinumab (Stelara)* *Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses	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 6 years to 17 years): Weight < 60 kg: 0.75 mg/kg Weight 60 to 100 kg: 45 mg Weight > 100kg: 90 mg	90 mg every 12 weeks
	PsA	Adult: 45 mg SC at weeks 0 and 4, followed by 45 mg every 12 weeks Pediatric (age 6 years to 17 years): Weight based dosing SC at weeks 0 and 4, then every 12 weeks thereafter. Weight < 60 kg: 0.75 mg/kg Weight ≥ 60 kg: 45 mg	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 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-use prefilled syringe: 45 mg/0.5 mL, 90 mg/mL
Single-dose vial for SC: 45 mg/0.5 mL
Single-dose vial for IV: 130 mg/26 mL (5 mg/mL)

References

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14. ClinicalTrials.gov. A study of the Safety and Effectiveness of Ustekinumab in Patients with Psoriatic Arthritis (PSUMMIT-1). Available at https://clinicaltrials.gov/ct2/show/NCT01009086. Accessed February 10, 2023.
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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
J3358	Ustekinumab, for intravenous injection, 1 mg

Revision Log

Reviews, Revisions, and Approvals	Revision Date	Approval Date

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed healthcare 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

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