MEDICAL MUTUAL®

Drug Policy

Policy:	**201012**	**Initial Effective Date: 12/22/2010**
Code(s):	**HCPCS J3357, J3358**	**Annual Review Date: 05/18/2023**
SUBJECT:	**Stelara™ (ustekinumab for subcutaneous [SC] injection – Centocor Ortho Biotech)** **Stelara IV (ustekinumab for intravenous infusion)**	**Last Revised Date: 05/18/2023**

☒Subject to Site of Care

Prior approval is required for some or all of the procedure codes listed in this Corporate Medical Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

Overview

Stelara is indicated for the treatment of those ≥ 6 years of age with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy, for adult patients ≥ 18 years of age with active psoriatic arthritis (PsA) alone or in combination with methotrexate (MTX), and for moderate to severe active Crohn's Disease, in patients who have failed or were intolerant to immunomodulators or corticosteroids, but never failed a tumor necrosis factor inhibitor (TNFi), or in patients who failed or were intolerant to at least on TNFi. Stelara is also indicated for the treatment of patients ≥ 18 years of age with moderate to severe active Ulcerative Colitis. Stelara is a human immunoglobulin G (IgG) 1κ monoclonal antibody against the p40 subunit of the interleukin (IL)-12 and IL-23 cytokines, which are involved in inflammatory and immune responses. It is administered by subcutaneous (SC) injection under the supervision of a physician, although with proper training patients may self-inject.

Stelara for intravenous IV infusion is indicated for the treatment of adults ≥ 18 years of age with moderate to severe active Crohn's disease, in patients who have failed or were intolerant to immunomodulators or corticosteroids, but never failed a tumor necrosis factor inhibitor (TNFi), or in patients who failed or were intolerant to at least one TNFi. It is a human immunoglobulin G (IgG) 1κ monoclonal antibody against the p40 subunit of the interleukin (IL)-12 and IL-23 cytokines, which are involved in inflammatory and immune responses. In Crohn's disease, a single weight-based dose is administered by IV infusion. For both Ulcerative Colitis and Crohn's Disease, a single, weight-based induction dose with the IV product is administered, followed by the recommended maintenance is Stelara for subcutaneous (SC) injection, given as a 90 mg SC injection administered 8 weeks after the initial IV dose, then once every 8 weeks (Q8W) thereafter.

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POLICY STATEMENT

This policy involves the use of Stelara. Prior authorization is recommended for medical benefit coverage of Stelara. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Stelara as well as the monitoring required for AEs and long-term efficacy, initial approval requires Stelara be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below. Stelara SC is subject to the **Inflammatory Conditions Care Value Step Therapy.**

Food and Drug Administration (FDA)-Approved Indications

1. Plaque Psoriasis

I. Initial Therapy. Approve for 3 months if the patient meets ALL of the following criteria (i, ii AND iii)):

- **i.** Patient meets ONE of the following conditions (a or b or c):
  - **a)** Patient has tried at least one of the following agents for at least 3 months for plaque psoriasis: an oral therapy for psoriasis (e.g., MTX, cyclosporine, acitretin tablets; oral methoxsalen plus ultraviolet A light (PUVA)); or
  - **b)** The patient has tried ONE biologic disease-modifying antirheumatic drug (DMARD) for at least 3 months [Refer to Appendix A for examples] OR
  - **c)** Patient has a contraindication to one oral agent for psoriasis such as MTX, as determined by the prescribing physician; AND
- **ii.** Patient is 6 years of age or older; AND
- **iii.** Stelara is prescribed by or in consultation with a dermatologist.

II. Patient is Currently Receiving Stelara. Approve if the patient has had a beneficial response as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Stelara.

Dosing in Plaque Psoriasis.

- Adult Subcutaneous Recommended Dosage

Weight Range (kilograms)	Recommended Dosage
Less than or equal to 100 kg	45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks
greater than 100 kg	90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks

- Pediatric (6 to 17 years old) Subcutaneous Recommended Dosage

- Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter.

Weight Range (kilograms)	Recommended Dosage
Less than 60 kg	0.75 mg/kg
60 kg to 100 kg	45 mg
Greater than 100 kg	90 mg

Approval Duration
Initial Approval = 3 months (90 days)
Re-authorization = 1 year (365 days)

2. Psoriatic Arthritis (PsA).

I. Initial Therapy. Approve for 6 months if Stelara is prescribed by or in consultation with a rheumatologist or a dermatologist.

II. Patient is Currently Receiving Stelara. Approve for 1 year if the patient has had a beneficial response (e.g., less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants [for example, C-reactive protein]), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Stelara.

Dosing in Psoriatic Arthritis.

- Adult Subcutaneous Recommended Dosage
  - The recommended dosage is 45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks
  - For patients with co-existent moderate-to-severe plaque psoriasis weighing greater than 100 kg, The recommended dosage is 90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks

- Pediatric (6 to 17 years old) Subcutaneous Recommended Dosage
  - Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter.

Weight Range (kilograms)	Recommended Dosage
Less than 60 kg	0.75 mg/kg
60 kg to 100 kg	45 mg
Greater than 100 kg with co-existent moderate-to-severe plaque psoriasis	90 mg

Approval Duration
Initial Approval = 6 months (180 days)
Re-authorization = 1 year (365 days)

3. **Crohn's Disease in an Adult, IV Induction Therapy** [Medical Benefit Only]**:** Approve a single dose, if the patient meets the following criteria (A, B, C, AND D):
   - **A)** The patient meets one of the following conditions (i or ii):
     - **i.** The patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
     - **ii.** The patient has tried one other agent for Crohn's disease (e.g., azathioprine, 6-mercaptopurine, methotrexate [MTX], OR Cimzia® [certolizumab pegol SC injection], Entyvio® [vedolizumab for IV infusion], Humira® [adalimumab SC injection] or adalimumab product, or infliximab IV infusion); AND
   - **B)** Stelara IV is prescribed by or in consultation with a gastroenterologist; AND
   - **C)** The patient is 18 years of age or older; AND
   - **D)** Site of care medical necessity must be met*.

   Note: Patients with fistulizing Crohn's disease or Crohn's disease of the ileal pouch must meet the above criteria for Crohn's disease in adults.

Stelara IV is indicated as a single dose, for moderate to severe active Crohn's disease, in patients who have failed or were intolerant to immunomodulators or corticosteroids, but never failed a TNFi, or in patients who failed or were intolerant to at least one TNFi. The recommended induction dose is weight-based IV infusion; maintenance dosing is with Stelara SC 90 mg as a SC injection 8 weeks after the initial intravenous dose, then 90 mg every 8 weeks thereafter.

Dosing in Crohn's Disease. Recommended Initial Adult Intravenous Dosage.

A single intravenous infusion using weight-based dosing:

Weight Range (kilogram)	Recommended Dosage
Up to 55 kg	260 mg (2 vials)
Greater than 55 kg to 85 kg	390 mg (3 vials)
Greater than 85 kg	520 mg (4 vials)

4. Crohn's Disease in an Adult, SQ maintenance therapy

- **A)** Initial SC Therapy. Approve (90-mg dose) for 6 months if the patient meets the following criteria (i, ii, iii and iv):
  - **i.** The patient meets one of the following conditions (a, b or c):
    - **a.** The patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
    - **b.** The patient has tried one conventional systemic therapy for Crohn's disease for at least 3 months (e.g., azathioprine, 6-mercaptopurine, or methotrexate [MTX]); OR
    - **c.** The patient has tried ONE biologic disease-modifying antirheumatic drug (DMARD) [Refer to Appendix A for examples] AND
  - **ii.** Stelara SC is prescribed by or in consultation with a gastroenterologist.
  - **iii.** The patient is 18 years of age or older; AND
  - **iv.** The patient has received a single induction dose with Stelara IV within 2 months of initiating therapy with Stelara SC;

B) Patients Currently Receiving Stelara (IV or SC). Approve for 1 year if the patient has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Stelara.
Note: Patients with fistulizing Crohn's disease or Crohn's disease of the ileal pouch must meet the above criteria for Crohn's disease in adults.

Approval Duration
Initial Approval = 6 months (180 days)
Re-authorization = 1 year (365 days)

5. Ulcerative Colitis Induction Therapy with Stelara IV [Medical Benefit Only]**:** Approve a single dose if the patient meets the following criteria (A, B, C, D and E):
A) The patient is 18 years of age or older; AND
B) Stelara IV will be used as induction therapy; AND
C) The patient has had a trial of one systemic agent for ulcerative colitis.
Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a biologic (e.g., an adalimumab product, an infliximab product, Simponi® [golimumab for SC injection], or Entyvio [vedolizumab injection]) also counts as a trial of one systemic agent for UC; AND
D) The agent is prescribed by or in consultation with a gastroenterologist.
E) Site of care medical necessity must be met*.

Dosing in Ulcerative Colitis. Recommended Initial Adult Intravenous Dosage.

A single intravenous infusion using weight-based dosing:

Weight Range (kilogram)	Recommended Dosage
Up to 55 kg	260 mg (2 vials)
Greater than 55 kg to 85 kg	390 mg (3 vials)
Greater than 85 kg	520 mg (4 vials)

6. Ulcerative Colitis, Stelara SQ maintenance therapy:
I. Initial Therapy. Approve (90mg dose) for 6 months days if the patient meets the following criteria (A, B, C, and D):
A) The patient is 18 years of age or older; AND
B) The patient has received a single induction dose with Stelara IV within 2 months of initiating therapy with Stelara SC; AND
C) The patient has had a trial of one systemic agent for ulcerative colitis.
Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a biologic (e.g., an adalimumab product, an infliximab product, Simponi® [golimumab for SC injection], or Entyvio [vedolizumab injection]) also counts as a trial of one systemic agent for UC; AND

D) The agent is prescribed by or in consultation with a gastroenterologist.

II. Continuation of Therapy: Approve for 1 year if the patient has had a response to therapy, as determined by the prescriber. Examples of a response to therapy include decreased stool frequency or rectal bleeding.

Approval Duration

Initial Approval = 6 months (180 days)
Re-authorization = 1 year (365 days)

CRITERIA NOT RECOMMENDED FOR APPROVAL:

Stelara has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent Biologic Therapy.** Stelara should not be administered in combination with another biologic agent for an inflammatory condition (e.g., TNF antagonists [Cimzia® {certolizumab pegol for SC injection}, Enbrel, Humira, Remicade, or Simponi], or Kineret® [anakinra for SC injection]). Combination therapy with two biologic agents is not recommended due to a higher rate of adverse effects with combinations and lack of additive efficacy.[6]

2. **Ankylosing Spondylitis (AS).** There is a published proof-of-concept trial evaluating Stelara in AS (TOPAS – UsTekinumab for the treatment Of Patients with active Ankylosing Spondylitis).[12] TOPAS was a prospective, open-label study evaluating Stelara 90 mg at Week 0, 4, and 16 in patients (n = 20) with AS. After Week 16, patients were followed through Week 28. Patients who previously failed to respond to TNF blockers were excluded, but patients who discontinued a TNF for reasons other than lack of efficacy were allowed to enroll. The primary endpoint was a 40% improvement in disease activity at Week 24 according to the ASAS criteria (ASAS40). Efficacy analysis was completed in the intent-to-treat (ITT) population which included all patients who received at least one dose of Stelara. In all, 65% of patients (95% confidence interval [CI]: 41%, 85%; n = 13/20) achieved an ASAS40 response at Week 24. There was at least a 50% improvement of the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) achieved by 55% of patients (95% CI: 32%, 77%; n = 11/20); improvement in other secondary endpoints were also noted. However, enthesitis (measured by MASES [Maastricht AS Entheses Score] and SPARCC [SPondyloArthritis Research Consortium of Canada] enthesitis indices) and the number of swollen joints were not significantly improved at Week 24. There was a significant reduction of active inflammation on magnetic resonance imaging (MRI) at Week 24 compared with baseline in sacroiliac joints.

3. **Concurrent use with Otezla.** No evidence to suggest that combination use of Otezla with Stelara is superior to monotherapy.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation and to deny reimbursement when it has determined that the services performed were not medically necessary, investigational and/or a pattern of practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must

be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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Prior approval is required for HCPCS Code J3357, J3358

Edits and Denials:

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Prior Approval: Prior approval is required for Stelara (HCPCS Code J3357 and J3358). Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician consultant for review if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Code J3357 and J3358** will edit with **Remark Code M3M or M4M** and will be adjudicated in accordance with the Corporate Medical Policy.

Liability: A participating provider will be required to write off charges denied as not medically necessary.

HCPCS Code(s):	
J3357	Ustekinumab, for subcutaneous injection, 1 mg
J3358	Ustekinumab, for Intravenous Injection, 1 mg (Effective date 1/1/2018)

Appendix A

	Mechanism of Action	**Examples of Inflammatory Indications***
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PsA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC

Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO IV formulation: CD
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, RA, PsA, UC
Xeljanz® (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indications (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis.