

STRIDESM (HMO) MEDICARE ADVANTAGE**Effective Date: April 15, 2017****Subject: Stelara® (ustekinumab)**

Background: Ustekinumab (Stelara®) is a human interleukin-12 and -23 antagonists approved by the United States Food and Drug Administration (FDA) in September 2009 for treatment of adults (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Supplemental FDA approval was issued in September 2013 for treatment of adults with active psoriatic arthritis (to be used alone or in combination with methotrexate).

- The safety and effectiveness of ustekinumab (Stelara®) in pediatric patients have not been evaluated.

In September 2016, FDA-approved indications were expanded to include treatment of moderately to severely active Crohn's disease in patients 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 blocker.

Ustekinumab (Stelara®) for the treatment of plaque psoriasis and psoriatic arthritis is administered subcutaneously and intended for use under the guidance and supervision of a physician. Ustekinumab (Stelara®) should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

- Ustekinumab (Stelara®) for the maintenance treatment of Crohn's disease is also for subcutaneous administration; however, patients should receive a onetime weight-based loading dose via intravenous infusion.

Ustekinumab (Stelara®) is available through Harvard Pilgrim StrideSM (HMO) medical benefits or pharmacy benefit, depending on how the drug is prescribed, dispensed, or administered. This policy only addresses instances when ustekinumab (Stelara®) is covered under Part B benefits. It does not address instances when ustekinumab (Stelara®) is covered under Part D benefits.

Authorization: Prior authorization from Harvard Pilgrim StrideSM (HMO) is required for all subcutaneous and intravenous use of ustekinumab (Stelara®).

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Harvard Pilgrim StrideSM (HMO) policies are based on medical science and relevant information including current Medicare coverage (including National and Local Coverage Determinations), Harvard Pilgrim medical policies, and Harvard Pilgrim StrideSM (HMO) Medicare Advantage Plan materials. These policies are intended to provide benefit coverage information and guidelines specific to the Harvard Pilgrim StrideSM (HMO) Medicare Advantage Plan. Providers are responsible for reviewing the CMS Medicare Coverage Center guidance; in the event that there is a conflict between this document and the CMS Medicare Coverage Center guidance, the CMS Medicare Coverage Center guidance will control.

Policy and Coverage Criteria:

Harvard Pilgrim StrideSM (HMO) covers ustekinumab (Stelara®) that is medically necessary for adults with moderate to severe plaque psoriasis, active psoriatic arthritis or moderately to severely active Crohn’s disease when treatment is reasonable and medically necessary, and ordered by the attending physician caring for the member.

Ustekinumab (Stelara™) may be authorized when medical record documentation confirms ALL the following:

1. Drug is prescribed by an appropriate specialist (as described below) for a member age 18 years or older;
2. Member has been diagnosed with a listed condition; AND
3. Condition-specific criteria listed below are met.

Condition	Criteria
<p>Plaque Psoriasis (moderate to severe disease)</p> <p>Dosing Recommendations:</p> <ul style="list-style-type: none"> • For patients weighing < 220 lbs (≤100 kg): 45 mg subcutaneous (SC) initially and 4 weeks later, followed by 45 mg SC every 12 weeks. • For patients weighing >220 lbs (100 kg): 90 mg SC initially and 4 weeks later, followed by 90 mg SC every 12 weeks. 	<p>Medical record documentation confirms criteria 1-3 are met:</p> <ol style="list-style-type: none"> 1. Ustekinumab (Stelara™) is prescribed by a board-certified or board-eligible dermatologist; AND 2. ANY of the following: <ul style="list-style-type: none"> • 10% or more body surface area is affected by plaque psoriasis; • 5 % or more of body surface area is affected by plaque psoriasis, AND psoriasis involves sensitive areas (hands, feet, face, or genitals); • Member has a Psoriasis Area and Severity Index (PASI) score of 10 or more; AND 3. EITHER of the following: <ul style="list-style-type: none"> • History of treatment failure after one course of systemic therapy including but not limited to methotrexate, azathioprine, or acitretin; OR • Contraindication to systemic therapy.
<p>Psoriatic Arthritis</p> <p>Dosing Recommendations: 45 mg subcutaneous (SC) initially and 4 weeks later,</p>	<p>Medical record documentation confirms ALL the following:</p> <ol style="list-style-type: none"> 1. Ustekinumab (Stelara™) is prescribed by a board-certified or board-eligible rheumatologist;

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Condition	Criteria
<p>followed by 45 mg SC every 12 weeks.</p> <p>For patients weighing >220 lbs (100 kg), with co-existent moderate-to-severe plaque psoriasis: 90 mg SC initially and 4 weeks later, followed by 90 mg SC every 12 weeks.</p>	<p>AND</p> <p>2. EITHER of the following:</p> <ul style="list-style-type: none"> • History of treatment failure with one oral or injectable disease-modifying anti-rheumatic drug (DMARD) agent including Leflunomide (Arava), Methotrexate (Rheumatrex, Trexall), Hydroxychloroquine (Plaquenil), or Sulfasalazine (Azulfidine); OR • Contraindication to an oral or injectable DMARD.

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Condition	Criteria
<p>Crohn's Disease</p> <p>Dosing Recommendations:</p> <ul style="list-style-type: none"> • For adult patients weighing less than 55 kg (121 lbs): A single intravenous (IV) infusion of 260 mg, followed by a 90 mg subcutaneous (SC) dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter. • For adult patients weighing 55-85 kg (121-187 lbs): A single IV infusion of 390 mg, followed by a 90 mg SC dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter. • For adult patients weighing more than 85 kg (187 lbs): A single IV infusion of 520 mg, followed by a 90 mg SC dose 8 weeks after the initial IV dose, then every 8 weeks thereafter. 	<p>Medical record documentation confirms ALL the following:</p> <ol style="list-style-type: none"> 1. Ustekinumab (Stelara™) is prescribed by a board-certified or board-eligible gastroenterologist; AND

Ongoing treatment is authorized when medical record documentation confirms efficacy of prior course(s) of treatment with ustekinumab (Stelara®), and coverage criteria (above) are met.

Exclusions:

Harvard Pilgrim StrideSM (HMO) does not cover investigational and unproven use of ustekinumab (Stelara®). Use of ustekinumab (Stelara®) is considered investigational and unproven when criteria above are not met.

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Coding:

Codes are listed below for informational purposes. The list may not be all-inclusive, and does not imply or guarantee coverage or provider reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Harvard Pilgrim policies apply.

CPT® Code	
J3357	Injection, ustekinumab, 1 mg (Stelara™)

ICD 10 Code	Description
K50.011	Crohn's Disease Of Small Intestine With Rectal Bleeding
K50.012	Crohn's Disease Of Small Intestine With Intestinal Obstruction
K50.013	Crohn's Disease Of Small Intestine With Fistula
K50.014	Crohn's Disease Of Small Intestine With Abscess
K50.018	Crohn's Disease Of Small Intestine With Other Complication
K50.019	Crohn's Disease Of Small Intestine With Unspecified Complications
K50.111	Crohn's Disease Of Large Intestine With Rectal Bleeding
K50.112	Crohn's Disease Of Large Intestine With Intestinal Obstruction
K50.113	Crohn's Disease Of Large Intestine With Fistula
K50.114	Crohn's Disease Of Large Intestine With Abscess
K50.118	Crohn's Disease Of Large Intestine With Other Complication
K50.119	Crohn's Disease Of Large Intestine With Unspecified Complications
K50.811	Crohn's Disease Of Both Small And Large Intestine With Rectal Bleeding
K50.812	Crohn's Disease Of Both Small And Large Intestine With Intestinal Obstruction
K50.813	Crohn's Disease Of Both Small And Large Intestine With Fistula
K50.814	Crohn's Disease Of Both Small And Large Intestine With Abscess
K50.818	Crohn's Disease Of Both Small And Large Intestine With Other Complication
K50.819	Crohn's Disease Of Both Small And Large Intestine With Unspecified Complications
K50.911	Crohn's Disease, Unspecified, With Rectal Bleeding
K50.912	Crohn's Disease, Unspecified, With Intestinal Obstruction
K50.913	Crohn's Disease, Unspecified, With Fistula
K50.914	Crohn's Disease, Unspecified, With Abscess

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ICD 10 Code	Description
K50.918	Crohn's Disease, Unspecified, With Other Complication
K50.919	Crohn's Disease, Unspecified, With Unspecified Complications
L40.0	Psoriasis Vulgaris
L40.50	Arthropathic Psoriasis, Unspecified
L40.51	Distal Interphalangeal Psoriatic Arthropathy
L40.52	Psoriatic Arthritis Mutilans
L40.53	Psoriatic Spondylitis
L40.59	Other Psoriatic Arthropathy

References:

1. *Highlights of Prescribing Information*. 1st ed.; 2012. Available at: <https://www.stelarainfo.com/pdf/prescribinginformation.pdf>. Accessed March 6, 2017.
2. Medicare Benefit Policy Manual. 1st ed.; 2017. Available at: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c15.pdf>. Accessed March 6, 2017.
3. The American Academy of Dermatology (AAD) has published new guidelines for the management of psoriasis and psoriatic arthritis. *Inpharma Weekly*. 2008;&NA;(1641):2. doi:10.2165/00128413-200816410-00003.
4. Sandborn W, Gasink C, Gao L et al. Ustekinumab Induction and Maintenance Therapy in Refractory Crohn's Disease. *New England Journal of Medicine*. 2012;367(16):1519-1528. doi:10.1056/nejmoa1203572.
5. Treatment of psoriasis. Uptodatecom. 2016. Available at: https://www.uptodate.com/contents/treatment-of-psoriasis?source=search_result&search=treatment%20of%20psoriasis&selectedTitle=1~150. Accessed March 6, 2017.
6. Treatment of psoriatic arthritis. Uptodatecom. 2016. Available at: https://www.uptodate.com/contents/treatment-of-psoriatic-arthritis?source=search_result&search=treatment%20of%20psoriatic%20arthritis&selectedTitle=1~146. Accessed March 6, 2017.
7. Gómez-García F, Epstein D, Isla-Tejera B, Lorente A, Vélez García-Nieto A, Ruano J. Short-term efficacy and safety of new biological agents targeting the interleukin-23-T helper 17 pathway for moderate-to-severe plaque psoriasis: a systematic review and network meta-analysis. *British Journal of Dermatology*. 2016. doi:10.1111/bjd.14814.
8. Muramatsu S, Kubo R, Nishida E, Shintani Y, Morita A. Serum interleukin-6 levels in response to biologic treatment in patients with psoriasis. *Journal of Dermatological Science*. 2016;84(1):e122. doi:10.1016/j.jdermsci.2016.08.366.

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9. Vergou T, Moustou AE, Antoniou C. Five-year experience with Ustekinumab for psoriasis: Real-life data of a single centre. *Journal of the European Academy of Dermatology and Venereology*. 2016;31(1):e40–e41. doi:10.1111/jdv.13658.
10. Ramiro S, Smolen JS, Landewé R, et al. Pharmacological treatment of psoriatic arthritis: A systematic literature review for the 2015 update of the EULAR recommendations for the management of psoriatic arthritis. *Annals of the Rheumatic Diseases*. 2015;75(3):490–498. doi:10.1136/annrheumdis-2015-208466.
11. Zweegers J, Otero M, Reek J, et al. Effectiveness of biologic and conventional systemic therapies in adults with chronic plaque psoriasis in daily practice: A systematic review. *Acta Dermato Venereologica*. 2016;96(4):453–458. doi:10.2340/00015555-2276.
12. Michaels BD, Del Rosso JQ. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. *Yearbook of Dermatology and Dermatologic Surgery*. 2012;2012:115–116. doi:10.1016/j.yder.2012.02.093.
13. Lebwohl M. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 5. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. *Yearbook of Dermatology and Dermatologic Surgery*. 2011;2011:113–114. doi:10.1016/j.yder.2011.02.069. Menter, A., Korman, NJ., Elmets, CA., et al. Guidelines of care for the management off 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(4): 643-59.
14. Menter, A., Korman, NJ., Elmets, CA., et al. Guidelines of care for the management off psoriasis and psoriatic arthritis: Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermtol*. 2009; 61(3): 451-85.
15. Gottlieb, A., Korman, NJ., Gordon, KB., et al. Guidelines of care for the management off psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. *J Am Acad Dermatol*. 2008; 58(5): 851-64.
16. Toedter GP, Blank M, Lang Y, Chen D, Sandborn WJ, de Villiers WJS. Relationship of C-Reactive protein with clinical response after therapy with Ustekinumab in Crohn’s disease. *The American Journal of Gastroenterology*. 2009;104(11):2768–2773. doi:10.1038/ajg.2009.454.
17. Sandborn, WJ., Feagan, BG., Fedorak, RN., et al. A randomized trial of Ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with moderate-to-severe Crohn’s disease. *Gastroenterology*. 2008; 135(4):1130-41.

Summary of Changes:

Date	Revision
1/11/17	Updated language and criteria for Crohn’s disease
12/14/16	Revised format, language. Delete language re: duration of authorization/re-authorization. Add background information, dosing recommendations, info

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	re: expanded FDA approved indications. Clarify exclusion for experimental and investigational use. Update references, coding.
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Approved by UMPCP: 1/11/17

- **Revised: 12/16; 1/17**
- **Initial Approval: 7/27/16**

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