Pharmacy Management Drug Policy

SUBJECT: Stelara ® (Ustekinumab) – for Crohn's Disease, Plaque Psoriasis and Psoriatic Arthritis
POLICY NUMBER: Pharmacy-59
ANNUAL REVIEW DATE: 1/1/2021
EFFECTIVE DATE: 9/25/2014 LAST
REVIEW DATE: 2/27/2020

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Stelara® (Ustekinumab) is a human monoclonal antibody that binds to and interferes with the proinflammatory cytokines, interleukin 12 (IL-12) and IL-23. Biological effects of IL-12 and IL-23 include natural killer cell activation and CD4+ T-cell differentiation and activation. Ustekinumab also interferes with the expression of monocyte chemotactic protein-1, tumor necrosis factor-alpha, interferon-inducible protein-10, and IL-8. Significant clinical improvement in psoriasis and psoriatic arthritis patients is seen in association with reduction of these proinflammatory signalers

Stelara® is indicated for:

- the treatment of adult and pediatric patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate
- reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis alone or in combination with methotrexate
- the treatment of moderately to severely active Crohn's disease in adult patients who have failed or were intolerant to treatment with immunomodulators or corticosteroids but never failed treatment with a tumor necrosis factor (TNF) blocker, OR who failed or were intolerant to treatment with one or more TNF blockers

Stelara® can be administered by a healthcare professional or can be self-administered if individual has been trained by a health care professional.

- If administered by a healthcare professional, it goes under the medical benefit.
- If self-administered, it goes under the pharmacy (Rx) benefit.

POLICY:

Based upon our assessment and review of the peer-reviewed literature Stelara® has been medically proven to be effective and therefore, **medically necessary** for the treatment of the following diagnoses if specific criteria are met:

A. Plaque Psoriasis

1. Member must be followed by a dermatologist or rheumatologist **AND**
2. Member must be at least 12 years of age **AND**
3. Member must have moderate to severe chronic plaque psoriasis that involves at least 10% of their body surface area. Consideration will be given to those who have severe disease of the hands or feet or other areas causing disruption in normal activities, but have less than 10% body surface area involvement. **AND**

4. Member must be a candidate for systemic therapy, i.e. Acitretin, methotrexate, or cyclosporine with a trial period of at least 3 months. If contraindications are present or had developed severe intolerance to the above-mentioned agents before 3 months, a trial of one of the other three criteria listed below must be present **OR**
5. If member does not qualify as stated above in **"4"**, then one of the following must be attempted for a reasonable period of time (at least 3 months):
    - **a.** UVB in combination with a topical therapy such as coal tar, steroids or tazarotene **OR**
    - **b.** PUVA in combination with topical corticosteroids **OR**
    - **c.** Medium/High potency topical steroids in combination with anthralin, calcipotriene, or tazarotene
6. Approved dosing is in chart listed below on page 3.

B. <u>Psoriatic Arthritis</u>

1. A diagnosis of definitive psoriatic arthritis established by a Rheumatologist or Dermatologist **AND**
2. Member must be at least 18 years of age **AND**
3. Member must be actively followed by and the drug prescribed by a Rheumatologist or Dermatologist **AND**
4. Member must have some clinical features of psoriatic arthritis such as: involvement of the DIP joints, an asymmetric distribution of joint disease, spondyloarthritis, sausage digits, new bone formation on radiographs, cutaneous findings, and the characteristic nail manifestations of psoriatic arthritis (nail pitting, onycholysis & other lesions, which include leukonychia, red spots in the lunula, and nail plate crumbling) all may be present.
5. Can be used alone or in combination with methotrexate or other DMARD (hydroxychloroquine, leflunomide, or sulfasalazine).
6. Approved dosing is in chart listed on page 3.

C. <u>Crohn's Disease</u>

1. Patient must have a diagnosis of moderately to severely active Crohn's disease made by a gastroenterologist [moderate to severe disease = Crohn's Disease Activity Index (CDAI) score of 220-450, typically described as having more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting or significant anemia] **AND**
2. Patient must be at least 18 years of age **AND**
3. Patient meets at least one of the following criteria:
    - **a.** Patient continues to experience disease flare despite complete and adequate therapy with a corticosteroid (such as prednisone or budesonide). Typically, response is noted within 14 days of initiating therapy **OR**
    - **b.** Patient is steroid-dependent (unable to taper off of steroids) despite treatment with azathioprine, 6-mercaptopurine or methotrexate **OR**
    - **c.** Documentation is provided that azathioprine, 6-mercaptopurine is ineffective, contraindicated, or not tolerated

4. Approved dosing:
   - **a.** Induction dosing - At week 0, a one-time weight-based IV loading dose (260 mg [55 kg or less], 390 mg [more than 55 kg to 85 kg], or 520 mg [more than 85 kg]) is given by a healthcare professional. This will be paid for under the medical benefit.
   - **b.** Maintenance dosing - starting at week 8, Stelara 90mg is given subcutaneously every 8 weeks. This can be self-injected under the Rx benefit or given subcutaneously by a healthcare professional under the medical benefit.

D. Ulcerative Colitis

1. Member must be actively followed by and the drug prescribed by a gastroenterologist AND
2. There must be documentation of failure or serious side effects to at least 2 of the following conventional therapies for at least 3 months:
   a. Thiopurines: azathioprine/6-mercaptopurine (6-MP)
   b. 5-Aminosalicylates: sulfasalazine, mesalamine, olsalazine
   c. Cyclosporine
   d. IV or oral steroids
3. Member must have had drug failure or serious side effects with Humira
4. Approved dosing:
   a. Induction dosing - At week 0, a one-time weight-based IV loading dose (260 mg [55 kg or less], 390 mg [more than 55 kg to 85 kg], or 520 mg [more than 85 kg]) is given by a healthcare professional. This will be paid for under the medical benefit.
   b. Maintenance dosing - starting at week 8, Stelara 90mg is given subcutaneously every 8 weeks. This can be self-injected under the Rx benefit or given subcutaneously by a healthcare professional under the medical benefit.

Dosing guidelines for Plaque Psoriasis (PP):

- **Initial request**: Week 0, 4 and then every 12 weeks thereafter
- **If dose or frequency increase is requested:** see 3rd column

If patient weighs:	Initial dose	If partial response by week 28 (or later)*:
≤ 100kg	45mg week 0, 4, 16, 28, etc.	90mg every 12 weeks; May increase to 90mg every 8 weeks after 24 weeks (or 3 doses) of 90mg every 12 weeks
> 100kg (TNF- naïve)	45mg week 0, 4, 16 etc. (may increase to 90mg every 12 weeks @ week 16 if no response)	90mg every 8 weeks if already on 90mg dose (by week 28)
> 100kg (previous TNF use)	90mg week 0, 4, 16, 28, etc.	90mg every 8 weeks
> 100kg and co-existent PP and PsA, regardless of TNF-history	90mg week 0, 4, 16, 28, etc.	90mg every 8 weeks

- **Pediatric dosing SC (> 12 years of age):**
  - **≤ 60kg: 0.75mg/kg at weeks 0, 4, and every 12 weeks thereafter**
  - **60kg to 100kg: 45mg at weeks 0, 4, and every 12 weeks thereafter**
  - **> 100kg: 90mg at weeks 0, 4, and every 12 weeks thereafter**

Dosing guidelines for Psoriatic Arthritis (PsA):

- **Initial request**: Week 0, 4 and then every 12 weeks thereafter
- **If dose or frequency increase is requested:** see 3rd column

If patient weighs:	Initial dose	If partial response by week 28 (or later)*:
Any weight	45mg week 0, 4, 16, 28, etc.	90mg every 12 weeks; May increase to 90mg every 8 weeks after 24 weeks (or 3 doses) of 90mg every 12 weeks
> 100kg (and previous TNF use)	90mg week 0, 4, 16, 28, etc.	90mg every 8 weeks
> 100kg and co-existent PP and PsA, regardless of TNF-history	90mg week 0, 4, 16, 28, etc.	90mg every 8 weeks

***** If there is **no response** to initial dosing other than increasing from 45mg to 90mg at week 16 if patient weighs > 100kg, then the dose increase request will **NOT** be allowed.

APPROVAL TIME PERIODS:

Line of Business	Rx Initial approval	Rx Recertification	Medical Initial approval	Medical Recertification
Medicaid Managed Care (MMC)/Child Health Plus (CHP)	2 years	2 years	6 months	12 months
Commercial/Exchange	2 years	2 years	Outpatient hospital: 6 months	Outpatient hospital: 6 months
			Home Care/Office Based: 2 years	Home Care/Office Based: 2 years
Medicare	Already defined in policy	Already defined in policy	Outpatient hospital: 6 months	Outpatient hospital: 6 months
			Home Care/Office Based: 2 years	Home Care/Office Based: 2 years

POLICY GUIDELINES:

1. Prior-authorization is contract dependent.
2. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.;

generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

3. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.
4. If Stelara® is being self-administered, it will be paid for under the pharmacy benefit. If Stelara® is being given in the office or by a healthcare professional, it would then go under the medical benefit.
5. Requests for 45 mg every 8 weeks will be denied as off label as there is no efficacy data for any weight.
6. Requests for any dose or frequency greater than 90mg every 8 weeks will be denied as there is no data available showing this is safe or effective.
7. While the FDA-approved dosing for persons weighing > 100kg with psoriasis is to start with 90mg dose, the 45mg dose was effective in clinical trials (PASI 75 response at week 12: 54% vs 68% in 45mg and 90mg, respectively). We will allow the dose increase to 90mg by week 16 if little to no improvement.
8. Involvement of the DIP joints, an asymmetric distribution of joint disease, spondyloarthritis, sausage digits, new bone formation on radiographs, cutaneous findings, and the characteristic nail manifestations of psoriatic arthritis all help to distinguish psoriatic arthritis from other inflammatory arthritis, including RA.
9. Stelara® is **not to be used in immunocompromised patients** due to the possible risk of serious infection
10. Stelara may increase the risk for malignancy although the impact on the development and course of malignancies is not fully defined. Rapidly appearing cutaneous squamous cell carcinomas (multiple) have been reported in patients receiving ustekinumab who were at risk for developing nonmelanoma skin cancer. Monitor all patients closely for the development of nonmelanoma skin cancer; closely follow patients >60 years of age, with a history of prolonged immunosuppression, and in patients with a history of PUVA treatment. Use with caution in patients with prior malignancy (use not studied in this population).
11. Tuberculosis (frequently disseminated or extrapulmonary at clinical presentation), invasive fungal infections, and other opportunistic infections have been observed in patients receiving Stelara®. All patients being considered for biologic therapy should be screened for latent tuberculosis infection, regardless of the presence of risk factors. Annual testing is recommended for patients who live, travel, or work in situations where tuberculosis exposure is likely.
12. Patients should not receive live attenuated herpes zoster vaccine while receiving Stelara®; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants.
13. Stelara, as well as other immunomodulating biologics not listed in this policy (Humira, Enbrel, Stelara, Cimzia, Remicade and biosimilars) should not be administered in combination with another biologic or targeted synthetic DMARD used for an inflammatory condition. Combination therapy is generally not recommended due to the added risk of immunosuppression, potential for a higher rate of adverse effects, and lack of evidence for additive therapy. NOTE: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with biologics and targeted synthetic DMARDs.

UPDATES:

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1/2020	Revised
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7/17	Revised
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REFERENCES:

1. Stelara (Ustekinumab) [package insert]. Horsham, PA: Janssen Biotech. Revised September 2016 Accessed Online June 2017.
2. Andrulonis R, Ferris LK. Treatment of severe psoriasis with ustekinumab during pregnancy. *J Drugs Dermatol*. 2012;11(10):1240.
3. Papp KA, Langley RG, Lebwohl M, et al, "Efficacy and Safety of Ustekinumab, a Human Interleukin-12/23 Monoclonal Antibody, in Patients with Psoriasis: 52-Week Results from a Randomised, Double-Blind, Placebo-Controlled Trial (PHOENIX 2)," *Lancet*, 2008, 371(9625):1675-84.
4. Papp KA, Griffiths CE, Gordon K, et al, "Long-Term Safety of Ustekinumab in Patients with Moderate-to-Severe Psoriasis: Final Results from 5 Years of Follow-Up," *Br J Dermatol*, 2013, 168(4):844-54.
5. Leonardi CL, Kimball AB, Papp KA, et al, "Efficacy and Safety of Ustekinumab, a Human Interleukin-12/23 Monoclonal Antibody, in Patients With Psoriasis: 76-Week Results from a Randomised, Double-Blind, Placebo-Controlled Trial (PHOENIX 1)," *Lancet*, 2008, 371(9625):1665-74.
6. Galvan-Banqueri M, Marin Gil R, Santos Ramos, B, et al, "Biological Treatments for Moderate-to-Severe Psoriasis: Indirect Comparison," *J Clin Pharm Ther*, 2013, 38(2):121-30.
7. Sandborn WJ, Gasink C, Gao LL, et al. "Ustekinumab induction and maintenance therapy in refractory Crohn's disease." *N Engl J Med*. 2012 Oct;367(16):1519-28.
8. McInnes IB, Kavanaugh A, PSUMMIT 1 Study Group, et al. Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial." *Lancet*. 2013;382(9894):780.
9. Gottlieb A, Menter A, et al. "Ustekinumab, a human interleukin 12/23 monoclonal antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial." *Lancet*. 2009;373(9664):633
10. Alice Gottlieb, Neil J. Korman, Kenneth B. Gordon, Steven R. Feldman, Mark Lebwohl, John Y.M. Koo, Abby S. Van Voorhees, Craig A. Elmets, Craig L. Leonardi, Karl R. Beutner, Reva Bhushan, Alan Menter Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: Overview and guidelines of care for treatment with an emphasis on the biologics *Journal of the American Academy of Dermatology*, *Volume 58, Issue 5*, *May 2008*, *Pages 851-864*
11. Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. *Archives of dermatology.* Jan 2012;148(1):95-102.
12. Ritchlin C, Rahman P, Kavanaugh A, et al: Efficacy and safety of the anti-IL-12/23 p40 monoclonal antibody, ustekinumab, in patients with active psoriatic arthritis despite conventional non-biological and

biological anti-tumour necrosis factor therapy: 6-month and 1-year results of the phase 3, multicentre, double-blind, placebo-controlled, randomised PSUMMIT 2 trial. Ann Rheum Dis 2014;
13. Engel T, Kopylov U: Ustekinumab in Crohn's disease; evidence to date and place in therapy. *Ther Adv Chronic Dis*. 2016 Jul; 7(4):208-214.
14. Harris K, Horst S, et al.: Patients with Refractory Crohn's Disease Successfully Treated with Ustekinumab. *Inflamm Bow Dis.* 02/2016 Volume 22, Issue 2.
15. Feagen BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2016;375:1946-1960.