ustekinumab (Stelara™)

**Policy #** 00242  
**Original Effective Date:** 11/18/2009  
**Current Effective Date:** 11/16/2016

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

**When Services May Be Eligible for Coverage**
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:
- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

**Plaque Psoriasis**
Based on review of available data, the Company may consider the use of ustekinumab (Stelara™)† for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy to be eligible for coverage.

**Patient Selection Criteria**
Coverage eligibility will be considered for ustekinumab (Stelara) for the treatment of plaque psoriasis when all of the following criteria are met:
- Patient is 18 years of age or older; and
- Patient has moderate to severe plaque psoriasis; and
- Patient has a negative purified protein derivative (PPD) test prior to treatment; and
- Patient has greater than 10% of body surface area or less than or equal to 10% body surface area with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).
- Patient has failed to respond to an adequate trial of one of the following treatment modalities:
  - Ultraviolet B; or
  - Psoralen positive Ultraviolet A; or
  - Systemic therapy (i.e. methotrexate, cyclosporine, acitretin).
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).

**Note:** FDA recommended dosage for patients weighing ≤ 100kg (220lbs) is 45mg initially and 4 weeks later, followed by 45mg every 12 weeks.

FDA recommended dosage for patients weighing > 100kg (220lbs.) is 90mg initially and 4 weeks later, followed by 90mg every 12 weeks.

**Psoriatic Arthritis**
Based on review of available data, the Company may consider the use of ustekinumab (Stelara) for the treatment of psoriatic arthritis to be eligible for coverage.
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Patient Selection Criteria
Coverage eligibility for the use of ustekinumab (Stelara) for the treatment of psoriatic arthritis will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; and
- Patient has active psoriatic arthritis; and
- Ustekinumab (Stelara) is used alone or in combination with methotrexate; and
- Patient has a negative purified protein derivative (PPD) test prior to treatment.
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs).
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)

Note: FDA recommended dosage is 45mg initially and 4 weeks later, followed by 45mg every 12 weeks.

For patients with co-existent moderate to severe plaque psoriasis weighing >100kg, the recommended dose is 90mg initially and 4 weeks later, followed by 90mg every 12 weeks.

Crohn’s Disease
Based on review of available data, the Company may consider the use of ustekinumab (Stelara) for the treatment of moderately to severely active Crohn’s disease to be eligible for coverage.

Patient Selection Criteria
Coverage eligibility for the use of ustekinumab (Stelara) for the treatment of Crohn’s Disease will be considered when all of the following criteria are met:

- Patient has a diagnosis of moderately to severely active Crohn’s disease; and
- Patient is 18 years of age or older; and
- Patient has failed or become intolerant to treatment with immunomodulators (e.g. azathioprine, 6-mercaptopurine) or corticosteroids OR the patient has failed or become intolerant to a tumor necrosis factor (TNF) blocker (e.g. Remicade®, Humira®); and
- Stelara is NOT being use concurrently with other biologic products (e.g. Humira, Remicade) for the treatment of moderately to severely active Crohn’s disease; and
- Patient has a negative purified protein derivative (PPD) test prior to treatment

Note: FDA recommended dosage is use of an initial Stelara intravenous infusion based on body weight (260 mg for those up to 55kg, 390 mg for those greater than 55 kg to 85 kg, or 520 mg for those greater than 85 kg) followed by subcutaneous Stelara 90 mg every 8 weeks thereafter (beginning 8 weeks after the initial intravenous infusion).

When Services Are Considered Investigational
Note: Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.
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Based on review of available data, the Company considers the use of ustekinumab (Stelara) when patient selection criteria are not met to be investigational* (with the exception of those denoted above as not medically necessary**).

Based on review of available data, the Company considers the use of ustekinumab (Stelara) for indications other than those listed above to be investigational.*

When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers the use of ustekinumab (Stelara) when any of the following criteria for their respective disease state listed below (and denoted in the patient selection criteria above) are not met to be not medically necessary**:

- For plaque psoriasis
  o Patient has greater than 10% of body surface area or less than or equal to 10% body surface area with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia)
  o Patient has failed to respond to an adequate trial of one of the following treatment modalities:
    - Ultraviolet B; or
    - Psoralen positive Ultraviolet A; or
    - Systemic therapy (i.e. methotrexate, cyclosporine, acitretin).

- For psoriatic arthritis
  o Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs)

Background/Overview
Stelara is a monoclonal antibody that inhibits proteins that contribute to the overproduction of skin cells. It is a biologic drug that inhibits interleukin-12 and interleukin-23. Stelara is available in 45 mg and 90 mg subcutaneous dosage forms as well as 130 mg single dose vials. The vials are only used for the treatment of Crohn’s Disease.

Plaque Psoriasis
Psoriasis is a common skin condition that is characterized by frequent episodes of redness, itching and thick, dry silvery scales on the skin. It is most commonly seen on the trunk, elbows, knees, scalp, skin folds and fingernails. This condition can appear suddenly or gradually and may affect people of any age; it most commonly begins between the ages of 15 and 35. Psoriasis is not contagious. It is an inherited disorder related to an inflammatory response in which the immune system targets the body’s own cells. It may be severe in immunosuppressed people or those who have other autoimmune disorders such as rheumatoid arthritis. The diagnosis is based on the appearance of the skin. A skin biopsy or scraping and culture of the skin patch may be needed to rule out other disorders. If joint pain is present and persistent, an x-ray may be used to evaluate for psoriatic arthritis. Treatment is focused on control of the symptoms and prevention of secondary infections. Lesions that cover all or most of the body may be acutely painful and require hospitalization. The body loses vast quantities of fluid and becomes susceptible to severe secondary infections that can involve internal organs and even progress to septic shock.
Psoriatic Arthritis
Psoriatic arthritis is an inflammatory arthritis that occurs in individuals with psoriasis. The arthritic portion typically presents asymmetrically and the psoriasis may precede or follow joint involvement. The joints most commonly affected are the distal interphalangeal joints of the fingers and toes. Diagnosis of psoriatic arthritis requires both clinical and radiological observations. In patients with psoriatic arthritis, the arthritic remissions tend to be more frequent and complete than rheumatoid arthritis, but progression to chronic arthritis with crippling can occur. Treatment for psoriatic arthritis is similar to that of rheumatoid arthritis and included disease modifying anti-rheumatic drugs, such as methotrexate. Phototherapy may also be an effective treatment option.

Crohn's Disease
Crohn's disease is a chronic autoimmune disease that can affect any part of the gastrointestinal tract but most commonly occurs in the ileum. As a result of the immune attack, the intestinal wall becomes thick, and deep ulcers may form. In addition to the bowel abnormalities, Crohn's disease can also affect other organs in the body. Typically, first line treatments such as corticosteroids, 6-MP and azathioprine are used to treat this condition.

FDA or Other Governmental Regulatory Approval
The FDA approved Stelara on September 25, 2009, for the treatment of adult patients (18 years of age or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. In September of 2013, Stelara was approved for the treatment of adults with active psoriatic arthritis. In September of 2016, Stelara gained FDA approval for the treatment of moderately to severely active Crohn's disease in those that have failed standard therapy (corticosteroids, immunomodulators) or those that have failed therapy with a TNF blocker.

Rationale/Source
This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Plaque Psoriasis
Stelara was evaluated for the treatment of plaque psoriasis in two multicenter, randomized, double-blind, placebo-controlled studies (Ps Study 1 and Ps Study 2). These studies enrolled 1,996 patients age 18 years of age and older with plaque psoriasis who had a minimum body surface area involvement of 10% and were candidates for phototherapy or systemic therapy. The patients were given either placebo, Stelara 45 mg of Stelara 90 mg. In both studies, the endpoints were the proportion of subjects who achieved at least a 75% reduction in the PASI score (PASI 75) from baseline to week 12 and treatment success on the Physician's Global Assessment. In regards to the primary endpoints in Ps Study 1, 3% of placebo patients
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reached PASI 75 vs. 67% in the Stelara 45 mg group vs. 66% in the Stelara 90 mg group. In regards to the primary endpoints in Ps Study 2, 4% of placebo patients reached PASI 75 vs. 67% in the 45 mg group vs. 76% in the 90 mg group.

Psoriatic Arthritis
Stelara was evaluated in psoriatic arthritis in two randomized, double-blind, placebo-controlled studies in adult patients with psoriatic arthritis despite therapy with non-steroidal anti-inflammatory drugs or disease modifying anti-rheumatic agents. These studies included 927 patients, and those patients were randomized to receive Stelara 45 mg, 90 mg, or placebo. The primary endpoint of the studies was the percentage of patients achieving ACR20 response at week 24. In both studies, a greater proportion of patients achieved ACR 20, ACR 50, and PASI 75 response in the Stelara 45 mg and 90 mg groups compared to placebo at week 24. In PsA study 1, ACR20 was achieved in 23% of placebo patients, 42% of Stelara 45 mg patients, and 50% of Stelara 90 mg patients. In PsA study 2, ACR20 was achieved in 20% of placebo patients, 44% of Stelara 45 mg patients, and 44% of Stelara 90 mg patients.

Crohn’s Disease
Stelara was evaluated in 3 randomized, double-blind, placebo-controlled clinical studies in adult patients with moderately to severely active Crohn’s disease. There were two 8-week intravenous induction studies (CD-1 and CD-2) followed by a 44-week subcutaneous randomized withdrawal maintenance study (CD-3) representing 52 weeks of therapy.

For CD-1 and CD-2, induction of clinical response at week 6 and clinical remission at week 8 was evaluated. CD-1 included patients that had failed or were intolerant to TNF inhibitors, while CD-2 included patients that were intolerant or had failed treatment with steroids, an immunomodulator, or both. There were 1,409 patients randomized in these two trials. The clinical response at week 6 for the placebo groups was 21% and 29% in trials CD-1 and CD-2, respectively. The clinical response at week 6 in the Stelara group was 34% and 56% for trials CD-1 and CD-2, respectively. The clinical remission at week 8 was 7% and 20% in the placebo groups for trials CD-1 and CD-2, respectively. The clinical remission at week 8 was 21% and 40% for trials CD-1 and CD-2, respectively. In these two studies, a greater proportion of patients treated with Stelara achieved clinical response at week 6 and clinical remission at week 8 compared to placebo. Clinical response and remission were significant as early as week 3 in Stelara treated patients and continued to improve through week 8.

CD-3 (the maintenance study) evaluated 388 patients who achieved clinical response at week 8 of induction with Stelara in studies CD-1 and CD-2. Patients were randomized to receive subcutaneous Stelara 90 mg every 8 week of placebo for 44 weeks. At 52 weeks from initiation of the induction dose, 36% of placebo patients had reached a clinical remission vs. 53% of patients in the Stelara treatment group. At the same time point, 44% of placebo patients had a clinical response vs. 59% in the Stelara group. At week 44, 47% of patients who received Stelara were steroid free and in clinical remission compared to 30% of patients in the placebo group.

References
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11/12/2009 Medical Policy Committee approval
11/04/2010 Medical Policy Committee approval
11/16/2010 Medical Policy Implementation Committee approval. No change to policy coverage.
11/03/2011 Medical Policy Committee review
11/01/2012 Medical Policy Committee review
05/02/2013 Medical Policy Committee review
05/22/2013 Medical Policy Implementation Committee approval. Reworded and reformatted the coverage section for clarity. Coverage eligibility unchanged.
10/10/2013 Medical Policy Committee review
10/16/2013 Medical Policy Implementation Committee approval. Added the new indication of Psoriatic Arthritis. Added criteria that requires Humira AND Enbrel prior to use of Stelara for Plaque psoriasis and psoriatic arthritis. Changed title since the drug gained a new indication. Modified the not medically necessary section to reflect changes.
10/02/2014 Medical Policy Committee review
10/15/2014 Medical Policy Implementation Committee approval. Removed the requirement that Humira AND Enbrel be used prior to Stelara.
10/08/2015 Medical Policy Committee review
10/21/2015 Medical Policy Implementation Committee approval. No change to coverage.
11/03/2016 Medical Policy Committee review
11/16/2016 Medical Policy Implementation Committee approval. Added the new indication for Crohn’s Disease. Updated Background info/rationale to coincide with new indication.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
04/01/2017 Coding update
07/01/2017 Coding update
Next Scheduled Review Date: 11/2017

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2015 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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<td>ICD-10 Diagnosis</td>
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community;
3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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