BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Ustekinumab (Stelara™)

Policy # 00242
Original Effective Date: 11/18/2009
Current Effective Date: 01/01/2014

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™)‡ ǂ 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 failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product (unless there is clinical evidence or patient history that suggests that the these products will be ineffective or cause an adverse reaction to the patient); 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.)*
- 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: Recommended dosage for patients weighing ≤ 100kg (220lbs) is 45mg initially and 4 weeks later, followed by 45mg every 12 weeks.

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

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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**.

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 failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs); 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 treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product (unless there is clinical evidence or patient history that suggests that the these products will be ineffective or cause an adverse reaction to the patient); 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 a negative purified protein derivative (PPD) test prior to treatment.

Note: 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.*

When Services Are Considered Investigational
Note: Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

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

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- Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product
- 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)
- 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
  - Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs)
  - Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product

Background/Overview

Ustekinumab 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. Since it affects the immune system, Ustekinumab may increase a patient's risk of infection and certain types of cancer.

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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
The FDA approved Ustekinumab (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. Stelara has been approved with Risk Evaluations and Mitigation Strategy (REMS) to ensure that benefits outweigh risks associated with the use of the medication. The REMS for Stelara includes a communication plan for healthcare providers and a medication guide for patients.

Centers for Medicare and Medicaid Services (CMS)
The CMS has no national coverage policy regarding Stelara for the treatment of psoriasis.

Rationale/Source

Individuals genetically deficient in IL-12/IL-23 are particularly vulnerable to disseminated infections from mycobacteria (including nontuberculous, environmental mycobacteria), salmonella (including nontyphi strains), and Bacillus Calmette-Guerin (BCG) vaccinations. Serious infections and fatal outcomes have been reported in such patients. It is not known whether patients with pharmacologic blockade of IL-12/IL-23 from treatment with Stelara will be susceptible to these types of infections. Appropriate diagnostic testing should be considered, e.g., tissue culture, stool culture, as dictated by clinical circumstances.

Stelara may increase the risk of infections and reactivation of latent infections. Serious bacterial, fungal and viral infections were observed in subjects receiving Stelara. Stelara should not be given to patients with any clinically important active infection. Stelara should not be administered until the infection resolves or is adequately treated. Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. Exercise caution when considering the use of Stelara in patients with a chronic infection or a history of recurrent infection. Serious infections requiring hospitalization occurred in the psoriasis development program. These serious infections included cellulitis, diverticulitis, osteomyelitis, viral infections, gastroenteritis, pneumonia and urinary tract infections.

Evaluate patients for tuberculosis infection prior to initiating treatment with Stelara. Do not administer Stelara to patients with active tuberculosis. Initiate treatment of latent tuberculosis prior to administering Stelara. Consider anti-tuberculosis therapy prior to initiation of Stelara in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed. Patients receiving Stelara should be monitored closely for signs and symptoms of active tuberculosis during and after treatment.

Stelara is an immunosuppressant and may increase the risk of malignancy. Malignancies were reported among subjects who received Stelara in clinical studies. In rodent models, inhibition of IL-12/IL-23p40 increased the risk of malignancy.

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The safety of Stelara has not been evaluated in patients who have a history of malignancy or who have a known malignancy.

One case of reversible posterior leukoencephalopathy syndrome (RPLS) was observed during the clinical development program which included 3,523 Stelara -treated subjects. The subject, who had received 12 doses of Stelara over approximately 2 years, presented with headache, seizures and confusion. No additional Stelara injections were administered and the subject fully recovered with appropriate treatment. RPLS is a neurological disorder not caused by demyelination or a known infectious agent. RPLS can present with headache, seizures, confusion and visual disturbances. Conditions with which it has been associated include preeclampsia, eclampsia, acute hypertension, cytotoxic agents and immunosuppressive therapy. Fatal outcomes have been reported. If RPLS is suspected, Stelara should be discontinued and appropriate treatment administered.

References

1. Ustekinumab (Stelara) [package insert]. Horsham, PA; Janssen Biotech, Inc., Revised September 2013.
2. U.S. Food and Drug Administration. Center for Drug Evaluation and Research. FDA Labeling Information. Ustekinumab (Stelara)® *http://www.fda.gov.*

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines (BCBSLAMPCG) are obtained from Current Procedural Terminology (CPT®)‡, copyright 2012 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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CPT is a registered trademark of the American Medical Association.

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

Code Type	Code
CPT	No code
HCPCS	J3357
ICD-9 Diagnosis	696.1 thru 696.8
ICD-9 Procedure	No code

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11/12/2009	Medical Policy Committee approval
11/18/2009	Medical Policy Implementation Committee approval. New policy.
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
11/16/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/01/2012	Medical Policy Committee review
11/28/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
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.

Next Scheduled Review Date: 10/2014

*****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. Food and Drug Administration (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; or
    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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.