Corporate Medical Policy

Ustekinumab (Stelara®)

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Origination:	02/2010
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Description of Procedure or Service

Plaque psoriasis is the most common form of psoriasis. It is characterized by raised, inflamed, red lesions covered with a silvery-white buildup of dead skin cells (scales). These are found primarily on the trunk, elbows, knees, scalp and finger or toe nails. The cause of psoriasis is related to the immune system, and more specifically, a type of white blood cell called a T lymphocyte or T cell. Normally, T-cells travel throughout the body to detect and fight off foreign substances, such as viruses or bacteria. If you have psoriasis, however, the T-cells attack healthy skin cells by mistake as if to heal a wound or to fight an infection. Normally, skin cells mature and shed after about a month. In psoriasis, the cell maturation speeds up, taking only three to four days. Because the lower layer of skin cells divides more rapidly than normal, dead cells accumulate in thicker patches on the skin's outermost layer (called the epidermis). Chief complaints of patients with moderate to severe psoriasis include scaling, itching, redness, and tightness of the skin with burning sensations. Exposed skin, especially cracked or bleeding areas, can act as potential sites of infection. Approximately 10% of patients who have psoriasis also develop an associated inflammation of their joints. Patients who have inflammatory arthritis and psoriasis are diagnosed as having psoriatic arthritis. Psoriatic arthritis can cause inflammation in body tissues away from the joints other than the skin, such as in the eyes, heart, lungs, and kidneys.

Initial treatment for stable plaque psoriasis is topical, including corticosteroids, emollients, anthralin, tar, retinoids, calcipotriene (Vitamin D analogue), and salicylic acid. Though corticosteroids are the mainstay of topical therapy, continuous use of these agents can cause tachyphylaxis (wearing off effect) and several side effects. Other treatments for plaque psoriasis include phototherapy, immunosuppressants, and systemic retinoids. Conservative treatment for psoriatic arthritis involves a combination of anti-inflammatory medications (NSAIDs) and exercise. If progressive inflammation and joint destruction occur despite NSAIDs treatment, more potent medications such as methotrexate (Rheumatrex, Trexall), corticosteroids, and antimalarial medications (such as hydroxychloroquine, or Plaquenil) may be used.

Crohn's disease is an idiopathic, chronic inflammatory condition that affects the intestinal tract. It can occur anywhere in the GI tract from the mouth to the anus. The characteristic presentation in Crohn's disease is abdominal pain and diarrhea, which may be complicated by intestinal fistulization or obstruction. Unpredictable flares and remissions characterize the long-term course.

Ustekinumab (Stelara®) is a human IgG1κ monoclonal antibody that binds with high affinity and specificity to the p40 protein subunit used by both the interleukin (IL)-12 and IL-23 cytokines. IL-12 and IL-23 are naturally occurring cytokines that are involved in inflammatory and immune responses, such as natural killer cell activation and CD4+ T-cell differentiation and activation. In *in vitro* models, ustekinumab was shown to disrupt IL-12 and IL-23 mediated signaling and cytokine cascades by disrupting the interaction of these cytokines with a shared cell-surface receptor chain, IL-12 β1.

Ustekinumab (Stelara®) is indicated for:

- the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.
- the treatment of adult patients with active psoriatic arthritis, alone or in combination with methotrexate.
- the treatment of adult patients with moderately to severely active Crohn's disease who have failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker or have failed or were intolerant to treatment with one or more TNF blockers.
- the treatment of adolescent patients (12 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Related Policies:

Infliximab
Light Therapy for Dermatologic Conditions
Ultraviolet Light Therapy in the Home Setting (UVB)
Measurement of Serum Antibodies to Infliximab, Adalimumab, Vedolizumab and Ustekinumab

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for Ustekinumab (Stelara®) when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

Please refer to Certificate for availability of benefits. This policy relates only to the services or supplies described herein. Benefits may vary according to benefit design, therefore certificate language should be reviewed before applying the terms of the policy.

Coverage for Ustekinumab (Stelara®) requires prior review.

When Ustekinumab (Stelara®) is covered

Ustekinumab (Stelara®) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis in adult patients if:

1. One of the following:
   a) the patient has tried and failed, is intolerant to, or has a clinical contraindication to phototherapy (i.e., puva or broadband or narrowband uvb); OR
   b) the patient has tried and failed, is intolerant to, or has a clinical contraindication to systemic therapy (methotrexate (oral or im), cyclosporine, or acitretin); AND

2. One of the following:
   a) the patient has body surface area (bsa) involvement of at least 5%; OR
   b) the patient has involvement of the palms, soles, head and neck, or genitalia, causing disruption in normal daily activities and/or employment; AND

3. The patient is not using Stelara in combination with another biologic agent; AND

4. The patient is being managed by a dermatologist; AND

5. If Stelara 90 mg is requested and the patient is new to therapy with Stelara, ONE of the following:
   a) The patient has a diagnosis of psoriasis AND the patient has failed (had an inadequate response to) a trial of 45mg for at least 3 months; OR

b) The patient weighs >100kg

Ustekinumab (Stelara®) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis in adolescent patients, age 12 years or older, who are candidates for phototherapy or systemic therapy.

Ustekinumab (Stelara®) may be considered medically necessary for the treatment of active psoriatic arthritis in patients if:

1. The patient is not using Stelara in combination with another biologic agent; AND

2. If Stelara 90 mg is requested and the patient is new to therapy with Stelara, ONE of the following:
   a) The patient has a diagnosis of psoriasis AND the patient has failed (had an inadequate response to) a trial of 45mg for at least 3 months; OR
   b) The patient has a dual diagnosis of psoriasis AND psoriatic arthritis AND the patient is >100kg.

Ustekinumab (Stelara®) may be considered medically necessary for the treatment of moderately to severely active Crohn's disease in patients who are 18 years of age or older if:

1. The patient has tried and failed, is intolerant to, or has a clinical contraindication to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate); AND

2. For patients new to therapy, therapy will begin with an initial intravenous infusion of Stelara; AND

3. The patient will not be treated with the 45mg injection; AND

4. In two months following the intravenous infusion of Stelara, the patient will begin therapy with subcutaneous injections of Stelara.

When Ustekinumab (Stelara®) is not covered

Stelara is considered investigational and therefore not covered when the criteria listed above are not met.

Coverage is not provided for the simultaneous use of more than one biologic drug.

Policy Guidelines

Ustekinumab (Stelara®) should only be administered by a healthcare provider to patients who will be closely monitored and have regular follow-up visits with a physician. After proper training in subcutaneous injection technique, a patient may self inject with Stelara® if a physician determines that it is appropriate. The first self-injection should be performed under the supervision of a qualified healthcare professional. If a patient or caregiver is to administer Stelara®, he/she should be instructed in injection techniques and their ability to inject subcutaneously should be assessed to ensure the proper administration of Stelara®. Refer to the FDA Medication Guide for Stelara® at http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125261s086lbl.pdf

Stelara® (ustekinumab) may increase the risk of infections and reactivation of latent infections. Serious bacterial, fungal, and viral infections, some requiring hospitalization, were reported. In patients with psoriasis, serious infections included diverticulitis, cellulitis, pneumonia, appendicitis, cholecystitis, sepsis, osteomyelitis, viral infections, gastroenteritis and urinary tract infections. In patients with psoriatic arthritis, serious infections included cholecystitis. In patients with Crohn's disease, serious or other

clinically significant infections included anal abscess, gastroenteritis, ophthalmic herpes, pneumonia, and listeria meningitis.

Patients should be evaluated for tuberculosis (TB) infection prior to initiating treatment with ustekinumab (Stelara®). It should not be given to patients with active TB. Anti-tuberculosis therapy should be considered in patients with a past history of latent or active tuberculosis when an adequate course of treatment cannot be confirmed prior to initiation of ustekinumab (Stelara®).

Ustekinumab (Stelara®) is an immunosuppressant and may increase the risk of malignancy.

Prior to initiating therapy with ustekinumab (Stelara®), patients should receive all immunizations appropriate for age as recommended by current immunization guidelines. Patients being treated with ustekinumab (Stelara®) should not receive live vaccines.

For treatment of plaque psoriasis in adults, the recommended dosing regimen for patients 100 kg or less is 45 mg subcutaneously initially and 4 weeks later, followed by 45 mg every 12 weeks. For patients greater than 100 kg, the dose is 90 mg subcutaneously initially and 4 weeks later, followed by 90 mg every 12 weeks. The recommended dosing regimen for subcutaneous treatment of plaque psoriasis in adolescents is weight based at the initial dose, 4 weeks later, then every 12 weeks thereafter, with patients weighing less than 60 kg receiving 0.75 mg/kg, 60 kg to 100 kg receiving 45 mg, and greater than 100 kg receiving 90 mg.

The recommended dosing regimen for psoriatic arthritis is 45 mg subcutaneously initially and 4 weeks later, followed by 45 mg subcutaneously every 12 weeks. For patients with coexisting moderate-to-severe plaque psoriasis and with body weight greater than 100 kg, the dose is 90 mg subcutaneously initially and 4 weeks later, followed by 90 mg subcutaneously every 12 weeks.

For treatment of Crohn's disease, the recommended dosing regimen is an initial single intravenous infusion using weight-based dosing. A subcutaneous 90 mg dose is given 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J3357, J3358, J3490, J3590, C9399*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

U.S. Food and Drug Administration. Prescribing information. Retrieved 1/29/2010 from http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/125261lbl.pdf

U.S. Food and Drug Administration. Approval letter, BLA 125261/0 dated September 25, 2009. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist

U.S. Food and Drug Administration. Center for Drug Evaluation and Research. Application number: 125261. Summary Review. Retrieved 1/29/2010 from

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Smith CH, Anstey AV, Barker JN, Burden AD, et al. British Association of Dermatologists' guidelines for biologic interventions for psoriasis 2009. Br J Dermatol 2009 Nov;161(5):987-1019. Retrieved on December 13, 2010 from http://guideline.gov/content.aspx?f=rss&id=15883

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Menter A, Korman NJ, et al. American Academy of Dermatology Work Group. 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. J Am Acad Dermatol 2011 Jul;65(1):137-74. Retrieved from
http://www.guideline.gov/content.aspx?id=36824

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Food and Drug Administration (FDA). Medication Information and Guide for Stelara® (Ustekinumab). Retrieved from
http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125261s086lbl.pdf

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National Institutes of Health (NIH) Clinical Trial NCT01077362. A Study of the Safety and Efficacy of Ustekinumab in Patients With Psoriatic Arthritis With and Without Prior Exposure to Anti-TNF Agents.
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Cuchacovich R, Perez-Alamino R, Garcia-Valladares I, Espinoza LR. Steps in the management of psoriatic arthritis: a guide for clinicians. Ther Adv Chronic Dis. 2012 Nov;3(6):259-69.

U.S. Food and Drug Administration. Prescribing information. Revised September 2013.
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Specialty Matched Consultant Advisory Panel review 10/2018

Specialty Matched Consultant Advisory Panel review 10/2019

Policy Implementation/Update Information

3/02/10	New policy issued. Ustekinumab (Stelara™) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis in patients who are 18 years of age or older; and have already been treated with phototherapy (i.e., PUVA or broadband or narrowband UVB) unless the patient is not a candidate for phototherapy or phototherapy is not available to the patient; and have already been treated with or are not a candidate for any other systemic treatments such as methotrexate (oral or IM), cyclosporin, and acitretin (Soriatane®). Notification date 3/02/10 for effective date of 6/08/10. (adn)
8/31/10	Billing Information updated to include code J3490. (mco)
1/1/11	J3490 and J3590 deleted from policy. New code specific to injection of Ustekinumab (Stelara™) added to Billing/Coding section: J3357. (mco)
2/15/11	Specialty Matched Consultant Advisory Panel review 1/2011. References updated. (mco)
7/1/11	Added quantity limitations to Policy Guidelines. Medical director review 6/2011. Notification date 7/1/11 for effective date of 10/1/11. (lpr)
2/7/12	Specialty Matched Consultant Advisory Panel review 1/2012. References updated. No changes to Policy Statements. (mco)
2/12/13	References updated. Updated related policies. Specialty Matched Consultant Advisory Panel review 1/2013. Trademark symbol ™ replaced throughout policy with Registered trademark symbol®. (mco)

7/16/13 Added the following statement to the Policy Guidelines section: "After proper training in subcutaneous injection technique, a patient may self inject with STELARA® if a physician determines that it is appropriate. The first self-injection should be performed under the supervision of a qualified healthcare professional. If a patient or caregiver is to administer STELARA®, he/she should be instructed in injection techniques and their ability to inject subcutaneously should be assessed to ensure the proper administration of STELARA®. Refer to the FDA Medication Guide for Stelara® at http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125261s086lbl.pdf" References updated. Medical Director review 6/2013. (mco)

10/15/13 FDA prescribing information updated 9/2013. Description section updated. "When Covered" section updated to include the following statement: "Ustekinumab (Stelara®) may be considered medically necessary for the treatment of active psoriatic arthritis in patients who are 18 years of age or older. Ustekinumab (Stelara®) may be used alone or in combination with methotrexate for the treatment of active psoriatic arthritis." References updated. Medical Director review 10/2013. (mco)

2/11/14 Specialty Matched Consultant Advisory Panel review 1/2014. Medical Director review 1/2014. No changes to Policy Statements. (mco)

5/27/14 "When Covered" section revised as follows: "Ustekinumab (Stelara™) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis in patients who are 18 years of age or older; and have already been treated with phototherapy (i.e., PUVA or broadband or narrowband UVB) unless the patient is not a candidate for phototherapy or phototherapy is not available to the patient; **or** have already been treated with or are not a candidate for any other systemic treatments such as methotrexate (oral or IM), cyclosporin, and acitretin (Soriatane®)." Medical Director review 5/2014. (mco)

3/31/15 References updated. Specialty Matched Consultant Advisory Panel review 1/2015. Medical Director review 1/2015. (td)

12/30/15 When Covered section revised to state, "Ustekinumab (Stelara®) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis in patients who are 18 years of age or older and: 1.one of the following: a)The patient has tried and failed, is intolerant to, or has a clinical contraindication to phototherapy (i.e., puva or broadband or narrowband uvb); or b) The patient has tried and failed, is intolerant to, or has a clinical contraindication to systemic therapy (methotrexate (oral or IM), cyclosporine, or acitretin); and 2. One of the following: a) The patient has Body Surface Area (BSA) involvement of at least 5%; OR b)The patient has involvement of the palms, soles, head and neck, or genitalia, causing disruption in normal daily activities and/or employment AND 3.The patient is not using stelara in combination with another biologic agent AND 4.The patient is being managed by a dermatologist AND 5. If Stelara 90 mg is requested and the patient is new to therapy with Stelara, ONE of the following: a) The patient has a diagnosis of psoriasis AND the patient has failed (had an inadequate response to) a trial of 45mg for at least 3 months OR b)The patient weighs >100kg Ustekinumab (Stelara®) may be considered medically necessary for the treatment of active psoriatic arthritis in patients who are 18 years of age or older and:1.The patient has tried and failed, is intolerant to, or has a clinical contraindication to phototherapy (i.e., puva or broadband or narrowband uvb) and 2.The patient is not using stelara in combination with another biologic agent AND 3.If Stelara 90 mg is requested and the patient is new to therapy with Stelara, ONE of the following: a) The patient has a diagnosis of psoriasis AND the patient has failed (had an inadequate response to) a trial of 45mg for at least 3 months OR b)The patient has a dual diagnosis of psoriasis AND psoriatic arthritis AND the patient is >100kg . Medical Director review 1/2016. Specialty Matched Consultant Advisory Panel review 1/27/2016. **Policy noticed 2/29/2016 for effective date 4/29/16**. (td)

12/30/16 Policy updated to include new indication for treatment of Crohn's Disease. Ustekinumab (Stelara®) may be considered medically necessary for the treatment of moderately to severely active Crohn's disease in patients who are 18 years of age or older if: 1. The patient has tried and failed, is intolerant to, or has a clinical contraindication to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate); AND 2. For patients new to therapy, therapy will begin with an initial intravenous infusion of Stelara; AND 3. The patient will not be treated with the 45mg injection; AND 4. In two months following the intravenous infusion of Stelara, the patient will begin therapy with subcutaneous injections of Stelara. Codes *J3490, J3590, C9399* added to Billing/Coding section. Specialty Matched Consultant Advisory Panel review 11/30/2016. (an)

1/27/17 In the "When Covered" section regarding medical necessity of Stelara for the indication of active psoriatic arthritis, the requirement for prior phototherapy was deleted. (an)

3/31/17 Added code C9487 to Billing/Coding section. (an)

6/30/17 Effective July 1, 2017: code C9487 deleted from Billing/Coding section and code Q9989 added. (an)

12/15/17 The following statement was added to the covered indications: Ustekinumab (stelara®) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis in adolescent patients, age 12 years or older, who are candidates for phototherapy or systemic therapy. Reference added. Codes C9487, Q9989 deleted. Code J3358 added. Specialty Matched Consultant Advisory Panel review 11/29/17. (an)

11/9/18 Updated Policy Guidelines section to provide clarification of dosing per specific indication. Added reference of policy "Measurement of Serum Antibodies to Infliximab, Adalimumab, Vedolizumab and Ustekinumab" to related policies in Description section. Minor typographical and grammatical changes made for clarity. References added. Specialty Matched Consultant Advisory Panel review 10/24/18. (krc)

10/29/19 Specialty Matched Consultant Advisory Panel review 10/16/2019. No change to policy intent. (krc)