



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date 7/15/2011
Next Review Date 7/15/2012
Coverage Policy Number 1017

Subject **Ustekinumab (Stelara™)**

Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	2
References	3

Hyperlink to Related Coverage Policies

Enbrel®
Humira®
Orencia®
Remicade®
Rituxan®
Simponi™

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers ustekinumab (Stelara™) as medically necessary for the treatment of moderate to severe plaque psoriasis in an adult (18 years of age or older) with EITHER of the following:

- history of a beneficial clinical response to ustekinumab
- history of an inadequate response or intolerance to **ONE preferred self-administered** tumor necrosis factor (TNF) antagonist [adalimumab (Humira®) OR etanercept (Enbrel®)]

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to ustekinumab (Stelara™) therapy.

FDA Approved Indications

Stelara is a human interleukin-12 and -23 antagonist indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

FDA Recommended Dosing

Stelara is intended for subcutaneous administration by a healthcare professional and under the supervision of a physician. Stelara is administered by subcutaneous injection. For patients weighing ≤ 100 kg (220 lbs), the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks. For patients weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.

Drug Availability

Stelara does not contain preservatives. Stelara is available in prefilled syringes or single-use vials containing 45 mg or 90 mg of ustekinumab. Each prefilled syringe is equipped with a needle safety guard.

General Background

Pharmacology

Ustekinumab is a monoclonal antibody to interleukins 12 (IL-12) and 23 (IL-23) labeled for treating moderate to severe plaque psoriasis in patients who are candidates for systemic treatments or phototherapy. It is the first biologic agent available in the U.S. that works by this mechanism of action. Other biologic agents labeled for treating plaque psoriasis include alefacept, adalimumab, etanercept, and infliximab.

Ustekinumab is an immunoglobulin G1-kappa monoclonal antibody specific to the p40 subunits of IL-12 and IL-23. Ustekinumab binds to IL-12 and IL-23 preventing them from activating IL-12R-beta1 receptors on various immune and inflammatory cells. Specific effects of this binding include preventing natural killer cell and IL-17 activation, reducing interferon-gamma production, and reducing CD4+ T-cell differentiation and activation. Steady state concentrations are reached by week 28. Ustekinumab does not accumulate when dosed every 12 weeks. The mean half-life ranges from 14.9 to 45.6 days.

Ongoing Studies

Stelara is being studied for use in psoriatic arthritis (PsA). At this time, however, there is insufficient published data in terms of safety and efficacy to support the use of Stelara for this indication.

A phase 3 study is currently in progress to determine the safety and efficacy of Stelara for PA. The study was initiated in Feb 2010 in the US, Canada, France, Germany and the UK in subjects previously treated with biologic anti-TNF agents. It is expected to be completed in Nov 2011. The primary endpoint is the proportion of patients with American College of Rheumatology (ACR) 20 response. Secondary endpoints are changes in total radiographic scores of the hands and feet, health assessment questionnaire score, ACR 50 and ACR 70 response.

Adverse Reactions

The most common adverse events with ustekinumab are nasopharyngitis, respiratory tract infection, and headache. Adverse event rates are similar between ustekinumab and placebo. Ustekinumab may increase the risk for serious infections. Screen all patients for active or latent tuberculosis prior to initiating therapy. Drug interactions have not specifically been studied with ustekinumab. Do not administer live vaccines during treatment with ustekinumab, or BCG vaccines within one year of treatment with ustekinumab due to increased infection risk.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

HCPCS Codes	Description
J3357	Injection, ustekinumab, 1mg

ICD-9-CM Diagnosis Codes	Description
696.1	Other psoriasis

References

1. A Study of the Safety and Efficacy of Ustekinumab in Patients With Psoriatic Arthritis. National Institutes of Health. Accessed Jun 20, 2011. Available at: <http://www.clinicaltrials.gov/show/NCT01009086>
2. Centocor Ortho Biotech. Stelara (ustekinumab) product label. Horsham, PA: Centocor Ortho Biotech. Oct 2010.
3. Chien AL, Elder JT, Ellis CN. Ustekinumab: a new option in psoriasis therapy. *Drugs*. 2009;69(9):1141-1152.
4. Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. *Ann Rheum Dis*. Mar 2005;64 Suppl 2:ii65-68; discussion ii69-73.
5. Gottlieb A, Korman NJ, Gordon KB, et al. 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. *J Am Acad Dermatol*. May 2008;58(5):851-864.
6. Gottlieb A, Menter A, Mendelsohn A, et al. Ustekinumab, a human interleukin 12/23 monoclonal antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial. *Lancet*. Feb 21 2009;373(9664):633-640.
7. Krueger GG, Langley RG, Leonardi C, et al. A human interleukin-12/23 monoclonal antibody for the treatment of psoriasis. *N Engl J Med*. Feb 8 2007;356(6):580-592.
8. 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*. May 17 2008;371(9625):1665-1674.
9. McEvoy GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc. 2011.
10. Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol*. May 2008;58(5):826-850.
11. O'Neill JL, Kalb RE. Ustekinumab in the therapy of chronic plaque psoriasis. *Biologics*. 2009;3:159-168.
12. 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*. May 17 2008;371(9625):1675-1684.
13. Patel RV, Clark LN, Lebwohl M, Weinberg JM. Treatments for psoriasis and the risk of malignancy. *J Am Acad Dermatol*. Jun 2009;60(6):1001-1017.
14. 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*. Oct 2008;135(4):1130-1141.

15. Scanlon JV, Exter BP, Steinberg M, Jarvis CI. Ustekinumab: treatment of adult moderate-to-severe chronic plaque psoriasis. *Ann Pharmacother.* Sep 2009;43(9):1456-1465.
16. Segal BM, Constantinescu CS, Raychaudhuri A, Kim L, Fidelus-Gort R, Kasper LH. Repeated subcutaneous injections of IL12/23 p40 neutralising antibody, ustekinumab, in patients with relapsing-remitting multiple sclerosis: a phase II, double-blind, placebo-controlled, randomised, dose-ranging study. *Lancet Neurol.* Sep 2008;7(9):796-804.
17. Toedter GP, Blank M, Lang Y, Chen D, Sandborn WJ, de Villiers WJ. Relationship of C-Reactive Protein With Clinical Response After Therapy With Ustekinumab in Crohn's Disease. *Am J Gastroenterol.* Aug 11 2009.

"CIGNA", "CIGNA HealthCare" and the "Tree of Life" logo are registered service marks of CIGNA Intellectual Property, Inc., licensed for use by CIGNA Corporation and its operating subsidiaries. All products and services are provided by such operating subsidiaries and not by CIGNA Corporation. Such operating subsidiaries include Connecticut General Life Insurance Company, CIGNA Health and Life Insurance Company, CIGNA Behavioral Health, Inc., CIGNA Health Management, Inc., and HMO or service company subsidiaries of CIGNA Health Corporation and CIGNA Dental Health, Inc. In Arizona, HMO plans are offered by CIGNA HealthCare of Arizona, Inc. In California, HMO plans are offered by CIGNA HealthCare of California, Inc. In Connecticut, HMO plans are offered by CIGNA HealthCare of Connecticut, Inc. In North Carolina, HMO plans are offered by CIGNA HealthCare of North Carolina, Inc. In Virginia, HMO plans are offered by CIGNA HealthCare Mid-Atlantic, Inc. All other medical plans in these states are insured or administered by Connecticut General Life Insurance Company or CIGNA Health and Life Insurance Company.