



# 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 ..... 5/15/2011  
Next Review Date ..... 5/15/2012  
Coverage Policy Number ..... 4014

Subject **Alefacept (Amevive®)**

## Table of Contents

Coverage Policy .....	1
General Background .....	2
Coding/Billing Information .....	3
References .....	3
Policy History .....	5

## Hyperlink to Related Coverage Policies

Enbrel®  
Humira®  
Remicade®

### 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. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA covers alefacept (Amevive®) as medically necessary for the treatment of chronic plaque psoriasis in an adult (≥18 years of age) with either of the following indications:**

- history of a beneficial clinical response to alefacept therapy
- **BOTH** of the following:
  - individual is a candidate for, or has previously received **ONE** of the following treatments:
    - Systemic therapy (e.g., methotrexate, cyclosporin, soriatane)
    - Phototherapy [narrow or broad band ultraviolet B (UVB), or psoralen plus ultraviolet A (PUVA)]
  - history of an inadequate response or intolerance to **ONE preferred self-administered** tumor necrosis factor (TNF) antagonist [adalimumab (Humira®) OR etanercept (Enbrel®)]

**Note: Coverage may be approved for up to 12 weeks. Coverage may be approved for re-treatment ONCE as long as the total lymphocyte and CD4+ T cell counts are within normal range and a minimum of 12 weeks has passed since the last course of therapy.**

**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 alefacept (Amevive®) therapy.**

---

## **FDA Approved Indications**

Alefacept is a biological agent labeled for the treatment of moderate-to-severe chronic plaque psoriasis for adult patients who are candidates for systemic therapy or phototherapy.

## **FDA Recommended Dosing**

The recommended dose of alefacept is 15 mg given once weekly as an intramuscular (IM) injection. The recommended regimen is a course of 12 weekly injections. Retreatment with an additional 12-week course may be initiated provided that CD4+ T lymphocyte counts are within the normal range, and a minimum of a 12-week interval has passed since the previous course of treatment. The CD4+ T lymphocyte counts of patients receiving alefacept should be monitored before initiating dosing and every two weeks throughout the course of the 12-week dosing regimen. If CD4+ T lymphocyte counts are below 250 cells/ $\mu$ L, alefacept dosing should be withheld and weekly monitoring instituted. Alefacept should be discontinued if the counts remain below 250 cells/ $\mu$ L for one month.

## **Drug Availability**

Amevive is supplied in either a carton containing four doses, or in a carton containing one dose. Each four-dose carton contains one removable drug/diluent pack for refrigeration, four 1 mL syringes, and eight 23 gauge, 1  $\frac{1}{4}$  inch needles. Each four-dose drug/diluent pack for refrigeration contains: four 15-mg single-use vials of Amevive and four 10 mL single-use diluent vials of Sterile Water for Injection. Each single-dose carton contains one removable drug/diluent pack for refrigeration, one syringe and two 23 gauge, 1  $\frac{1}{4}$  inch needles. Each single-dose drug/diluent pack for refrigeration contains: one 15-mg single-use vial of Amevive and one 10 mL single-use diluent vial of Sterile Water for Injection.

## **General Background**

### **Pharmacology/Disease Overview**

In clinical practice, the severity of a patient's psoriasis is evaluated by combining the objective assessment (e.g. body surface area (BSA) of involvement, disease location, thickness) and subjective assessment of the physical, financial, and emotional impact of the disease on the patient's life. This subjective assessment is combined with the physician's global assessment of psoriasis to determine psoriasis severity and appropriate therapy.

Alefacept is fusion protein that prevents the activation of T lymphocytes involved in the pathogenesis of psoriasis. In placebo-controlled trials, alefacept demonstrated improvement in psoriasis-specific indices when compared to baseline values and patients taking placebo. Alefacept is effective when given either intravenously or intramuscularly. The first course of therapy with alefacept is attributed to the greatest clinical improvement and a second course is well-tolerated and increases efficacy. Clinical response is related to reductions in lymphocyte counts. Repeat courses of alefacept show equal to greater benefit and may increase duration of response; however, data concerning usage beyond two treatment cycles are limited. Rebounds in psoriasis after completion of therapy have not been reported with alefacept, indicating it acts as remittive therapy rather than an immunosuppressive.

### **Guidelines**

#### **National Psoriasis Foundation**

The National Psoriasis Foundation recommends two-tiered system that categorizes patients based on treatment plans as candidates for localized therapy or for systemic therapy and/or phototherapy. Localized therapy, which includes topical treatments and excimer laser treatments, is recommended for patients with psoriasis that affects less than 5% BSA. Appropriate therapies include, but are not restricted to, topical corticosteroids, topical cholecalciferol analogs, combinations of these 2, topical retinoids, tar preparations, anthralin, keratolytics, and excimer (UV-B) laser treatments. In general, the effects of topical therapy should become evident within the first two to three weeks of use. Clearing of scale is usually observed first, followed by flattening of the treated plaques. Resolution of erythema may take six to eight weeks. Systemic therapy and/or phototherapy, which includes broad and narrowband phototherapy, photochemotherapy (PUVA), systemic agents, and biologics, is recommended for patients with psoriasis affecting greater than 5% BSA, for those with less than 5% BSA affected in vulnerable areas, such as the face, genitals, hands or feet, and for other forms of psoriasis, including but not limited to erythrodermic, pustular, and guttate. In addition, patients with limited affected areas and

inadequate response to localized therapy or impairment in physical or mental functioning should also be considered candidates for systemic and/or phototherapy treatment.

### **American Academy of Dermatology (AAD)**

The AAD published a consensus statement on psoriasis therapies. The document is intended to be used as a guide to the evaluation and treatments of psoriasis until evidence based guidelines are developed. Within this document, the authors state that BSA should not generally be used to determine which therapy to select; moderate and severe disease overlap and individuals with limited disease can be considered moderate for the purposes of selecting a therapy. Topical therapies are recommended for limited plaque disease. For moderate to severe disease, the AAD recommends phototherapy, targeted phototherapy, narrowband UVB, photochemotherapy with psoralen and UVA light (PUVA), topicals and systemic treatments.

### **Clinical Efficacy**

Two controlled clinical studies included 1060 patients who had chronic (i.e., duration of one year or longer) plaque psoriasis with involvement of at least 10% of the body surface area and who were candidates for or had previously received systemic therapy or phototherapy. In these studies, 14 or 21% of patients receiving alefacept 7.5 mg intravenous (IV) or 15 mg intramuscular (IM) once weekly, respectively, achieved a response (i.e., reduction in Psoriasis Area and Severity Index [PASI] score of at least 75% compared with baseline) at two weeks following a 12-week course of therapy, compared with 4–5% of patients receiving placebo. An additional 7–11% of patients receiving alefacept achieved a response (i.e., reduction in PASI score of at least 75% compared with baseline) beyond two weeks post-treatment. Response rate at two weeks following a second 12-week course of IV or IM alefacept therapy was 26%, or 30%, respectively.

In both clinical studies, onset of response (reduction in PASI score of at least 50% compared with baseline) reportedly was observed 60 days after initiation of alefacept therapy. The median duration of response (maintenance of 75% or greater reduction in PASI score) after a 12-week course of therapy with alefacept 7.5 mg IV or 15 mg IM once weekly was 3.5 or two months, respectively. However, patients who achieved at least a 75% reduction in baseline PASI score during or after a single 12-week course of IV alefacept therapy maintained a 50% or greater reduction in PASI score for a median of seven months. The duration of response appeared to be longer after a second course of IV alefacept therapy; however, median duration of response was not determined, since the study was terminated after one year.

### **Adverse Reactions/Contraindications**

Alefacept should not be used concurrently with other immunosuppressive agents or in patients currently receiving phototherapy. The concomitant use of low-potency topical corticosteroids was permitted during clinical studies.

The most serious adverse reactions were lymphopenia, malignancies, serious infections requiring hospitalization, and hypersensitivity reactions. Commonly observed adverse events seen in the first course of placebo-controlled clinical were pharyngitis, dizziness, increased cough, nausea, pruritus, myalgia, chills, injection site pain, injection site inflammation, and accidental injury. The only adverse event that occurred at a 5% or higher incidence among was chills which occurred predominantly with intravenous administration. The most common events resulting in discontinuation of treatment with Amevive were CD4+ T lymphocyte levels below 250 cells/ $\mu$ L, headache, and nausea.

---

## **Coding/Billing Information**

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

**Covered when medically necessary:**

<b>HCPSC Codes</b>	<b>Description</b>
J0215	Injection, alefacept, 0.5 mg

<b>ICD-9-CM</b>	<b>Description</b>
-----------------	--------------------

<b>Diagnosis Codes</b>	
696.1	Other psoriasis

## References

1. Astellas Pharma US, Inc. Amevive (alefacept) prescribing information. Deerfield, IL: Astellas Pharma US, Inc. Feb 2011.
2. Bandy V. Alefacept: A T-cell-specific immunosuppressant to treat moderate to severe plaque psoriasis. *Formulary*. July 2002;37:346-353.
3. Callen JP, Krueger GG, Lebwohl M, McBurney EI, Mease P, Menter A, Paller AS, Pariser DM, Weinblatt M, Zimmerman G; AAD. AAD consensus statement on psoriasis therapies. *Am Acad Dermatol*. 2003 Nov;49(5):897-9.
4. Christophers E. Targeting T-cell subsets to achieve remission. *J Eur Acad Dermatol Venereol*. Jul 2003;17 Suppl 2:6-11.
5. Cooper JC, Morgan G, Harding S, et al. Alefacept selectively promotes NK cell-mediated deletion of CD45R0+ human T cells. *Eur J Immunol*. Mar 2003;33(3):666-675.
6. Ellis CN, Mordin MM, Adler EY. Effects of alefacept on health-related quality of life in patients with psoriasis: results from a randomized, placebo-controlled phase II trial. *Am J Clin Dermatol*. 2003;4(2):131-139.
7. Finlay AY, Salek MS, Haney J, For The Alefacept Clinical Study Group F. Intramuscular alefacept improves health-related quality of life in patients with chronic plaque psoriasis. *Dermatology*. 2003;206(4):307-315.
8. Gottlieb AB, Chaudhari U, Mulcahy LD, Li S, Dooley LT, Baker DG. Infliximab monotherapy provides rapid and sustained benefit for plaque-type psoriasis. *J Am Acad Dermatol*. Jun 2003;48(6):829-835.
9. Granstein RD. New treatments for psoriasis. *N Engl J Med*. Jul 26 2001;345(4):284-287.
10. Karrer S, Eholzer C, Ackermann G, Landthaler M, Szeimies RM. Phototherapy of psoriasis: comparative experience of different phototherapeutic approaches. *Dermatology*. 2001;202(2):108-115.
11. Katz HI, Prawer SE, Medansky RS, et al. Intermittent corticosteroid maintenance treatment of psoriasis: a double-blind multicenter trial of augmented betamethasone dipropionate ointment in a pulse dose treatment regimen. *Dermatologica* 1991;183:269-74.
12. Koo J, Lebwohl M. Duration of remission of psoriasis therapies. *J Am Acad Dermatol*. Jul 1999;41(1):51-59.
13. Kraan MC, van Kuijk AW, Dinant HJ, et al. Alefacept treatment in psoriatic arthritis: reduction of the effector T cell population in peripheral blood and synovial tissue is associated with improvement of clinical signs of arthritis. *Arthritis Rheum*. Oct 2002;46(10):2776-2784.
14. Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T. The impact of psoriasis on quality of life: results of a 1998 National Psoriasis Foundation patient-membership survey. *Arch Dermatol*. Mar 2001;137(3):280-284.
15. Krueger GG, Ellis CN. Alefacept therapy produces remission for patients with chronic plaque psoriasis. *Br J Dermatol*. Apr 2003;148(4):784-788.
16. Krueger GG, Papp KA, Stough DB, Loven KH, Gulliver WP, Ellis CN. A randomized, double-blind, placebo-controlled phase III study evaluating efficacy and tolerability of 2 courses of alefacept in patients with chronic plaque psoriasis. *J Am Acad Dermatol*. Dec 2002;47(6):821-833.

17. Krueger GG. Clinical response to alefacept: results of a phase 3 study of intravenous administration of alefacept in patients with chronic plaque psoriasis. *J Eur Acad Dermatol Venereol.* Jul 2003;17 Suppl 2:17-24.
18. Lebwohl M, Christophers E, Langley R, Ortonne JP, Roberts J, Griffiths CE. An international, randomized, double-blind, placebo-controlled phase 3 trial of intramuscular alefacept in patients with chronic plaque psoriasis. *Arch Dermatol.* Jun 2003;139(6):719-727.
19. Lowe NJ, Gonzalez J, Bagel J, Caro I, Ellis CN, Menter A. Repeat courses of intravenous alefacept in patients with chronic plaque psoriasis provide consistent safety and efficacy. *Int J Dermatol.* Mar 2003;42(3):224-230.
20. Luba KM, Stulberg DL. Chronic plaque psoriasis. *Am Fam Physician.* 2006;73(4):636-44.
21. Mason J, Mason AR, Cork MJ. Topical preparations for the treatment of psoriasis: a systematic review. *Br J Dermatol* 2002;146:351-64.
22. Ortonne JP, Lebwohl M, Em Griffiths C. Alefacept-induced decreases in circulating blood lymphocyte counts correlate with clinical response in patients with chronic plaque psoriasis. *Eur Dermatol.* Mar-Apr 2003;13(2):117-123.
23. Ortonne JP. Clinical response to alefacept: results of a phase 3 study of intramuscular administration of alefacept in patients with chronic plaque psoriasis. *J Eur Acad Dermatol Venereol.* Jul 2003;17 Suppl 2:12-16.
24. Pariser DM, Bagel J, Gelfand JM, Korman NJ, Ritchlin CT, Strober BE, Van Voorhees AS, Young M, Rittenberg S, Lebwohl MG, Horn EJ; National Psoriasis Foundation. National Psoriasis Foundation clinical consensus on disease severity. *Arch Dermatol.* 2007 Feb;143(2):239-42.

## Policy History

<b>Pre-Merger Organizations</b>	<b>Last Review Date</b>	<b>Policy Number</b>	<b>Title</b>
CIGNA HealthCare Great-West Healthcare	5/30/2008	4014	Alefacept (Amevive®)

“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.