



**BlueCross BlueShield
of Alabama**

Name of Policy:

AMEVIVE[®] (alefacept)

Policy #: 098

Category: Pharmacology

Latest Review Date: August 2011

Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

- 1. The technology must have final approval from the appropriate government regulatory bodies;*
- 2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
- 3. The technology must improve the net health outcome;*
- 4. The technology must be as beneficial as any established alternatives;*
- 5. The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

- 1. In accordance with generally accepted standards of medical practice; and*
- 2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
- 3. Not primarily for the convenience of the patient, physician or other health care provider; and*
- 4. 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.*

Description of Procedure or Service:

Psoriasis is a chronic autoimmune skin disease in which skin cells multiply 10 times faster than the normal rate causing scaling and inflammation. Excess cells pile up on the skin's surface, forming red, raised, scaly plaques that can be painful and disfiguring.

AMEVIVE[®] is the first biologic treatment approved by the FDA for psoriasis. AMEVIVE[®] (alefacept) is an immunosuppressive dimeric fusion protein that consists of the extracellular CD2-binding portion of the human leukocyte function antigen-3 (LFA-3) linked to the Fc portion of human IgG1. AMEVIVE[®] interferes with lymphocyte activation by specifically binding to the lymphocyte antigen, CD2, and inhibiting LFA-3/CD2 interaction. These interactions play a role in the pathophysiology of chronic plaque psoriasis. Treatment with AMEVIVE[®] results in a dose dependent reduction of CD4+ and CD8+ T lymphocyte counts.

Policy:

Effective for dates of on or after August 23, 2011:

AMEVIVE[®] (alefacept) meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the treatment of adult patients with moderate to severe chronic plaque psoriasis when the following criteria are met:

- ~~Minimum involvement of 10% body surface area~~
- Must have tried previous therapies (phototherapy or other systemic medications such as methotrexate)
- ~~CD4+ count > 250, monitored weekly~~
- No history of systemic malignancy
- Given in weekly doses for 12 weeks, cannot be repeated for 12 weeks
- If patient has positive response, can repeat for one additional cycle, data is limited on the safety and efficacy of AMEVIVE[®] beyond two courses of treatment.

Effective for dates of service prior to August 23, 2011:

AMEVIVE[®] (alefacept) meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the treatment of adult patients with moderate to severe chronic plaque psoriasis when the following criteria are met:

- Minimum involvement of 10% body surface area
- Must have tried previous therapies (phototherapy or other systemic medications such as methotrexate)
- CD4+ count > 250, monitored weekly
- No history of systemic malignancy
- Given in weekly doses for 12 weeks, cannot be repeated for 12 weeks
- If patient has positive response, can repeat for one additional cycle, data is limited on the safety and efficacy of AMEVIVE[®] beyond two courses of treatment.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Two randomized, double-blind, placebo-controlled studies in adults with chronic (greater than one year) plaque psoriasis and a minimum body surface area of 10% who were candidates for or had previously received systemic therapy or phototherapy evaluated AMEVIVE[®]. 553 patients were randomized into three cohorts and included ages 16-84 years. Each study consisted of once-weekly administration for 12 weeks (IV for study 1 of 7.5 mg AMEVIVE[®] per bolus and either AMEVIVE[®] 10 or 15 mg IM for study 2) of placebo or AMEVIVE[®]. In study 1, the median duration of response (maintenance of 75% or greater reduction in the PASI, the Psoriasis Area and Severity Index) was 3.5 months for AMEVIVE[®] treated patients and 1 month for placebo treated patients. Study 2 (IM route) had a median duration of response approximately 2 months for both AMEVIVE[®] and placebo treated patients. Most patients who had responded to either AMEVIVE[®] or placebo maintained a 50% or greater reduction in PASI through the 3-month observation period. For course 2, 52 patients crossed over to the placebo and maintained a 50% or greater reduction in PASI through the 3-month observation period. In the retreatment, study 1 patients who were less than clear by the Physicians' Global Assessment (PGA) and the CD4+ count was above the lower limit of normal were eligible for a second treatment. The median reduction in PASI score was greater in patients who received a second course of AMEVIVE[®] compared to patients who received placebo. Data on the safety and efficacy beyond two courses are limited.

In September 2005, Biogen issued an update to the prescribing information stating: "The recommended dose of Amevive[®] is 7.5mg given once weekly as an IV bolus or 15 mg given once weekly as an 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 or patients receiving Amevive[®] should be monitored before initiating dosing every two weeks throughout the course of the 12-week dosing regimen".

(This update is from Biogen and no update has been issued from the FDA regarding additional treatments beyond the second course of treatment and every two weeks testing of CD4+ counts.)

November 2008 Update

No new studies were identified that would alter the coverage statement of this policy.

August 2011 Update

Dunn and Feldman (2010) reviewed data from clinical trials that provided new insights into the efficacy, safety, and cost effectiveness of alefacept as a treatment for psoriasis. They concluded that over the past decade, numerous studies have shown the safety, efficacy, and cost effectiveness of alefacept as a therapy for moderate to severe psoriasis. Those studies demonstrated that although alefacept is not the most efficacious or cost effective treatment, it seems to be, at least in their opinion, one of the safest treatments, if not the single safest biologic treatment, available. They did not find any reports of opportunistic infections with alefacept, as have been reported with TNF inhibitors. However, far fewer patients have received alefacept compared with those who have received TNF antagonists, thereby limiting the extent to which we know the overall safety profile of alefacept.

Alefacept is slower to act than and is not as effective as TNF inhibitors for most psoriasis patients. However, the efficacy of alefacept for a particular patient is, as of now, unpredictable. In practice, there is no single right treatment for all, as some patients place more weight on efficacy, others on safety, and others on the convenience of the dosing regimen. For patients who want the safest biologic therapy (and certainly for those who have failed other options), alefacept may be a good choice of treatment, and it may also have a role in multitherapeutic approaches to treating psoriasis.

Key Words:

AMEVIVE[®], alefacept, psoriasis, plaque psoriasis, CD4+

Approved by Governing Bodies:

U.S. Food and Drug Administration approval was given on January 31, 2003 for the treatment of adults with moderate-to-severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Covered if covered by the Participating Home Plan

BellSouth/AT&T contracts: No special requirements

FEP contracts: No special requirements

Wal-Mart: Special benefit consideration may apply. Refer to member's benefit plan.

Pre-certification/Pre-determination requirements: Not required

Coding:

CPT coding:

Effective January 1, 2004:

J0215 Injection, Alefacept, 0.5 mg

References:

1. American Academy of Dermatology: Public Resources. *Psoriasis*, <http://www.aad.org/pamphlets/Psoriasis.html>.
2. Astellas Pharma US, Inc. Amevive (alefacept) prescribing information. Deerfield, IL: Astellas Pharma US, Inc. August 2011.
3. BIOGEN, Inc. Amevive[®] labeling information, February 2003.
4. BIOGEN, Inc. *FDA approves Biogen's Amevive[®] (alefacept) for treatment of psoriasis*, January 31, 2003, http://www.biogen.com/site/content/news/pr_detail.asp?id=202.

5. Drake, Lynn A., Ceilley, Roger I., et al. *Guidelines of care for psoriasis*, American Academy of Dermatology Association, <http://www.aadassociation.org/guidelines/psoriasis.html>.
6. Dunn KL, Feldman SR. *Alefacept Treatment for Chronic Plaque Psoriasis*. *Skin Therapy Lett.* 2010 Apr;15(4):1-3. Retrieved on August, 2011 from <http://www.skintherapyletter.com/2010/15.4/1.html>.
7. Krueger, Gerald G., Papp, Kim A., et al. *A randomized, double-blind, placebo-controlled phase III study evaluating efficacy and tolerability of 2 courses of alefacept in patients with chronic plaque psoriasis*, *Journal of the American Academy of Dermatology*, December 2002, Vol. 47, No. 6, pp. 821-833.
8. National Institute of Arthritis and Musculoskeletal and Skin Diseases: Health Topics. *Questions and answers about psoriasis*, January 2002, <http://www.niams.nih.gov/hi/topics/psoriasis/psoriafs.htm>.

Policy History:

Medical Policy Group, March 2003 (1)

Medical Policy Administration Committee, March 2003

Available for comment April 1-May 16, 2003

Medical Policy Group, November 2005 (1)

Medical Policy Group, November 2008 (1)

Medical Policy Group, August 2011 (1) Update to Policy, Key Points and References

Medical Policy Administration Committee, September 2011

Available for comment September 22 through November 7, 2011

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.