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ALEFACEPT (Amevive®) Preauthorization Criteria for Approval

Medications and Dosage Forms Included in Criteria

Generic Name	Brand Name	Dosage Form
Alefacept	Amevive®	Intramuscular injection

FDA Approved Indications

Amevive® (alefacept) is indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy.¹

Description

The purpose of the Amevive (alefacept) preauthorization criteria is to support the use of first-line agents in the treatment of chronic plaque psoriasis. Requirements of the criteria include having prior or current treatment with first-line agents, meeting the recommendations of clinical trials and product labeling, and having a diagnosis of plaque psoriasis that covers at least ten percent of the body surface area and which has persisted for more than six months and a normal CD4 lymphocyte count.

Criteria

Initial Evaluation

1. Has the patient been treated with Amevive within the past 12 months?
If yes, see renewal evaluation.
If no, continue to 2.
2. Has the patient been diagnosed with chronic plaque psoriasis?
If yes, continue to 3.
If no, do not approve.
3. Has the patient had symptoms of plaque psoriasis for more than 6 months?
If yes, continue to 4.
If no, do not approve.
4. Does the patient have body surface area involvement of 10 percent or more?
If yes, continue to 5.
If no, do not approve.
5. Has the patient been treated with one or more topical or systemic antipsoriatic agents (e.g., topical corticosteroids, topical coal tar products, tazarotene, cyclosporine, methoxsalen, anthralin, calcipotriene, methotrexate, or acetrelin)?
If yes, continue to 6.
If no, do not approve.
6. Does the patient have a normal CD4 lymphocyte count (250 cells/ μ L or greater)?
If yes, approve for 12 weeks.
If no, do not approve.

Renewal Evaluation

1. Has the patient been previously treated with Amevive in the last 12 months?
If yes, continue to 2.
If no, see initial evaluation.
2. Did previous treatment with Amevive result in remission of the disease or improvement in the severity of symptoms (e.g., decrease in body surface area affected, decrease in plaque induration, scaling, or erythema)?
If yes, continue to 3.
If no, do not approve.
3. Has there been a minimum of 12 weeks since the end of the previous course of Amevive therapy?
If yes, continue to 4.
If no, do not approve.
4. Does the patient have a normal CD4 lymphocyte count (250 cells/ μ L or greater)?
If yes, approve for 12 weeks.
If no, do not approve.

Rationale

The purpose of the Amevive (alefacept) Preauthorization Criteria is to provide approval to patients prescribed Amevive that have tried first-line therapy and meet product labeling recommendations. Alefacept has been selected for preauthorization due to recommendations by practice guidelines for chronic plaque psoriasis and their use after first-line agents have been tried.²⁻⁴ The majority of patients can be managed with topical therapy.²⁻⁴

Topical corticosteroids is documented as the most commonly prescribed treatment for psoriasis and is consistently considered initial therapy in treatment algorithms.^{4,5} Corticosteroids are not the only option for initial treatment as corticosteroids can cause skin atrophy.⁵ Alternatives include coal tar, anthralin, vitamin D₃ analogues (calcipotriene), topical retinoids (tazarotene), and intralesional injection of corticosteroids.⁵ It is possible that patients may not adequately respond to initial treatment or topical treatments may not suffice for widespread psoriatic lesions. Systemic treatment or phototherapy are generally prescribed in these instances. These treatments include the combination of psoralen plus ultraviolet A (UVA), commonly known as PUVA. Other systemic agents include methotrexate, acitretin, and cyclosporine.²⁻⁵

Psoriasis is a chronic inflammatory, T-cell-mediated autoimmune disease characterized by periods of spontaneous remission and relapse. Alefacept interferes with lymphocyte activation by specifically binding to the lymphocyte antigen, CD2, and inhibiting LFA-3/CD2 interaction.¹ Activation of T lymphocytes involving the interaction between LFA-3 on antigen-presenting cells and CD2 on T lymphocytes plays a role in the pathophysiology of chronic plaque psoriasis.¹ The majority of T lymphocytes in psoriatic lesions are of the memory effector phenotype characterized by the presence of the CD45RO marker, express activation markers (e.g., CD25, CD69) and release inflammatory cytokines, such as interferon γ .¹ Alefacept also causes a reduction in subsets of CD2+ T lymphocytes (primarily CD45RO+), presumably by bridging between CD2 on target lymphocytes and immunoglobulin Fc receptors on cytotoxic cells, such as natural killer cells.¹ Treatment with alefacept results in a reduction in circulating total CD4+ and CD8+ T lymphocyte counts.¹ CD2 is also expressed at low levels on the surface of natural killer cells and certain bone marrow B lymphocytes.¹ Therefore, the potential exists for alefacept to affect the activation and numbers of cells other than T lymphocytes.¹ In clinical studies of alefacept, minor changes in the numbers of circulating cells other than T lymphocytes have been observed.¹

Alefacept has shown efficacy in the treatment of moderate to severe psoriasis although its place in therapy is still to be determined based on lack of trials comparing alefacept to other therapies and the

potential for serious side effects.^{1,3} However, alefacept has provided the longest psoriasis remission time among the current biologic medications available for psoriasis treatment.⁶

Commonly observed adverse events seen in the first course of placebo-controlled clinical trials with at least a 2% higher incidence in the alefacept-treated patients compared to placebo-treated patients were: pharyngitis, dizziness, increased cough, nausea, pruritus, myalgia, chills, injection site pain, injection site inflammation, and accidental injury.¹ The only adverse event that occurred at a 5% or higher incidence among alefacept-treated patients compared to placebo-treated patients was chills (1% placebo vs. 6% alefacept), which occurred predominantly with intravenous administration.¹ The most serious adverse reactions were lymphopenia, malignancies, serious infections requiring hospitalization, and hypersensitivity reactions.¹

Explanation of PA Criteria

The purpose of the PA criteria is to ensure that patients have a documented diagnosis of chronic plaque psoriasis and meet requirements recommended in the package labeling, clinical trials, and practice guidelines. Guidelines recommend the use of biological intervention in patients with severe disease defined as a Psoriasis Area and Severity Index (PASI) score of 10 or more and/or a body surface area (BSA) of 10% or greater.⁷ Furthermore, patients must have psoriasis symptoms for at least 1 year as evaluated in clinical trials.^{8,9} A trial of at least one topical or systemic therapeutic agent is required for approval to determine if the psoriasis is resistant to current treatment. Alefacept can induce dose-dependent reductions in circulating CD4+ and CD8+ T lymphocyte counts and a course of alefacept therapy should not be initiated in patients with a CD4+ T lymphocyte count below normal.¹ The CD4+ T lymphocyte counts of patients receiving alefacept should be monitored every 2 weeks throughout the course of the 12-week dosing regimen.¹ If CD4+ T lymphocyte counts are below 250 cells/ μ L, alefacept dosing should be withheld and weekly monitoring instituted.¹ Alefacept should be discontinued if the counts remain below 250 cells/ μ L for one month.¹ The PA Criteria requires normal CD4+ lymphocyte counts before initiation of therapy and upon renewal of therapy.

For renewal of therapy after the initial course of therapy, evidence of disease improvement must be documented. Clinical trials involving alefacept defined a response to treatment as a reduction in score on the PASI of at least 75% from baseline at two weeks following the 12-week treatment period.^{1,8,9} Other treatment responses included achieving a scoring of "almost clear" or "clear" by Physician Global Assessment (PGA) and a reduction in PASI of at least 50% from baseline two weeks after the 12-week treatment period.^{1,8,9} If patients improve on initial therapy they may be approved through the PA evaluation process for additional therapy. Furthermore, if retreatment is needed after the initial course of therapy, product labeling recommends that CD4+ lymphocyte counts be normal and retreatment is at least 12 weeks after the previous treatment course.¹ These same recommendations are requirements within the renewal PA criteria.

References

1. Amevive® (alefacept) [package insert]. Deerfield, IL: Astellas Pharma US, Inc., October 2006.
2. Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. *J Am Acad Dermatol* 2008;58(5):826-50.
3. Luba KM, Stulberg DL. Chronic plaque psoriasis. *Am Fam Physician* 2006;73(4):636-44.
4. Pardasani AG, Feldman SR, Clark AR. Treatment of psoriasis: an algorithm-based approach for primary care physicians. *Am Fam Physician* 2000;61:725-33,736.
5. Peters BP, Weissman FG, Gill MA. Pathophysiology and treatment of psoriasis. *Am J Health-Syst Pharm* 2000;57:645-62.
6. Papp KA. The long-term efficacy and safety of new biological therapies for psoriasis. *Arch Dermatol Res* 2006;298:7-15.
7. Smith CH, Anstey AV, Barker JNWN, et al. British association of dermatologists guidelines for use of biological interventions in psoriasis 2005. *British J Dermatol* 2005;153:486-97.
8. Lebwohl M, Christophers E, Langley R, et al. An international, randomized, double-blind, placebo-controlled phase 3 trial of intramuscular alefacept in patients with chronic plaque psoriasis. *Arch Dermatol* 2003;136:719-27.
9. Krueger GG, Papp KA, Stough DB, 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. *J Am Acad Dermatol* 2002;47:821-33.

Billing/Coding

CODES	NUMBER	DESCRIPTION
GPI	90250515*****	Alefacept
HCPCS	J0215	Injection, alefacept, 0.5 mg
	S0193	Injection, alefacept 7.5 mg (includes dose packaging)
	C9212	Injection, alefacept, for intramuscular use, per 7.5 mg

Type of Service	Prescription Drug	
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Place of Service	Outpatient	
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Update Information

Date	Action	Reason
07/01/08	Replace PA criteria	New PA criteria

Preauthorization Criteria History

06/26/08	Reviewed by QMC
07/01/08	Preauthorization criteria original effective date
June 2009	Next Review