**BENEFIT DESCRIPTION AND LIMITATIONS OF COVERAGE**

**ITEM:** Amevive® (alefacept, injection)

**PRODUCT LINES:** Commercial HMO/PPO/CDHP

**COVERED UNDER:**
- HMO: Medical (provider setting)
- PPO/CDHP: Rx

**DESCRIPTION:** Binds to CD2, a receptor on the surface of lymphocytes, inhibiting their interaction with leukocyte functional antigen 3 (LFA-3). Interaction between CD2 and LFA-3 is important for the activation of T lymphocytes in psoriasis. Activated T lymphocytes secrete a number of inflammatory mediators, including interferon gamma, which are involved in psoriasis. Since CD2 is primarily expressed on T lymphocytes, treatment results in a reduction in CD4+ and CD8+ T lymphocytes, with lesser effects on other cell populations (NK and B lymphocytes).

**CPT/HCPCS Code:** J0215

**Company Supplying:** Biogen Idec

**Setting:** administered by intravenous (IV) or intramuscular (IM) infusion every week

**Coverage Criteria:** Express Scripts, Inc. monograph dated 10/19/2011

**Approval Period:** 12 weeks (see detail) or as otherwise noted for indication

**Recommended Authorization Criteria**

Coverage of alefacept is recommended in those who meet one of the following criteria:

**FDA-Approved Indications**

1. **Plaque psoriasis.** Authorization can be given for 12 weeks of therapy for patients who meet *all of* the following criteria a, b, and c:
   a. Alefacept is prescribed by a dermatologist or in consultation with a dermatologist,
   b. Patient has minimum BSA involvement with plaque psoriasis of ≥ 5%.
   Exceptions can be made to the requirement for ≥ 5% BSA involvement in the following instances (i or ii):
   i. Patients with plaque psoriasis of the palms, soles, head and neck, nails, intertriginous areas or genitalia are not required to have a minimum BSA involvement OR
   ii. The patient who meets all three of the following conditions is not required to have a minimum BSA involvement:
      - Patient has had an inadequate response to a 3-month trial of either topical therapy **OR** localized phototherapy with UVB or oral methoxsalen plus ultraviolet A (UVA) light (PUVA) and
      - Patient has had an inadequate response to a 3-month trial of systemic therapy (See c. below for list) or has contraindications to all of these and
      - Patient has significant disability or impairment in physical or mental functioning, according to the treating physician.
Note: Patients who meet both the criteria 1bii are not required to meet 1c below.

and

c. Patient has tried a systemic therapy or phototherapy for 3 months with one of the following agents: acitretin (Soriatane®), cyclosporine, methotrexate, adalimumab (Humira®), etanercept (Enbrel®), infliximab (Remicade®), or ustekinumab (Stelara™) or has tried phototherapy with UVB or PUVA for psoriasis. Rarely, a patient may have contraindications to nearly all of these other therapies and exceptions can be made on a case-by-case basis. (Due to its toxicity, alefacept therapy should be reserved for patients who have not responded well or are intolerant to other standard systemic therapy. In addition, the National Psoriasis Foundation Clinical Consensus, states that there currently are no prognostic factors that ascertain which therapies will be most efficacious and least toxic.)

(In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria above and the criterion for repeated courses.)

Approval Period:
After at least 12 weeks off alefacept therapy, patients may be reauthorized for a second 12 weeks of therapy. The above criteria (a, b, and c) do not have to be met for the second course of therapy. Authorization may be given for two 12-week courses in 48 weeks, provided there is a 12-week period off alefacept between courses.

d. Limited information is available in patients who have received more than two courses of alefacept, but in a follow-up study of 1,869 patients, some patients have received nine courses of alefacept. Alefacept FDA-approved dosing is for a 12-week course and a minimum of a 12-week interval since the previous course. In a small open-label trial in 20 patients, the efficacy and safety of administering alefacept for 12 weeks vs. 16 weeks was evaluated. Another extension study found that patients (n = 175) dosed with additional courses of alefacept (up to five courses) experienced similar safety profiles as patients completing one or two courses with alefacept.

Other Uses with Supportive Evidence

2. Psoriasis of hand and/or foot (may be palmoplantar pustulosis, palmoplantar pustular psoriasis, or palmar plantar pustulosis). Approve for up to 4 months (16 weeks) using the criteria above for plaque psoriasis regardless of type of psoriasis.

After at least 16 weeks off alefacept therapy, patients may be reauthorized for another 16 weeks of therapy. The above criteria for plaque psoriasis (a, b, and c) do not have to be met for the second course of therapy. Authorization may be given for two 16-week courses in 48 weeks provided there is a 16-week period off alefacept between courses. Some patients may have used 12 weeks of therapy for this indication. In this case, they should be off alefacept for at least 12 weeks before reauthorizing another course.

Hand or foot psoriasis may involve the palms of the hands, soles of the feet, or the dorsal surface of the hands or feet, and may be plaque-type and/or pustular-type (palmoplantar pustulosis). Some patients may not have psoriasis on other parts of the body. Hand and foot psoriasis is often refractory to treatment. Systemic therapy and phototherapy are often used. Alefacept has been effective for hand or foot psoriasis in two open-label studies. In one study in patients with palmoplantar pustular psoriasis (n = 15), 15 mg of alefacept was given IM once weekly for 8 weeks and then 30 mg once weekly for an additional 8 weeks. Severity of psoriasis improved with much of the improvement occurring after 10 weeks of therapy. In a second study in patients with palmar plantar pustulosis (n = 15), 15 mg of alefacept was given once weekly for 16
weeks. Maximal improvement was noted 8 to 16 weeks after therapy ended. Larger well-controlled trials are needed. Information on repeat courses is not available.

3. **Psoriatic arthritis (PsA).** Approve for 12 weeks of therapy if patient has tried adalimumab (Humira), etanercept (Enbrel), infliximab (Remicade), or golimumab (Simponi) for at least 3 months AND the patient will be receiving alefacept in combination with methotrexate. After at least 12 weeks off alefacept therapy, patients may be reauthorized for a second 12 weeks of therapy. Authorization may be given for two 12-week courses in 48 weeks, provided there is a 12-week period off alefacept between courses.

Adalimumab, etanercept, golimumab, and infliximab are FDA-approved for PsA and have shown efficacy in well-controlled trials in reducing signs and symptoms of active arthritis and to inhibit the progression of structural damage and improve physical function in patients with PsA. In a double-blind, placebo-controlled Phase II trial, patients with active PsA despite therapy with methotrexate for at least 3 months were randomized to IM alefacept 15 mg (n = 123) or placebo (n = 62) once weekly for 12 weeks in combination with methotrexate. This was followed by 12 weeks of observation with methotrexate therapy continuing in both groups. At Week 24, 54% of patients on alefacept/methotrexate attained an American College of Rheumatology (ACR) 20 response vs. 23% of patients on placebo/methotrexate (P < 0.001). ACR 50 and ACR 70 responses were numerically better for alefacept/methotrexate than for placebo/methotrexate but did not reach statistical significance. Mean reductions in tender and swollen joint counts were -8.0 vs. -6.3, respectively. In an open-label extension phase, patients (n = 160) who received ≥ 8 doses of alefacept or placebo injections during the double-blind phase were treated with an additional 12 weekly alefacept 15 mg IM injections while continuing their stable methotrexate dose, followed by 12 weeks of observation. At Week 24, 55% of patients on alefacept/methotrexate and 51% of patients on placebo/methotrexate in the double-blind phase achieved an ACR 20 response. Psoriatic arthritis disease activity was evaluated by reduction from baseline in ACR rating. Change in modified Sharp-van der Heijde radiographic scores were measured to assess erosion and joint space narrowing in each patient at baseline and at Week 24 of each phase of the study. Of the patients who were previously treated with alefacept plus MTX, the proportion of patients achieving an ACR 50 and ACR 70 increased from 17% and 7% to 34% and 12%, respectively. At baseline, the mean modified Sharp-van der Heijde score was 61.8 in the placebo-treated group compared to 84.8 in the alefacept-treated group indicating more joint damage at baseline in the alefacept treatment group. There was not a statistically significant difference in the change in modified Sharp-van der Heijde scores in either phase of the study between the two treatment groups. Additional larger trials are needed.

**Lichen planus.** Approve for 12 weeks if patient has tried at least two systemic therapies for this indication (e.g., phototherapy, acitretin, oral corticosteroid, mycophenolate mofetil, azathioprine, cyclosporine, oral tacrolimus, methotrexate). In case reports, 15 mg of alefacept once weekly for 12 weeks was effective in reducing the affected mucosal surface area and in reducing pain in patients with generalized or erosive mucosal lichen planus. Larger studies are needed. Information is not available on repeat courses.

**Exclusions**

Coverage of alefacept is not recommended in the following circumstances:
1. Alefacept should not be given in combination with a TNFα antagonist (e.g., adalimumab [Humira®], certolizumab pegol [Cimzia®], etanercept [Enbrel®], golimumab [Simponi™], infliximab [Remicade®], anakinra (Kineret®), or ustekinumab (Stelara™)). Patients receiving other immunosuppressive agents should not receive concurrent therapy with alefacept due to the possibility of excessive immunosuppression.

2. Rheumatoid arthritis. Published studies showing efficacy are not available.

3. Graft versus host disease (GVHD). Four studies have evaluated the use of alefacept in GVHD. In the first study, three patients with extensively pretreated, refractory GVHD were treated with alefacept and had rapid and clinically significant improvement in their GVHD. In the second study, 12 patients with extensively pretreated, refractory GVHD were treated with alefacept. Nine of the 11 evaluable patients showed response (10 of 12 evaluable episodes). The response was marked (three episodes), moderate (two episodes), or minimal (four episodes). In two of the responding patients, the response was only temporary and progression appeared under alefacept treatment (therefore treatment was stopped). With a 30-month median follow-up, 6 of 12 patients are alive: five with stable or improved GVHD, and one with progression. In the third study, seven patients with steroid resistant/dependent acute GVHD were treated with alefacept and all demonstrated response. In the fourth study, 16 patients (13 patients were steroid refractory, three patients were steroid dependent) previously treated with at least cyclosporine and steroids, were treated with alefacept for acute GVHD. Thirteen of the 16 patients showed a response. All complete responses were durable. Three of the responding patients had a relapse of acute GVHD a median of 278 days after alefacept. Five patients developed chronic GVHD. Other clinical trials evaluating alefacept for the treatment of GVHD are underway.

4. Alopecia areata or alopecia universalis. A randomized, double-blind, placebo-controlled, multicenter, 12-week study evaluated the use of alefacept in adult patients with chronic, severe, scalp alopecia areata (AA). Forty-five patients were randomized to treatment with weekly IM injections of alefacept 15 mg (n = 23) or placebo (n = 22) followed by observation for 12 weeks. Severity of Alopecia Tool (SALT) scores were comparable in both treatment groups at baseline. At the end of Week 12 and Week 24, there was not a significant change in SALT scores in either treatment group. Two patients in both the alefacept and placebo groups experienced at least a 50% improvement in SALT scores at Week 12. In the alefacept treatment group, only one of these patients was able to maintain this improvement at Week 24. Alefacept was not effective for treatment of alopecia areata.

5. Pyoderma gangrenosum. In an open-label pilot study four patients with idiopathic pyoderma gangrenosum received 15 mg of alefacept weekly for 20 weeks followed by 12 weeks of followup. At Week 32, two patients had attained clear or almost clear status (remission) and the other two patients had a marked improvement. Further studies are needed.

6. Atopic dermatitis. In a pilot study, nine adults with moderate to severe atopic dermatitis were treated with 30 mg of alefacept weekly for 8 weeks, and then if there was not a 50% reduction in the Eczema Area Severity Index (EASI) score, they continued another 8 weeks of 30 mg weekly. If there was a > 50% decrease in the EASI, the patients continued with 15 mg weekly for another 8 weeks. Patients were allowed to continue antihistamines. At Week 18, one patient attained an EASI 50 score and one an EASI 90 score. Five of nine patients did not finish the study due to lack of efficacy or worsening of disease. In another open-label study, 10 patients with atopic dermatitis were treated for 12 weeks with alefacept 15 mg IM weekly. All patients had significant improvement with mean percentage improvement in EASI of 78% at Week 12.
and 86% at Week 22; EASI 50 and EASI 75 were not reported. Additional studies are needed to establish safety and efficacy.

7. **Children ≤ 16 years of age.** The safety and efficacy of alefacept in pediatric patients has not been studied. In one of the clinical trials, patients ≥ 16 years were eligible, and in other trials patients were ≥ 18 years.

8. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### APPROVAL:

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