Raptiva®
Step Therapy Criteria

<table>
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<tr>
<th>Brand</th>
<th>generic</th>
<th>Dosage Form</th>
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<tr>
<td>Raptiva®</td>
<td>efalizumab</td>
<td>Injection, subcutaneous</td>
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FDA-APPROVED INDICATIONS

Raptiva® (efalizumab) is indicated for the treatment of adult patients (18 years or older) with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

RATIONALE FOR SELECTING

Raptiva has been selected for step therapy because the majority of patients experiencing active disease can be successfully managed with topical therapy. Alternatives to topical corticosteroids, which may cause skin atrophy, include the following; coal tars; calcipotriene ointment, a synthetic vitamin D₃ analogue; tazarotene, a topical retinoid; anthralin; and intralesional corticosteroid injections. When patients have psoriasis that is refractory to topical therapy or affected areas are too widespread for topical treatment, phototherapy or systemic therapy are generally prescribed. Alternatives include combination therapy with oral or topical psoralens and UVA radiation (PUVA) and systemic agents such as methotrexate, cyclosporine, the retinoid, acitretin, and the biologic agents Enbrel and Amevive.

Raptiva is an immunosuppressive recombinant humanized IgG1 monoclonal antibody that binds to CD11a, the α subunit of lymphocyte function-associated antigen-1 (LFA-1). This binding inhibits multiple key pathogenic steps; activation of T lymphocytes, adhesion of T lymphocytes to endothelial cells, and migration of T lymphocytes to sites of inflammation including psoriatic skin. Lymphocyte activation and migration to skin play a role in the pathophysiology of chronic plaque psoriasis.

Data submitted to the FDA for approval of Raptiva included four efficacy trials in patients with moderate-to-severe stable, plaque psoriasis. Patients enrolled had long-standing psoriasis (median of 19 years), and 66 percent have had a history of systemic therapy for psoriasis. The median psoriasis area and severity index (PASI) score was 19 and median body surface area involvement was 30 percent. Raptiva 1.0 mg/kg/week and Raptiva 2.0 mg/kg/week were compared to placebo after 12 weeks of treatment for the primary endpoint of 75 percent improvement from baseline in PASI scores. The proportion of patients who experienced 75 percent or greater improvement in PASI scores ranged from 18 percent to 37 percent in the four studies. The 2.0 mg/kg/week dose of Raptiva was not significantly more effective than the 1.0 mg/kg/week dose.

For patients who responded to Raptiva therapy in the initial 12 weeks of treatment and were allowed to continue therapy, 77 percent maintained their full clinical response during an additional 12-week treatment period as compared to 20 percent of those who were switched to placebo.
(p<0.0001). When Raptiva was used to retreat responders who relapsed (loss of 50 percent of treatment effect) after discontinuation of therapy, approximately one third of patients demonstrated improvement. For patients who were considered non-responders after the initial 12 weeks of treatment and allowed to continue for a total of 24 weeks of treatment, an additional 11 percent to 14 percent of patients demonstrated 75 percent or greater improvement in PASI scores.

The most frequently reported adverse events included headache, non-specific infection (e.g., common colds), nausea, chills, pain, and fever. Raptiva was associated with a higher incidence of adverse events than placebo and the incidence was highest after the initial injection but decreased with each subsequent injection. At the third dose, the incidence was similar between the active treatment group and placebo-treated group.

No deaths in psoriasis trials have been linked to Raptiva treatment. Malignancies in the initial treatment portion of trials were few (n=4) and similar in Raptiva-treated patients, controls, and external cohorts although numbers of cases were too small to make any conclusions concerning cancer risk. In the first 12 weeks of controlled trials, serious infections occurred in 0.4 percent of Raptiva-treated patients compared with 0.1 percent of placebo-treated patients. One opportunistic infection was reported, *Legionella* pneumonia.

Platelet counts at or below 52,000 cells/μL occurred in 8 (0.3%) Raptiva-treated patients during clinical trials. No abnormal platelet counts were reported in placebo-treated patients. Five of the eight patients received a course of systemic corticosteroids. Response to steroid treatment suggests an immune-mediated thrombocytopenia and assessment of platelet counts is recommended periodically during therapy. Other potentially autoimmune and/or inflammatory adverse events such as transverse myelitis, pneumonitis, idiopathic hepatitis, and serum sickness have also been reported in Raptiva-treated patients.

During clinical trials 19 of 2589 (0.7%) Raptiva patients had serious worsening of psoriasis during treatment or after discontinuation of therapy including psoriatic erythroderma and pustular psoriasis. Some patients required hospitalization and alternative antipsoriatic therapy.

**INITIAL AUTOMATIC STEP THERAPY EDIT FUNCTIONALITY**

The overall process for step therapy requires that another drug or drugs be tried for a specific quantity of drug in the previous time period before the claim drug. The patient must have evidence of the applicable drug-specific edit(s) in the patient’s prescription drug history.

Raptiva® edit

In order for a Raptiva claim to pay automatically the patient must have evidence of a claim for a topical or systemic psoriasis treatment in their medication history within the past six months. Topical treatment that will allow automatic payment for Raptiva include coal tar products (GPI 9052*********), anthralin, (GPI 902500*********), topical corticosteroids, (GPI 9055*********), calcitriol, (GPI 902500*********), and tazarotene, (GPI 902500*********). A claim for Raptiva will also pay automatically if there is evidence of a claim for systemic methotrexate (GPI 21300050****** or 66250050******), cyclosporine (GPI 9940202030****), acitretin (GPI 90250510******), or methoxsalen (GPI 90250560******) or previous use of a biologic agent, Enbrel (GPI 66290030******) or Amevive (GPI 90250515******) if, within the six month look-back time frame and there has been a minimum of 30 days between the apparent end of Enbrel or Amevive therapy and the new claim.

Raptiva claims will also pay automatically if there is evidence of Raptiva therapy (GPI 90250527******) within 90 days prior to the new claim. The 90 day parameter is intended to identify current use and prevent disruption of previously established therapy. The claims system is designed to identify a Raptiva claim with a days supply that ends within the 90-day look-back parameter.
If the patient has met any of the requirements defined above, the claim for Raptiva will be paid automatically under the patient’s current prescription benefit. If the patient does not meet the step therapy criteria, then the claims adjudication system will reject the claim and a Point of Sale message will indicate that a prior authorization is necessary. The Prior Authorization (PA) Criteria for Approval would then be applied to requests submitted by the patient’s practitioner for evaluation.

CLINICAL RATIONALE FOR STEP THERAPY FUNCTIONS

Step therapy Electronic Edit
The intent of the initial step therapy edit is to electronically identify patients that have been previously treated with topical or systemic antipsoriatic agents or Raptiva. The majority of patients with psoriasis can be effectively treated with topical agents, corticosteroids being the most prescribed and most effective. Chronic plaque psoriasis is a disease with symptoms that wax and wane and treatment may be intermittent. Therefore, the step edit function will require one claim for one of the designated agents in the previous 180 days.

Prior Authorization (PA) Criteria for Approval
The intent of the PA Criteria for Approval is to ensure that patients have been diagnosed with chronic plaque psoriasis and are properly selected according to product labeling and/or clinical studies and/or guidelines.

The PA Criteria for Approval will require a diagnosis of chronic plaque psoriasis. A trial of at least one topical or systemic antipsoriatic agent or prior use of Raptiva will be required before treatment with Raptiva will be approved. According to American Academy of Dermatology Guidelines of Care for Psoriasis, the majority of patients can be successfully treated with topical agents. Initial approval for Raptiva will be for six months. Clinical trials involving extension of therapy for 12 weeks beyond the initial 12-week period indicates that some patients may become responders to therapy if continued beyond 12 weeks. Prior use of the biological agents Enbrel or Amevive will be considered as a previous systemic antipsoriatic agent and use of Raptiva will be approved if there will be a minimum of 30 days between therapies. The thirty-day interval is to assure elimination of the previous TNF-blocking agent before administration of a second agent.

For continuation of Raptiva therapy beyond the initial six months, there should be evidence of improvement in disease severity. In clinical trials improvement was assessed by improvement in PASI, an evaluation tool that takes into consideration the percent of body surface area affected and the nature and severity of the psoriatic changes within the affected regions (erythema, infiltration/plaque thickness, and desquamation) or a six category scale (Physician Global Assessment) ranging from “very severe” to “clear.” Renewals of therapy may be approved for an additional 12 months of therapy. Currently, there is little data evaluating the efficacy of continuous Raptiva treatment.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Initial and Renewal Evaluation
1. Has the patient been previously treated with Raptiva in the past 90 days?
   If yes, approve for 12 months. If no, continue to 2.

2. Has the patient been diagnosed with chronic plaque psoriasis?
   If yes, continue to 3. If no, deny.

3. 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 acitretin)?
   If yes, approve for 6 months. If no, continue to 4.

4 Has the patient been previously treated with Enbrel or Amevive?
   If yes, continue to 5. If no, deny.
5. Will Enbrel or Amevive be discontinued before the first dose of Raptiva?  
   If yes, approve for 6 months.  If no, deny.

CONCLUSION
Step therapy electronic edits are designed to identify patients electronically by their medication history. The prior authorization process provides a member-specific review process. Practitioner provided patient-specific parameters are taken into consideration and are reviewed by a physician.

REFERENCES
5. FDA’s Dermatologic and Ophthalmic Drugs Advisory Committee meeting. September 9, 2003. Available at http://www.fda.gov/ohrms/dockets/ac/cder03.html#DermatologicandOphthalmicDrugs

Document History
Original Prime Standard approved by UMC 02/2004
Client specific modifications 07/2005
Annual Review with changes approved by External UMC 11/2005
Annual Review with changes, Client Specific criteria approved by HCSC Corporate Clinical Committee 12/2005
[correction of Enbrel GPI included with AR]