



# BlueCross BlueShield of Nebraska

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## EFALIZUMAB (Raptiva®) Preauthorization Criteria for Approval

### Medications and Dosage Forms Included in Criteria

Generic Name	Brand Name	Dosage Form
Efalizumab	Raptiva®	Subcutaneous injection

### 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.<sup>1</sup>

### Description

The purpose of the Raptiva (efalizumab) 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 which has persisted for more than six months.

### Criteria

#### Initial Evaluation

1. Has the patient been treated with Raptiva within the past 6 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 acetretin)?  
If yes, approve for 6 months.  
If no, do not approve.

#### Renewal Evaluation

1. Has the patient been previously treated with Raptiva?  
If yes, continue to 2.  
If no, see initial evaluation.

2. Did initial treatment with Raptiva 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 the patient been previously treated with Raptiva and has now relapsed after discontinuation of therapy?  
If yes, approve for 6 months.  
If no, continue to 4.
4. Is Raptiva being prescribed as continuous therapy to improve or maintain symptoms of plaque psoriasis?  
If yes, approve for 12 months.  
If no, do not approve.

## Rationale

The purpose of the Raptiva (efalizumab) Preauthorization Criteria is to provide approval to patients prescribed Raptiva that have tried first-line therapy and meet product labeling recommendations. Efalizumab 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.<sup>2-4</sup> The majority of patients can be managed with topical therapy.<sup>2-4</sup>

Topical corticosteroids is documented as the most commonly prescribed treatment for psoriasis and is consistently considered initial therapy in treatment algorithms.<sup>4,5</sup> Corticosteroids are not the only option for initial treatment as corticosteroids can cause skin atrophy.<sup>5</sup> Alternatives include coal tar, anthralin, vitamin D<sub>3</sub> analogues (calcipotriene), topical retinoids (tazarotene), and intralesional injection of corticosteroids.<sup>5</sup> 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.<sup>2-5</sup>

Efalizumab 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 efalizumab to other therapies and the potential for serious side effects.<sup>1,6</sup> Guidelines recommend on the use of efalizumab when the disease is severe, the psoriasis fails to respond to standard systemic therapies or the patient is intolerant to, or has a contraindication to, these treatments.<sup>6,7</sup>

Psoriasis is a chronic inflammatory, T-cell-mediated autoimmune disease characterized by periods of spontaneous remission and relapse. Efalizumab classified as an immunosuppressive recombinant humanized IgG1 kappa isotype monoclonal antibody that binds to human CD11a, the  $\alpha$  subunit of leukocyte function antigen-1 (LFA-1), which is expressed on all leukocytes, and decreases cell surface expression of CD11a.<sup>1</sup> Efalizumab inhibits the binding of LFA-1 to intercellular adhesion molecule-1 (ICAM-1), thereby inhibiting the adhesion of leukocytes to other cell types.<sup>1</sup> Interaction between LFA-1 and ICAM-1 contributes to the initiation and maintenance of multiple processes, including activation of T lymphocytes, adhesion of T lymphocytes to endothelial cells, and migration of T lymphocytes to sites of inflammation including psoriatic skin.<sup>1</sup> Lymphocyte activation and trafficking to skin play a role in the pathophysiology of chronic plaque psoriasis.<sup>1</sup> In psoriatic skin, ICAM-1 cell surface expression is upregulated on endothelium and keratinocytes.<sup>1</sup> CD11a is also expressed on the surface of B lymphocytes, monocytes, neutrophils, natural killer cells, and other leukocytes.<sup>1</sup> Therefore, the potential exists for efalizumab to affect the activation, adhesion, migration, and numbers of cells other than T lymphocytes.<sup>1</sup>

The most common adverse reactions associated with efalizumab were a first dose reaction complex that included headache, chills, fever, nausea, and myalgia within two days following the first two injections.<sup>1</sup> These reactions are dose-level related in incidence and severity and were largely mild to moderate in severity when a conditioning dose of 0.7 mg/kg was used as the first dose.<sup>1</sup> The most serious adverse reactions observed during treatment with efalizumab were serious infections, malignancies, thrombocytopenia, hemolytic anemia, arthritis events, and psoriasis worsening and variants.<sup>1</sup> In clinical trials conducted evaluating treatment beyond 12 weeks found that adverse effect frequency and intensity were similar to placebo during the second treatment and subsequent treatment periods.<sup>8</sup> Immune-mediated thrombocytopenia and immune-mediated hemolytic anemia are serious side effects to treatment.<sup>1,8</sup> Assessment of platelet counts is recommended upon initiating and periodically while receiving efalizumab treatment due to severe thrombocytopenia. It is recommended that assessments be more frequent when initiating therapy (e.g., monthly) and may decrease in frequency with continued treatment (e.g., every 3 months). End-organ toxicity has not been observed during clinical trials.<sup>8</sup> Efalizumab is an immunosuppressive agent and has the potential to increase the risk of infection and reactivate latent, chronic infections.<sup>1</sup> Efalizumab should not be administered to patients with clinically important infections.<sup>1</sup> Caution should be exercised when considering the use of efalizumab in patients with a chronic infection or history of recurrent infections.<sup>1</sup> If a patient develops a serious infection, efalizumab should be discontinued.<sup>1</sup>

Worsening of psoriasis and psoriasis variants is a possibility during and after treatment with efalizumab.<sup>1</sup> A recent analysis of rebound and relapse with efalizumab therapy indicated a 3% incidence of worsening during treatment and a 14% incidence after abrupt discontinuation of therapy.<sup>9</sup> Interestingly, the incidence of rebound was associated with level of response to treatment.<sup>9</sup> Rebound was observed in 72% of nonresponder patients and 10% in patients that had achieved a PASI-75.<sup>9</sup>

### **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.<sup>6</sup> Furthermore, patients must have psoriasis symptoms for at least 6 months.<sup>6</sup> 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. Extension of treatment beyond the initial 12 weeks has been evaluated and some patients may respond to therapy beyond the 12 week period.<sup>8</sup> The potential for response after the initial 12 weeks of treatment has been accounted for in the criteria as approvals are for 6 months.

For renewal of therapy after the initial 6 months, evidence of disease improvement must be documented. Documentation of improvement is usually assessed by the PASI score or the static Physician Global Assessment (sPGA). The PASI is a composite score that takes into consideration both the fraction of body surface area affected and the nature and severity of the psoriatic changes within the affected regions (erythema, infiltration/plaque thickness, and desquamation).<sup>1</sup> The sPGA is a 6 category scale ranging from "very severe" to "clear" indicating the physician's overall assessment of the psoriasis severity focusing on plaque, scaling and erythema.<sup>1</sup> If patients improve on initial therapy they may be approved through the PA evaluation process for additional therapy. If a patient has relapsed after cessation of therapy, approval may be granted for repeat therapy, however, improvement must be documented after six months for continuation of therapy.

### **References**

1. Raptiva® (efalizumab) [package insert]. South San Francisco, CA: Genentech, Inc., June 2005.
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. 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.
7. National Institute for Health and Clinical Excellence (NICE). Technology appraisal guidance 103: Etanercept and efalizumab for the treatment of adults with psoriasis. Available at: <http://www.nice.org.uk/TA103>. Accessed June 2008.
8. Papp KA. The long-term efficacy and safety of new biological therapies for psoriasis. *Arch Dermatol Res* 2006;298:7-15.

## Billing/Coding

CODES	NUMBER	DESCRIPTION
GPI	90250527*****	Efalizumab
HCPCS	S0162	Injection, efalizumab, 125 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