Along with traditional systemic therapies, the American Academy of Dermatology recommends four biologic agents as first-line treatment for psoriasis patients who are candidates for systemic therapy.

Evaluating New Therapies for Psoriasis

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Psoriasis is one of the most common skin disorders, affecting approximately 1 in 50 Americans (NPF 2004). This immune-mediated disease, which is incurable and chronic, is characterized by periods of remission and relapse.

More than 4.5 million Americans have been diagnosed with one of the five recognized types of psoriasis: plaque, guttate, inverse, erythrodermic, and pustular. Plaque psoriasis accounts for about 80 percent of these diagnoses.

In plaque psoriasis, the skin may have well-defined areas that are thick, red, raised, and covered with silvery scales. These patches, or plaques, may be found anywhere on the body, though it is more common to find them on the elbows, knees, scalp, lower back, face, palms, and soles. An associated arthritis, psoriatic arthritis, develops in approximately 10 to 30 percent of people with psoriasis. Annual costs of managing patients with psoriasis are estimated to exceed $3 billion (NPF 2004).

Psoriatic plaques itch and may cause burning or pain. Moreover, the disfigurement and discomfort caused by the disease significantly affect quality of life. The physical impact of psoriasis is measured by the extent of the body area involved. Mild psoriasis is defined as involvement of less than 2 percent of body area. Moderate psoriasis involves between 3 and 10 percent of the body; involvement greater than 10 percent is classified as severe psoriasis.

This classification does not capture patient disability or diminished quality of life, however. For example, psoriasis that affects the knees of a carpet layer or tile installer presents a greater burden than does plaque of the same size on the back or trunk. Likewise, psoriasis on those areas that are not typically covered by clothing is of greater concern to a patient than is "hidden" psoriasis.

Patients with moderate to severe chronic plaque psoriasis require long-term therapy to control their symptoms; about one third of patients need systemic therapy or phototherapy to control their disease (Greaves 1995). Fortunately, most patients have limited forms of the disease, involving small areas of skin and characterized by spontaneous exacerbations and periods of remission. Nevertheless, patients with moderate or severe disease may need years of aggressive therapy to control their symptoms and to improve their quality of life.

Many available systemic therapies, however, are unsuitable for chronic administration due to the risk of cumulative toxicity (Tristani-Firouzi 1998). Because of the associated risk of toxicity and adverse events, these agents have been administered intermittently, with periodic discontinuation of therapy and monitoring for severe side effects. This cyclical therapy results in cycles of remission and recurrence of disease.

Increased knowledge of the role of the immune system in the pathogenesis of psoriasis has led to the development of biologic agents that specif-

ically target the pathogenesis of psoriasis (Krueger 2002).

These agents act on the immune system, disrupting the cycle that results in symptom flares. Developing agents that are not simply immunosuppressive, but rather target specific areas of the immune system, may result in reduced toxicity. The goal of therapy with these new agents is to achieve continuous disease control without interruptions, thus breaking the cycle of remission and recurrence.

AVAILABLE TREATMENTS

Traditional therapies

Because no cure exists for psoriasis, treatments are aimed at managing symptoms and improving quality of life. Historically, treatments were structured in a stepwise approach. Topical treatments were used initially, phototherapy was considered to be second-line, and finally, systemic therapies were employed.

With increased knowledge of the disease process, current approaches to psoriasis treatment tailor therapy to the individual patient. Assessment of the severity of the disease, the type of psoriasis, the location on the body, and the individual's age and medical history may lead to the initiation of systemic treatment at the time of diagnosis.

The fact that the disease often is cyclical does complicate the management and clinical tracking of therapy for patients with psoriasis. The size, character, and location of psoriatic plaques, as well as symptoms of psoriasis may improve or worsen over time. In addition, a prior response to treatment is not always a predictor of response with the next flare; skin may become resistant to some treatments.

Topical treatments for management of psoriasis include topical steroids, coal tar, calcipotriene, anthralin, salicylic acid, tazarotene, and moisturizers. These agents are not without adverse effects but are considered low-risk therapy options when compared with alternative agents.

Patients who have moderate to severe psoriasis may benefit from treatment with phototherapy. Phototherapy options include PUVA (psoralen combined with ultraviolet A), ultraviolet B (UVB), and laser treatment. Phototherapy sessions take a considerable amount of time — 2 or 3 visits are required weekly for many months — thus affecting quality of life. Additionally, PUVA therapy is associated with an increased risk of skin cancer.

Systemic treatments are reserved for patients with moderate to severe psoriasis. The use of the older systemic therapies, such as cyclosporine, methotrexate, and retinoids, is associated with a high frequency of adverse effects — including hepatotoxicity, nephrotoxicity, teratogenicity, and malignancy — that limit their usefulness.

It is generally recommended that these treatment options be used for a maximum of only 1 to 2 years. Patients commonly are switched from one therapy to another in an effort to avoid the cumulative toxicity associated with long-term use. Also, many people abandon therapy as either too time-consuming or dangerous and become socially reclusive.

Biologic agents

A better understanding of the pathophysiology of psoriasis has enabled the development of biologic agents that target the cascade initiated by the activation of T cells. Excessive keratinocyte proliferation and abnormal differentiation were once believed to be the cause of psoriasis (Krueger 2002).

Psoriasis is now understood to be a T cell-mediated disease. Although the underlying cause of the disease is not completely understood, activated T cells are present in the skin of patients with psoriasis. The activation of T cells is the first step in a cascade of inflammatory events, which continues with the migration of T cells into the skin tissue and culminates in the secretion of cytokines, such as tumor necrosis factor-alpha (TNF-alpha).

The proliferation of T cells in psoriasis begins with an antigen bound to class I or class II major histocompatibility complex molecules presenting on the surface of a dendritic antigen-presenting cell (APC) being recognized by a T cell (Krueger 2002).

The first interaction that occurs between a T cell and an APC is the binding of lymphocyte function-associated antigen type 1 (LFA-1) on the surface of T cells with intercellular adhesion molecule-1 (ICAM-1).

Additionally, numerous accessory or costimulatory signals are important for optimal T cell activation, including CD28, CD80, CD40, and CD86, among others. APC maturation is controlled by granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-4 (IL-4), and TNF-alpha. Following activation, T cells proliferate and differentiate. It is the sum of all these factors that contributes to the continued movement of inflammatory cells into the skin and the increased activity of keratinocytes.

To date, the U.S. Food and Drug Administration has approved three entities for treatment of psoriasis: alefacept, etanercept, and efalizumab. Infliximab, currently FDA-approved for treatment of rheumatoid arthritis and Crohn's disease, is in phase 3 clinical trials for the treatment of psoriasis. Adalimumab (Humira), which is a monoclonal antibody against TNF-alpha, is FDA-approved for patient-administered treatment of rheumatoid arthritis. It also is in early phase 3 clinical trials for psoriasis.

No comparative trials between any of the biologic agents have been con-

ducted. Health care providers and managed care decision makers therefore must familiarize themselves with the differences among these products to make informed decisions regarding product selection and formulary inclusion (Table 1).

For the purpose of clinical trials, the Psoriasis Area and Severity Index (PASI) is used to quantify disease severity. This measure assesses overall severity and coverage of psoriasis, taking into account the area involved on the head, trunk, arms, and legs.

Disease severity in each region is assessed by examining the degree of plaque erythema (redness), thickness, and scaling. The composite PASI score ranges from 0 (no disease) to 72 (maximal disease).

The FDA has established a primary outcome measure for the evaluation of agents to treat psoriasis, which is the proportion of patients who achieve a reduction in PASI score of 75 percent or more, relative to baseline (PASI-75).

Mechanism of action

Recently, it has been suggested that biologic therapies for psoriasis can be classified according to four different strategies for addressing immunomodulation (Table 2). The agents discussed in this article execute three of those strategies.

Reducing the number of pathogenic T cells is one means by which alefacept appears to function. Alefacept is a fusion protein consisting of the extracellular CD2-binding portion of LFA-3 and the Fc portion of human IgG1. Presumably because the Fc portion of the fusion protein binds to the immunoglobulin Fc receptors of cytotoxic cells, alefacept reduces the number of CD2+ lymphocytes, through granzyme-mediated apoptosis (Ellis 2001). Clinical improvement in patients who are receiving alefacept has been correlated with reduced memory T cell counts (Gordon 2003a). Additionally, alefacept binds to CD2 on the surface of T cells,

TABLE 1 Summary of attributes of biologic agents for psoriasis

	Alefacept	Efalizumab	Etanercept	Infliximab
Trade name	Amevive	Raptiva	Enbrel	Remicade
Manufacturer	Biogen Idec	Genentech	Amgen/Wyeth	Centocor
FDA approval for psoriasis	January 2003	October 2003	April 2004	in phase 3 trials
Description	fusion protein (components of LFA-3 and IgG1)	humanized monoclonal IgG1 antibody	fusion protein (components of the p75 TNF receptor and IgG1)	chimeric monoclonal IgG1 antibody
Molecular target	CD2, a subunit of LFA-3, expressed by activated T cells	CD11a, a subunit of LFA-1, expressed by all leukocytes	TNF-alpha (also binds to TNF-beta)	TNF-alpha
Administration	intramuscular (IM)	subcutaneous	subcutaneous	intravenous infusion
Frequency	15 mg once weekly for 12 weeks; 2nd 12-week course may be initiated after elapse of at least 12 weeks	weekly, beginning with conditioning dose of 0.7 mg/kg, followed by 1 mg/kg thereafter	50 mg twice weekly for 3 months, followed by reduction to maintenance dose of 50 mg weekly	3 mg/kg or 5 mg/kg at 0, 2, and 6 weeks *(dosing used in recent phase 2 trial)*
Onset of response	slow	moderately rapid	moderately rapid	rapid
Monitoring	required	required	not required	required
Average wholesale price — usual single dose	15 mg IM — $995.00	125 mg — $360.15	initial: 100 mg — $690.16 maintenance: 50 mg — $345.08	100 mg — $691.61

LFA-1=lymphocyte-function–associated antigen type 1, LFA-3=lymphocyte-function–associated antigen type 3, TNF=tumor necrosis factor.

which thereby prevents the interaction of CD2 on T cells with LFA-3 on APCs; such an interaction is a component of T cell activation.

Efalizumab is a monoclonal antibody that binds to CD11a, the alpha chain of LFA-1, which is expressed on the surface of T cells (and all other leukocytes) (Raptiva PI). Efalizumab decreases the cell-surface expression of CD11a and also prevents LFA-1 from binding to ICAM-1 on other cell types, notably endothelial cells and keratinocytes. In psoriatic skin, expression of ICAM-1 is upregulated on the surface of these cells, and the interaction between LFA-1 and ICAM-1 plays a role in the activation of T cells, adhesion of T cells to endothelial cells, and migration of T cells to sites of inflammation.

Infliximab, which is also a monoclonal antibody, binds both free and receptor-bound TNF-alpha, and blocks its activity by preventing it from binding with its receptors. Additionally, it lyses TNF-alpha–expressing T cells (Remicade PI).

TNF-alpha also is blocked by etanercept, a fusion protein consisting of the extracellular binding portion of the human TNF receptor and the Fc portion of human IgG1. Etanercept is not specific for TNF-alpha, however, as it also binds TNF-beta (also known as lymphotoxin-alpha).

Administration and monitoring

The biologic agents differ in their administration and monitoring requirements. Infliximab and alefacept both necessitate administration by health care personnel (and hence entail the extra expense that is associated with office visits), while both etanercept and efalizumab can be self-administered subcutaneously.

Alefacept is given as a weekly intramuscular dose necessitating health care personnel intervention. (The manufacturer has discontinued distributing an intravenous product.) Alefacept can cause lymphopenia, and it is recommended that patients receiving alefacept therapy for psoriasis receive weekly CD4+ T lymphocyte counts during the 12-week treatment course and that treatment be withheld if counts are below 250 cells/microliter (Amevive PI).

Infliximab is administered via intravenous infusion. In studies with infliximab for psoriasis, the dose has been administered in three separate infusions, each given over 90 minutes. Administration of infliximab requires administration and observation by a health care professional, because of the potential for infusion reactions. An increased risk of infection has been observed when infliximab is used in patients with rheumatoid arthritis or Crohn's disease, including reactivation of latent tuberculosis. Patients should be monitored closely for signs and symptoms of infection.

Etanercept is self-administered as a subcutaneous injection. The recommended starting dose for the treatment of plaque psoriasis in adults is 50 mg twice weekly, which is twice the typical weekly dose used for treatment of other diseases for which etanercept is approved (rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis). After 3 months, the dose for psoriasis patients should be reduced to 50 mg per week. The manufacturer suggests no specific monitoring parameters (Enbrel PI).

Efalizumab is self-administered as a weekly subcutaneous injection. An initial conditioning dose is required. The Raptiva PI recommends the monitoring of platelets every month for the first 3 months and every 3 months thereafter. In terms of ease and frequency of administration, the self-administered agents may hold an advantage over the other biologics, but the preferences of patients and physicians will vary.

Onset of response

The biologic agents have exhibited differences in the rate of response to therapy. The response to infliximab appears to be rapid, with a statistically significant difference between active drug and placebo seen after a single dose (Sobell 2003). In a small (N=33) randomized, placebo-controlled trial enrolling patients with moderate to severe psoriasis, the median time to response was 4 weeks (Chaudhari 2001).

Response to both etanercept and efalizumab also is rapid, with results that can be seen as early as 4 weeks (Enbrel PI, Raptiva PI). Yet, onset of response to alefacept is much slower, at 60 days (Amevive PI). These differences in onset of response may have important financial implications in managed care. The rapid onset of

TABLE 2 Mechanism of action of biologic therapies for psoriasis

Strategy	Biologic agent	Molecular target
Reduction of pathogenic T cells	Alefacept	CD2
Inhibition of T cell activation and migration	Efalizumab	CD11a
Immune deviation	Etanercept	TNF-alpha
Blocking activity of inflammatory cytokines	Infliximab	TNF-alpha

SOURCE: SINGRI 2002

response allows decisions about continuing treatment with etanercept, efalizumab, or infliximab to be made at an early stage, and hence after a comparatively modest financial outlay, whereas patients receiving alefacept require a full course of treatment before the effectiveness of the treatment can be determined. Frequently in the day-to-day practice, the selection of which biologic agent to use for an individual patient may depend more on which agent will result in the lowest out-of-pocket cost for the patient rather than the comparative safety, efficacy, route of administration, onset of action, or duration of response.

Duration of response

Following the discontinuation of efalizumab after 24 weeks of therapy, PASI-50 was maintained in 30 percent of patients during a follow-up period of 12 weeks (Lebwohl 2003). The response of psoriasis to treatment with infliximab or alefacept has persisted for weeks after discontinuation of active treatment. After the initial 3 intravenous infusions of infliximab, clinical response has been maintained for up to 6 months in about half the patients, without any additional treatment (Gottlieb 2003). Continued response to alefacept has persisted for a median of 10 months before retreatment was required, and no disease rebound has been observed following cessation of alefacept therapy (Krueger 2003). The National Psoriasis Foundation defines rebound as a PASI exceeding 125 percent of baseline within 12 weeks of discontinuation of treatment. Psoriasis has been reported to rebound in less than 1 percent of patients following discontinuation of efalizumab.

Adverse events

Although the biologic agents are considered safer than traditional systemic immunosuppressive treatments for psoriasis, they are not free from adverse effects. As with any immunosuppressive agent, these agents have the potential to cause an increased risk of infection and malignancy.

Adverse events associated with efalizumab therapy have been primarily mild to moderate (Raptiva PI, Gordon 2003b, Lebwohl 2003). Pooled safety data from the four phase 3 efalizumab studies include 2,335 patients — 1,620 patients treated with efalizumab and 715 patients treated with placebo (Raptiva PI). These data constitute one of the largest safety cohorts for biologic psoriasis therapy to date in randomized, placebo-controlled trials. The safety profile for efalizumab was consistent across all four studies. No increased T cell depletion, risk of malignancy, end-organ toxicity, or infection has been observed (Raptiva PI). A conditioning dose must be given when initiating therapy to help reduce the occurrence of a first-dose reaction (headache, nausea, fever, and vomiting).

Antibodies to efalizumab have developed during treatment in 6.3 percent of patients but have not been associated with adverse events and have not necessitated discontinuation of therapy; neither has their development led to a need for a dosing increase.

Adverse events associated with the administration of infliximab for FDA-approved indications have in-

TABLE 3 Percentage of efalizumab-treated patients achieving PASI-75 and PASI-90 scores at 3-month intervals, out to 30 months

		Intent-to-treat analysis (n=339)								
	Month 3	Month 6	Month 9	Month 12	Month 15	Month 18	Month 21	Month 24	Month 27	Month 30
PASI-75	41%	44%	46%	49%	50%	46%	48%	47%	47%	50%
PASI-90	13%	19%	21%	22%	25%	29%	26%	27%	25%	29%
		Maintenance group analysis (n=290)								
PASI-75		52%	57%	57%	58%	56%	56%	56%	58%	58%
PASI-90		22%	24%	26%	29%	33%	30%	31%	30%	34%
		As-treated analysis (n varies)								
		(n=290)	(n=269)	(n=247)	(n=228)	(n=202)	(n=194)	(n=182)	(n=170)	(n=159)
PASI-75		52%	58%	62%	64%	67%	68%	66%	72%	78%
PASI-90		22%	25%	27%	31%	39%	34%	36%	35%	45%

PASI=Psoriasis Area and Severity Index.

SOURCE: GOTTLIEB 2004

cluded headaches and infusion reactions (Remicade PI). Antibodies have been documented in approximately 10 percent of patients; patients developing antibodies are more likely to experience infusion reactions (Sobell 2003, Remicade PI). The clinical significance of the antibodies is yet to be fully defined; they may affect the ability of the drug to work effectively over time. Anaphylactic-like reactions have been reported in postmarketing experience when infliximab has been used for approved indications. There has been an association with an increased rate of mortality when infliximab is used in patients with New York Heart Association Class III and Class IV heart failure (Remicade PI).

Injection site reactions are the most common adverse events associated with administration of etanercept. Antibodies to etanercept have been detected in approximately 6 percent of patients. These antibodies have not been correlated with clinical response or adverse effects. Because etanercept has been available for several years for other indications, its safety profile when used for conditions other than psoriasis is well defined; no T cell depletion, end-organ toxicity, or association with increased risk of either malignancy or infection has been observed (Weinberg 2003).

The mechanism of action of alefacept leads to a reduction in circulating total CD4+ and CD8+ T lymphocytes (Ellis 2001). This effect is dose-dependent and necessitates weekly monitoring of the CD4+ cell counts throughout therapy. Alefacept therapy has been associated with treatment-emergent malignancies in less than 2 percent of patients. Approximately 3 percent of the patients who are treated with alefacept develop antibodies during therapy. No adverse effects or effects on clinical response have been linked to the formation of antibodies. Hypersensitivity reactions also have been reported (Amevive PI).

LONG-TERM THERAPY WITH BIOLOGICS

Because psoriasis is a chronic disorder, long-term data on continuous administration of the biologic agents are desirable. To some extent, etanercept and infliximab are more familiar entities, because their safety and tolerability profiles have been well characterized through their longer use to treat conditions other than psoriasis.

Worldwide, infliximab has been used by more than 500,000 patients, and etanercept enjoyed extensive off-label utilization for psoriasis prior to the recent approval of its indication for the condition. Alefacept and efalizumab are less well known, due to the fact that they received their initial indications, for psoriasis, relatively recently. Interim 30-month results recently have been reported, however, from an open-label, multicenter, phase 3 study that was designed to evaluate the safety, tolerability, and efficacy of continuous efalizumab therapy for up to 3 years in patients with moderate to severe chronic plaque psoriasis (Gottlieb 2004). This is the longest continuous trial examining continuous use of any biologic agent in the treatment of psoriasis.

Patients were enrolled in the maintenance arm of the trial if they had achieved PASI-50 compared with baseline or a static Physician Global Assessment (sPGA) grade of mild, minimal, or clear after the initial 12 weeks of efalizumab treatment. The sPGA provides an indication of the physician's overall assessment of psoriasis and focuses on scaling, erythema, and plaque.

The primary efficacy measure was the percentage of patients with 75 percent or greater improvement in PASI at week 12 and at the end of each 3-month segment, compared with baseline. The impact of efalizumab on PASI scores was analyzed in three ways: intent-to-treat analysis, maintenance group analysis, and patients continuing on therapy (as-treated) analysis.

The intent-to-treat analysis included all 339 patients initially enrolled in the study, even if they failed to qualify for the maintenance phase. Patients who discontinued treatment during the first 12 weeks were classified as achieving less than PASI-50 at 12 weeks. If patients discontinued during the maintenance phase, their last PASI score was carried forward for analysis. Table 3 shows the percentage of patients who received up to 30 months of continuous efalizumab therapy and achieved 75 percent or 90 percent improvement in their PASI scores.

During the maintenance phase, 46 percent (133/290) of the subjects discontinued treatment.

In general, efalizumab therapy was well tolerated, with only 1 to 2 percent of patients discontinuing treatment due to adverse events during each 3-month maintenance treatment segment. The rate of serious adverse events ranged from 1.0 percent to 5.5 percent. Clinically significant adverse events remained generally stable during each 3-month segment.

In summary, treatment with efalizumab appears to be safe and efficacious up to at least 30 months of continuous weekly subcutaneous dosing, suggesting that the 1-year efficacy and safety limit cited in the current product labeling understates its benefits for patients afflicted with this chronic disease.

CONCLUSION

The addition of the biologic agents provides health care practitioners with more options in the management of patients with plaque psoriasis. These agents vary substantially

with respect to mechanism of action, mode and frequency of administration, time to onset of response, duration of response, and monitoring requirements.

At present, it is not possible to predict which patients will respond to which biologic agents. Biologic agents that are known for their relatively rapid onset of response (e.g., efalizumab, etanercept, infliximab) may be attractive as first choices, because they minimize financial outlay in the event of treatment failure.

Patients who respond to a 12-week course of alefacept may maintain their response for several months without the need for additional alefacept treatment; others may require a second 12-week course. This response pattern stands in contrast to that observed with efalizumab or etanercept, in which patients who respond to the treatment generally require continuous weekly treatment to maintain their response. Nonetheless, the new data reported above suggest that, in patients who respond to efalizumab, the agent can be used with confidence in its safety for up to 30 months of continuous treatment.

In a consensus statement on psoriasis therapies, the American Academy of Dermatology notes that all four biologic agents discussed in this article should be considered along with the traditional systemic therapies as first-line agents for patients who are candidates for systemic therapies (Callen 2003). Such patients are defined as those with psoriasis on the palms and soles, head and neck, or genitalia, or who have more than 5 percent of their skin surface involved.

Thus, the standard of care for treatment of psoriasis is changing, and health care organizations need to be familiar with the nuances of the different biologic products to make informed formulary decisions in the absence of head-to-head trials.

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REFERENCES

Amevive (alefacept) [package insert]. Cambridge, Mass.: Biogen Inc. August 2004.

Callen JP, Krueger GG, Lebwohl M, et al. AAD consensus statement on psoriasis therapies. *J Am Acad Dermatol.* 2003;49:897–899.

Chaudhari U, Romano P, Mulcahy LD, et al. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: a randomised trial. *Lancet.* 2001; 357:1842–1847.

Ellis CN, Krueger GG, for the Alefacept Clinical Study Group. Treatment of chronic plaque psoriasis by selective targeting of memory effector T lymphocytes. *N Engl J Med.* 2001;345: 248–255.

Enbrel (etanercept) [package insert]. Thousand Oaks, Calif.: Immunex Corp. 2004.

Gordon KB, Vaishnaw AK, O'Gorman J, et al; Alefacept Clinical Study Group. Treatment of psoriasis with alefacept: correlation of clinical improvement with reductions of memory T-cell counts. *Arch Dermatol.* 2003a;139: 1563–1570.

Gordon K, Papp K, Hamilton T, et al. Efalizumab for patients with moderate to severe plaque psoriasis. A randomized controlled trial. *JAMA.* 2003b; 290:3073–3080.

Gottlieb AB. Infliximab for psoriasis. *J Am Acad Dermatol.* 2003;49(2 suppl): S112–S117.

Gottlieb AB, Hamilton TK, Caro I, et al. Efficacy and safety outcomes of extended efalizumab therapy in patients with moderate to severe chronic plaque psoriasis: an update. Presented at: American Academy of Dermatology ACADEMY 2004 meeting, New York, July 29, 2004.

Greaves MW, Weinstein GD. Treatment of psoriasis. *N Engl J Med.* 1995;332: 581–588.

Krueger J. The immunologic basis for the treatment of psoriasis with new biologic agents. *J Am Acad Dermatol.* 2002;46:1–23.

Krueger GG, Ellis C. Alefacept therapy produces remission for patients with chronic plaque psoriasis. *Br J Dermatol.* 2003;148:784–788.

Lebwohl M, Tyring S, Hamilton T, et al. A novel targeted T-cell modulator, efalizumab, for plaque psoriasis. *N Engl JMed.* 2003;349:2004–2013.

NPF (National Psoriasis Foundation). Psoriasis Facts. 2004. Available at: «http://www.psoriasis.org». Accessed Sept. 17, 2004.

Raptiva (efalizumab) [package insert]. South San Francisco, Calif.: Genentech Inc. October 2003.

Remicade (infliximab) [package insert]. Malvern, Pa.: Centocor Inc. March 2004.

Singri P, West D, Gordon K. Biologic therapy for psoriasis: the new therapeutic frontier. *Arch Dermatol.* 2002;138: 657–663.

Sobell JM, Hallas SJ. Systemic therapies for psoriasis: understanding current and newly emerging therapies. *Semin Cutan Med Surg.* 2003;22:187–195.

Tristani-Firouzi P, Krueger G. Efficacy and safety of treatment modalities for psoriasis. *Cutis.* 1998;61 (suppl 2): 11–21.

Weinberg J, Saini R. Biologic therapy for psoriasis: the tumor necrosis factor inhibitors infliximab and etanercept. *Cutis.* 2003;71:25–29.