The National Psoriasis Foundation estimates that approximately 7 million Americans have psoriasis, with more than 200,000 new cases diagnosed annually. Some of these cases may not represent disease onset but the emergence of psoriasis sufferers as they learn about new treatments. Approximately 2 million patients have the moderate to severe form of the disease and are candidates for systemic therapy.

Outpatient treatment costs for psoriasis are estimated at $1.6 to $3.2 billion annually. In the commercial managed care population, psoriasis treatment consumes about $7 per member per year (PMPY), including prescription drugs and physician services.

The potential market for new biologic agents is significant. If all patients with moderate to severe disease were treated with a biologic agent, the potential cost would approach $5 billion annually, which translates to $15 PMPY for the entire managed care population.

Psoriasis usually starts in young adults, with the mean age of onset being 28 years. Of new cases, 10 to 15 percent occur in children under 10 years old. Most patients have the limited form of the disease involving small areas of skin and characterized by spontaneous exacerbations and remissions, and this form is most appropriately treated with topical medications. Patients with moderate to severe disease require more aggressive therapy to control the symptoms and preserve quality of life. Given the early age of onset, decades of therapy might be required. In special circumstances, limited forms of psoriasis can be disabling if, for example, the hands, feet, or face are affected; treating such patients with a systemic medication might be justified.

A significant number of people with psoriasis have trouble with activities of daily living and psychosocial activities (Table 1). The Short-Form 36 health survey instrument measures the physical and mental impact of disease on the quality of life. When patients with a variety of illnesses were surveyed, psoriasis ranked very high among medical conditions commonly recognized as negatively affecting quality of life (Rapp 1999). In the physical outcome category, psoriasis was exceeded only by congestive heart failure. In the mental outcome category, only major depression and chronic lung disease were thought to have a more significant impact than did psoriasis. This survey’s results clearly imply that participants perceived coping with psoriasis to be more difficult than coping with major medical conditions such as cancer, heart attack, arthritis, and diabetes.

For varying practical and technical reasons, current systemic treatments have been poorly accepted by patients and their dermatologists. In a survey of National Psoriasis Foundation members, 39 percent of respondents reported having severe disease. Among this group, 79 percent said psoriasis had a negative impact on their social or physical life. Fifty-nine percent indicated that their physicians could be more helpful in enabling them to live with psoriasis; 78 percent expressed frustration with their...
Continuing education is offered to physicians, pharmacists, nurses, and case managers who read this newsletter. The Chatham Institute designates this educational activity for a maximum of 2.0 category 1 credits toward the AMA Physician’s Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Purpose and overview
This activity focuses on pharmaceutical innovation and the role of pharmaceutical products in the treatment of patients with plaque psoriasis. Advancements in biotechnology have led to the development of new products that lead to improvements in clinical outcomes and quality of life with fewer side effects. The economic and cost benefits achieved through appropriate use of modern medicine are also discussed. This newsletter is derived from “Treating Psoriasis as a T-Cell Mediated Disease,” an online presentation.

Educational needs assessment
“Treating Psoriasis as a T-Cell Mediated Disease” was chosen as the topic for this newsletter through a critical assessment of current medical literature, advisory board meetings, and local market feedback forums. Scientists have recently learned that psoriasis is an immune system-mediated disorder that the new biologic agents are well designed to treat. Two unique biologically derived psoriasis therapies, alefacept and efalizumab, were recently approved by the U.S. Food and Drug Administration. Both drugs target T-cells that mediate the inflammation and overproduction of skin cells in psoriasis.

To provide their patients with these new treatments, health care professionals need to learn to implement the biologic regimens and manage potential complications associated with the targeted therapy. Case managers need to understand the issues unique to biologics, such as new cost-benefit structures, supply and distribution channels, and compliance issues surrounding injectable medications. Managed care organizations need to respond to the emergence of these new therapies by designing plan benefits and providing guidelines for psoriasis treatment that incorporate biologic therapies.

With the current influx of new biologic therapies, it is imperative to keep managed care executives current on clinical, disease state, and patient demographic information with respect to the expanding therapeutic options that are available for moderate to severe plaque psoriasis.

In response to these educational needs, The Chatham Institute partnered with leading dermatology experts to design the content for the CE-accredited Internet program that served as the basis for this newsletter.

Educational objectives
After reading this publication, the participant should be able to:

- Understand developments that have led to the treatment of plaque psoriasis as an immune-system mediated disorder that can be treated with biologically engineered products.
- Examine the pathogenesis of plaque psoriasis and strategies that have been developed for targeting the immune system in psoriasis.
- Discuss current treatment options for patients who have moderate to severe plaque psoriasis.

Target audiences
Managed care professionals, including medical and pharmacy directors, chief medical officers and other senior managers in managed care organizations, nurses, and case managers.

Continuing education credit sponsored by The Chatham Institute.

Conflicting interest and disclosure of significant relationships
As an accredited provider, The Chatham Institute requires that its

This activity has been planned and implemented in accordance with the ACCME Essential Areas, Elements, and Policies.

Pharmacy accreditation
The Chatham Institute is approved by the American Council on Pharmaceutical Education (ACPE) as a provider of continuing pharmaceutical education.

This activity provides 2.0 contact hours (0.2 CEU) of continuing education for pharmacists. Credit will be awarded upon successful completion of the post-test and the activity evaluation.

ACPE Universal Program Number (UPN):
812-000-04-006-H01
Release date: April 15, 2004
Expiration date: April 15, 2005
Medium: Newsletter

Nursing accreditation
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Provider approved by the California Board of Registered Nursing, Provider Number CEP12433, for 2.0 contact hours.

Case manager accreditation
This program has been approved for 1 hour with the Commission for Case Manager Certification.

Planning committee members
Cyndi Grimes, managing director, The Chatham Institute; Timothy P. Search, RPh, group publisher, MANAGED CARE, a division of MediMedia USA; Paula R. Sirois, senior science editor, custom publications, MediMedia USA Managed Markets Publishing.

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Faculty disclosure
Craig Leonardi, MD, acknowledges that he has a consulting relationship with Genentec, Amgen, and Centocor. He also acknowledges that he has received grant and/or research support from Genentech, Amgen, Centocor, Abbott, and Biogen. He has served on speakers’ bureaus for Amgen and Genentech. Leonardi’s presentation does not include any discussion of off-label use of the products discussed.

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This model, patients generally needed to fail therapies at one level before moving to another. Additionally, each escalation introduced treatments carrying additional risk or inconvenience.

Generally, patients start with over-the-counter emollients and other products. The next step has been to use prescription agents, including topical steroids, topical vitamin-D analogues, and topical retinoids. When these treatments failed, phototherapy was commonly recommended, including broadband (BB) and narrow-band (NB) ultraviolet B (UVB), PUVA (administration of an oral or topical sensitizing drug, psoralen, followed by exposure to ultraviolet A), and treatment of limited forms of psoriasis using a UVB-targeted phototherapy laser.

Each of these treatment modalities has strengths and weaknesses. For example, BB-UVB is most commonly available but usually necessitates 3 treatments weekly. NB-UVB induces more rapid clearing with longer remissions, but as a relatively new modality is available in a fraction of the offices offering phototherapy. PUVA is most likely to clear the psoriasis and is the most remittive, but psoralen may be associated with nausea. Also, because psoralen takes at least 8 hours to be cleared from the blood, the

### TABLE 1  NEGATIVE EFFECTS OF PSORIASIS ON ACTIVITIES OF DAILY LIVING AND PSYCHOSOCIAL ACTIVITIES, BY AGE GROUP (%)

<table>
<thead>
<tr>
<th>Activities of daily living</th>
<th>18–34 years (n = 1916)</th>
<th>35–54 years (n = 6625)</th>
<th>≥55 years (n = 8891)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleeping</td>
<td>20</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Sexual activity</td>
<td>27</td>
<td>27</td>
<td>13</td>
</tr>
<tr>
<td>Using hands</td>
<td>8</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Walking</td>
<td>7</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>Performing job duties</td>
<td>10</td>
<td>12</td>
<td>9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychosocial activities</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Interacting in workplace</td>
<td>18</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>Interacting with family or spouse</td>
<td>15</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Developing and maintaining friendships</td>
<td>15</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Being excluded from public facility</td>
<td>7</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Getting a job</td>
<td>5</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Contemplated suicide</td>
<td>10</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

SOURCE: KRUEGER 2001
eyes and skin must be protected from sun exposure during this period. Regardless of the type of phototherapy used, there is an increased incidence of photodamage and skin cancer with long-term therapy. Lentigines, multiple freckling, and burning are well-known side effects of phototherapy (Lebwohl 2001). As a consequence of long-term therapy, some patients develop squamous cell carcinomas and, less commonly, malignant melanoma. From a practical perspective, phototherapy requires the patient to come into the office 2 or 3 times each week, for months at a time. The relatively slow onset of action makes compliance difficult. Also, the specialized and expensive equipment requires dedicated office space and, in busy offices, a dedicated phototherapy technician.

Traditionally, systemic immunosuppressive therapy was the final step for patients who were unable to obtain phototherapy or for those who failed it. Systemic agents include cyclosporine, methotrexate, acitretin (Soriatane), and in some cases, oral steroids. These agents are easy to administer, relatively inexpensive, and efficacious for generalized disease.

Nevertheless, the toxicity of systemic medications severely limits long-term usage. Cyclosporine carries the risk of lymphoma, hypertension, and renal toxicity; the U.S. Food and Drug Administration has limited the use of this medication in psoriasis to 12 months.

Patients taking methotrexate must undergo routine monitoring for hepatotoxicity and bone marrow suppression. Long-term methotrexate treatment is associated with a dose-related risk of cirrhosis, ranging from 3 percent among psoriasis patients who have received a cumulative methotrexate dose of 1.5 g or less, to 20 to 25 percent among patients who have received a cumulative dose of 4 g. For this reason, a liver biopsy is recommended after each 1.5 g increase in the cumulative dose (1 to 3 years for the average patient).

Acitretin is associated with hyperlipidemia and hepatotoxicity; monitoring is therefore necessary during therapy. Teratogenicity is a significant issue with this drug. Due to its long half-life and storage in fat, the postdosing pregnancy avoidance period is 3 years, even after taking a single tablet. For this reason, females of childbearing potential rarely are offered the drug.

Given these limitations, patients with moderate to severe psoriasis are sometimes treated in cycles in which the systemic treatment is initiated when the condition worsens and then withdrawn before safety-related side effects occur. Treatment withdrawal results in worsening of the psoriasis and the cycle’s renewal. In attempting to forestall adverse events, the rotational or sequential approach also has been applied: short courses of different systemic medications are employed as monotherapy, or in combination, to limit exposure or reduce the dose required. This strategy is not especially promising for either the patient or the treating physician.

AN IMMUNE DISORDER

Twenty-five years ago, psoriasis was perceived predominantly as an epidermal proliferation disorder; the skin’s immune response was perceived as secondary. Psoriasis now is understood to be a T-cell mediated disorder of the immune system, with epidermal proliferation being an end result (Gordon 2002).

Several strategies for targeting the immune system have been developed. By interfering with the antigen-dependent activation of T cells, the secondary (co-stimulatory) signals can be blocked. Other alternatives are to prevent T-cell proliferation or to alter the balance between Th1 and Th2 cells. Another approach is to prevent the interaction of T cells with vascular endothelial cells and target cells in the skin. Additionally, inflammatory cytokines released as a consequence of the inflammatory cascade such as TNF-alpha (tumor necrosis factor alpha) or IL-8 (interleukin-8) can be inactivated.

BIOLOGIC DRUGS

To date, the FDA has approved two biologic drugs for the treatment of psoriasis (Table 2), alefacept and efalizumab. Amgen has applied to the FDA for a psoriasis indication for etanercept, which already has become the best-selling biologic agent for psoriasis. The FDA’s decision is expected by mid-2004. In addition, infliximab and adalimumab are among other agents in clinical trials for use in psoriasis. These agents are all TNF inhibitors and are beyond the scope of this article, which focuses on the two FDA-approved, T-cell mediated therapies for psoriasis — alefacept and efalizumab.

| TABLE 2 BIOLOGIC AGENTS UNDER EVALUATION FOR TREATMENT OF PSORIASIS |
|---------------------------------|------------------|------------------|
| **Agent**           | **Manufacturer** | **Phase**       |
| Alefacept (Amevive) | Biogen Idec   | Approved 2003   |
| Efalizumab (Raptiva) | Genentech   | Approved 2003   |
| Etanercept* (Enbrel) | Immunex     | Submitted; approval expected 2004 |
| Infliximab* (Remicade) | Centocor  | 3               |
| Denileukin difitox (Ontak) | Ligand  | 2               |
| Onercept [r-hTBP-1] | Serono     | 2               |
| Adalimumab* (Humira) | Abbott   | 2               |
| Anti-IL-12 | Centocor | 2               |
| SMART Anti-IFN-g | Protein Design Labs | 1/2          |

*Has FDA approval for treatment of other diseases.
Alefacept, a T-cell depleting agent, is a recombinant fusion glycoprotein comprising the extracellular portion of leukocyte function-associated antigen type 3 (LFA-3) fused with the Fc portion of IgG1. LFA-3 is present on antigen-presenting cells and binds to CD2, which is expressed on all T cells. CD2 is upregulated on the surface of the memory-effector (CD45RO+) T cells that are involved in the generation of psoriatic lesions. By binding with CD2, alefacept disrupts the immunologic synapse (Grakoui 1999) through prevention of the interaction of CD2 with LFA-3. This step reduces the efficiency of T-cell activation, both as a primary and a secondary process. Also, the Fc portion of alefacept can bind simultaneously with the CD16 (Fcγ receptor III) receptors of natural killer (NK) cells, resulting in apoptosis of the memory-effector T cells (Ellis 2001).

The net effect is to deplete the pool of memory-effector CD4+ and CD8+ lymphocytes. The FDA recommends that during treatment the CD4+ lymphocyte counts of patients should be monitored weekly throughout the 12-week dosing period of alefacept. If the counts of CD4+ lymphocytes drop below 250 cells/µL, dosing should be withheld; if the counts remain below 250 cells/µL for 1 month, alefacept should be discontinued.

Alefacept was originally developed in two formulations — for intravenous infusion and for intramuscular injection. Nevertheless, in October 2003, Biogen (now known as Biogen Idec) discontinued the IV formulation because the vast majority of dermatologists preferred the IM mode of administration.

In a phase 3 trial, patients (N = 507) were randomly assigned to receive alefacept 15 mg IM (n = 166), alefacept 10 mg IM (n = 173), or placebo (n = 168) for 12 weeks and were followed for an additional 12 weeks (Lebwohl 2003). The patients were middle aged (mean, 45.2 years; range, 18 to 80), male (66 percent), and white (90 percent), with a mean disease duration of 19 years (range, 2 to 77) and a median Psoriasis Area and Severity Index (PASI) of 14.2 (range, 3.4 to 58.8).

The FDA’s benchmark for evaluating psoriasis drugs is a 75 percent reduction in PASI, or PASI-75. This research tool takes into consideration disease extent and severity in four body sites (head, arms, trunk, and legs). Because PASI is complicated and time-consuming, outside of the research setting, dermatologists never use it to characterize psoriasis.

The primary endpoint was PASI-75 at 14 weeks — 2 weeks after treatment completion. This endpoint was achieved by 21 percent of patients receiving alefacept 15 mg IM, 12 percent of patients receiving alefacept 10 mg IM, and 5 percent of patients receiving placebo. Biogen also uses a private analysis of PASI responses that assesses overall response rate. The metric is a cumulative indicator of response, by which a patient who achieves PASI-75 at any time during the 12 weeks of dosing or the 12-week observation period is considered a treatment success. The overall response rate (patients achieving PASI-75 at any point) was 33, 28, and 13 percent in the 15 mg, 10 mg, and placebo groups, respectively. A 50 percent PASI reduction (PASI-50) at any point was achieved by 57 percent of the 15 mg group, 53 percent of the 10 mg group, and 35 percent of the placebo group.

These data also show that 79 percent of patients receiving alefacept 15 mg IM did not reach the primary endpoint; 67 percent failed to achieve a PASI-75 response at any time. Yet among those who achieved PASI-75 during the 12 weeks of therapy, a durable and sustainable remission was observed, as these patients maintained a PASI-50 for a mean of 216 days (Gordon 2002, Mehlis 2003).

Alefacept was well tolerated, with an adverse event profile that was comparable to placebo. Two mild infections (a sore throat and a cold) occurred in the two alefacept-treated patients whose CD4+ cell counts fell below 250 cells/µL, and the study drug was continued. Serious adverse event rates were comparable in the placebo group (6 percent) and the alefacept groups (15 mg, 4 percent; 10 mg, 5 percent), and no serious adverse events were considered drug-related.

**EFALIZUMAB, A HUMANIZED MONOCLONAL ANTIBODY**

As indicated by the *zumab* portion of its generic name, efalizumab is a humanized monoclonal antibody. It is an antibody directed against CD11a, a part of leukocyte function-associated antigen type 1 (LFA-1). About 3 percent of the amino acid sequences in efalizumab retain their murine heritage, but these appear to be insufficient to promote the development of neutralizing antibodies, as can occur with use of the chimeric monoclonal antibody infliximab. The patient administers efalizumab subcutaneously, once weekly.

In areas of inflammation, ICAM-1 is upregulated on the surface of endothelial cells as well as on keratinocytes in psoriatic skin. Efalizumab prevents trafficking of T cells into the dermis by preventing the binding of LFA-1 to ICAM. Unlike alefacept, efalizumab does not deplete lymphocytes systemically.

In clinical trials, a dose of 2 mg/kg/wk was no more efficacious than a dose of 1 mg/kg/wk. Efalizumab thus is given clinically at the latter dosage (up to a maximum of 200 mg for a single dose) for 11 weeks, following an initial dose of 0.7 mg/kg. In pooled data from three clinical trials, 27.9 percent of patients receiving efalizumab 1 mg/kg/wk (n = 763) achieved PASI-75 after 12 weeks of treatment — vs. 3.8 percent of those receiving placebo (n = 479); PASI-50 rates were 57.0 percent for efalizumab 1 mg/kg/wk and 14.6 percent for placebo.

A statistically significant (*P* < .005) difference in mean PASI scores between efalizumab and placebo was seen as early as week 2. This represents some early improvement and indicates that efalizumab has a fairly rapid onset of action, in contradistinction to that seen with alefacept, which necessitates completion of the entire 12-week course of therapy before the drug’s effectiveness can be determined. With efalizumab, effectiveness or lack thereof often becomes evident much sooner.

In a 24-week study in which patients received either placebo or efalizumab
for the first 12 weeks, followed by efalizumab 1 mg/kg/wk for the next 12 weeks, PASI-75 was achieved by 26.6 percent of the efalizumab group (n = 369) after 12 weeks vs. 4.3 percent of the placebo group (n = 187), with PASI-50 being achieved by 58.5 and 13.9 percent of the efalizumab and placebo groups, respectively (Menter 2003). After 24 weeks of continuous efalizumab therapy, PASI-75 and PASI-50 rates had increased to 43.8 percent and 66.6 percent, respectively. In other words, the longer efalizumab is given, the better it seems to work.

Interim results of an ongoing 36-month open-label study suggest this effect continues in the long term (Gottlieb 2003). In this study, patients who achieved a PASI-50 response after an initial 12-week treatment period are continuing weekly treatment for 3 years. The study design includes three treatment periods, as follows. During the first 12-week treatment period, patients received efalizumab 2 mg/kg/wk. During weeks 8 through 12, patients also were treated with either fluocinolone acetonide or white petrolatum.

In the maintenance period following week 12, patients received efalizumab 1 mg/kg/wk. In the case of relapse, defined as the loss of 50 percent of PASI improvement achieved at week 12, the patient ended participation in the current 12-week segment and started the next segment at 2 mg/kg/wk. During weeks 13 through 60, the dose for relapsed patients could be increased to a maximum of 4 mg/kg/wk, if clinically indicated. After week 60, further dose escalation was not allowed.

Through 24 months of continuous efalizumab therapy, PASI-75 response has been maintained or improved. During the first 3 months of treatment, 41.3 percent of patients (n = 339) achieved PASI-75, and 13.0 percent achieved PASI-90. In the maintenance phase (n = 290), 57.2 percent of patients achieved PASI-75 at month 12 and 55.9 percent at month 21. PASI-90 rates were 25.9 percent and 30.0 percent at months 12 and 21, respectively.

CONTINUING EDUCATION POST-TEST

Please tear out the combined answer sheet/evaluation form. On the answer sheet on page 7, place an X through the box of the letter corresponding with the correct response for each question. There is only one correct answer to each question.

1. Psoriasis is best described as stemming from a/an:
   a. Drug-drug interaction.
   b. Environmental pollutant.
   c. Immune disorder.
   d. Vitamin deficiency.

2. Utilization of systemic immunosuppressive agents for treating psoriasis is limited primarily by:
   a. High cost.
   b. Lack of efficacy.
   c. Complicated modes of administration.
   d. Toxicity.

3. Alefacept binds to:
   a. CD2 on T cells.
   b. CD16 receptor on natural killer cells.
   c. CD 20 on B cells.
   d. a and b
   e. a and c
   f. b and c

4. If counts of CD4+ T lymphocytes remain below 250 per µL for 1 month during alefacept therapy, alefacept treatment should be:
   a. Carefully monitored.
   b. Discontinued.
   c. Reduced to half the recommended dose.
   d. Increased to twice the recommended dose.

5. Efalizumab is a:
   a. Small molecule.
   b. Fusion protein.
   c. Humanized monoclonal antibody.
   d. Chimeric monoclonal antibody.

6. Efalizumab is administered via:
   a. Subcutaneous injection.
   b. Intramuscular injection.
   c. Intravenous infusion.
   d. Gel capsule.

7. The chief advantage that biologic treatments appear to offer over systemic treatments for psoriasis is:
   a. Greater safety.
   b. Greater efficacy.
   c. Lower cost.
   d. a and b
   e. a and c
   f. b and c

8. In treating patients with psoriasis, biologic agents should be considered for use only after systemic immunosuppressive agents have been found to be inadequate.
   a. True
   b. False

9. According to the National Psoriasis Foundation, which of the following statistics are correct?
   a. Seven million Americans are affected with psoriasis.
   b. There are 200,000 new cases diagnosed annually.
   c. Approximately 2 million patients have moderate to severe psoriasis, making them candidates for systemic therapy.
   d. All the above.
   e. None of the above.

10. Regarding the presentation of psoriasis, which is correct?
    a. Mean age of onset is 28 years.
    b. 10 to 15 percent of cases occur in children under 10 years old.
    c. It is common to see spontaneous exacerbations and remissions throughout the course of the disease.
    d. All the above.
    e. None of the above.

After the first few injections of efalizumab, there is an increased incidence of headache, chills, nausea, myalgia, and fever. By the third dose, there is no difference in any of those acute adverse events compared with placebo. The first dose of efalizumab therefore is 0.7 mg/kg to minimize these initial adverse events.

Another adverse event is the phe- continued on page 8
CONTINUING EDUCATION ANSWER SHEET/ 
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Treating Psoriasis as a T-Cell Mediated Disease

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EXAMINATION:
Place an X through the box of the letter that represents the
best answer to each question on page 6. There is only ONE
answer per question. Place all answers on this form:

A.  B.  C.  D.  E.  F.
1.  [ ]  [ ]  [ ]  [ ]  [ ]  [ ]
2.  [ ]  [ ]  [ ]  [ ]  [ ]  [ ]
3.  [ ]  [ ]  [ ]  [ ]  [ ]  [ ]
4.  [ ]  [ ]  [ ]  [ ]  [ ]  [ ]
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6.  [ ]  [ ]  [ ]  [ ]  [ ]  [ ]
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8.  [ ]  [ ]  [ ]  [ ]  [ ]  [ ]
9.  [ ]  [ ]  [ ]  [ ]  [ ]  [ ]
10. [ ]  [ ]  [ ]  [ ]  [ ]  [ ]

Program Evaluation
So that we may assess the value of this self-study program,
we ask that you please fill out this evaluation form.

A. Have the activity’s objectives been met?
   Yes      No
   ___ ___ Understand developments that have led to the
treatment of plaque psoriasis as an immune-
system mediated disorder that can be treated
with biologically engineered products.
   ___ ___ Examine the pathogenesis of plaque psoriasis and
   strategies that have been developed for targeting
   the immune system in psoriasis.
   ___ ___ Discuss current treatment options for patients
   who have moderate to severe plaque psoriasis.

B. Was this publication fair, balanced, and free of
   commercial bias?
   ___ ___ If no, please explain:
   ____________________________________________

C. Did this educational activity meet my needs, contribute
to my personal effectiveness, and improve my ability to:
   Strongly Strongly
   Treat/manage patients?  54321 N/A
   Communicate with patients?  54321 N/A
   Manage my practice?  54321 N/A
   Other _________________  54321 N / A

D. Effectiveness of this method of presentation:
   Excellent Very Good Good Fair Poor
   5 4 3 2 1

E. Time spent reading this publication: Hours __Minutes___

What other topics would you like to see addressed? ________

Comments: ____________________________________________

_________________________________________________________________
nomenon of rebound, which can occur when efalizumab is discontinued abruptly. Rebound is defined by the National Psoriasis Foundation as a PASI that exceeds 125 percent of the baseline within 12 weeks after discontinuation, as is seen when cyclosporine (or less commonly, methotrexate) treatments are stopped. During the phase 3 trials, 19 patients experienced serious worsening of their psoriasis after stopping therapy. While the majority of these events occurred while off therapy, four of these cases occurred shortly after efalizumab had been restarted. Rebound is best avoided by using efalizumab continuously, or by transitioning the patient onto an alternative form of psoriasis therapy. For the majority of efalizumab-treated patients who stop therapy, the mean time to relapse was 9 weeks, in contrast to the longer time seen with those who respond to alefacept.

Eight patients in the safety database for efalizumab (N = 2762) developed what was thought to be immune-mediated thrombocytopenia (<52,000 cells/μL). Each case led to discontinuation of efalizumab. For this reason, the FDA recommends that platelets should be checked monthly during treatment initiation and then quarterly thereafter.

**FINANCIAL CONSIDERATIONS**

Both of these medications raise concerns about reimbursement and cost of failure. Because it is administered via IM injection in the physician’s office, alefacept usually is classified as a medical benefit. Due to its slow onset of action, the entire 12 weeks of alefacept will likely be administered before its effectiveness (or lack thereof) can be determined. A 12-week course of therapy will cost roughly $11,000, with an additional $2,000 dollars expended on weekly laboratory tests (CD4 + counts) and office visits. Given that most patients will require two courses of therapy in their first year, the total cost of alefacept can approach $24,000. Alternatively, it will be difficult to justify a second course of therapy if an inadequate response occurs after the first course.

Efalizumab, in contrast, is administered subcutaneously by the patient and is usually classified as a pharmacy benefit and is distributed through a network of specialty pharmacies at a cost of about $343 a dose per week for 12 weeks.

Although efalizumab is best used as a continuous treatment, with an annual cost of about $14,000, its rapid onset of action allows for an early decision to be made about continuing therapy, at a fraction of the cost of that seen with a single course of alefacept.

These new agents will alter the traditional paradigm of psoriasis treatment, enabling patients to get off the therapeutic roller coaster and onto safer therapy. The biologics have favorable efficacy profiles, and they appear to be far safer than currently used systemic therapies. Recently, the American Academy of Dermatology issued a consensus statement on psoriasis care that puts biologics on equal footing with traditional systemic treatments (Callen 2003). In the eyes of many dermatologists, the biologics are first-line systemic therapies for those patients who require long-term systemic treatment for their psoriasis.

**REFERENCES**


