Managed Care Best Practices
In the Treatment and Management of Psoriasis
Based on a conference in Orlando, Fla., Feb. 3, 2003

HIGHLIGHTS

• Overview of Psoriasis: Update on Current and Emerging Treatment Options

• The Cost of Psoriasis

• Managed Care’s Perspective on Treatment of Plaque Psoriasis

• SPECIAL PRESENTATION AND ROUNDTABLE DISCUSSION
Improving the Standard of Care for Patients With Psoriasis

Continuing education credit for pharmacists and physicians sponsored by The Chatham Institute

Supported by an unrestricted educational grant from Genentech
The emergence of biologic response modifiers for the treatment of plaque psoriasis heralds a promising era for a patient population that has long been underserved. It’s going to be exhilarating to have a curative therapy for psoriasis, and patients and physicians have high expectations for this paradigm shift in treatment. Managed care organizations, too, will rapidly take notice as the pharma-therapeutic focus moves from older drugs to the new biologics. The issues inherent in this transition were discussed at “Managed Care Best Practices in the Treatment and Management of Psoriasis,” a meeting in Orlando, Fla., Feb. 3, 2003. There, an expert panel of managed care medical and pharmacy directors, dermatologists, clinical researchers, and employers learned about the evolution of therapy, economic implications of the disease, and managed care’s attitudes toward newer treatments. We also discussed the American Academy of Dermatology’s (AAD) new consensus statement on treatment of psoriasis. These presentations are excerpted herein.

Are biologics better? We know from controlled clinical trials that these drugs are highly effective, compared with clinical outcomes for methotrexate, cyclosporine, and ultraviolet light therapies. It seems clear that the newer agents are safe, and while information about long-term side effects is limited at this time, we do know the risks of administering older therapies and the expenses associated with monitoring patients for those side effects.

There is much work to be done. Patients are frustrated with their treatments and are looking for something new; managing their expectations will be extremely important. Part of this involves educating the profession, as not all dermatologists prescribe systemic drugs for patients with moderate to severe psoriasis; the AAD will take a leading role in educating physicians. Another part involves the creativity that health plans must adopt in offering coverage for biologics without allowing the cost of care to reach levels that would make these agents less accessible.

It’s an exciting time that offers a new opportunity to provide more effective care for psoriasis patients. I encourage all parties, including health care professionals and payers, to focus on providing these promising new therapies to those who stand to benefit from them most.
Managed Care Best Practices
In the Treatment and Management of Psoriasis
A CONTINUING EDUCATION ACTIVITY

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About this publication

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Continuing education credit is offered to physicians and pharmacists who read pages 3 through 21 of this publication, complete the post-test on page 22, and fill out the appropriate evaluation form on either page 23 (physicians) or 24 (pharmacists).

**Purpose and overview**

This activity is designed to educate health care practitioners and managed care professionals about current and emerging treatments for plaque psoriasis. The narratives in this section are excerpted from presentations and panel discussions on Feb. 3, 2003, at “Managed Care Best Practices in the Treatment and Management of Psoriasis,” held in Orlando, Fla.

Recent developments in the etiology of psoriasis have prompted development of new therapeutic agents. Biologic response modifiers under development and coming to market show promise in clinical trials, prompting physicians, patients, and payers to request information about the status and effectiveness of current and emerging therapies. The agenda for this meeting was developed on the basis of faculty perceptions of significant trends or issues.

**Educational objectives**

After reading this, the participant should be able to:

1. Discuss the prevalence of plaque psoriasis, etiology of disease, and comorbidities in patients with moderate to severe psoriasis.
2. Describe the range of therapies available to patients with moderate to severe disease.
5. Illustrate the economic burden of psoriasis on the health care system and society at large.
6. Outline potential considerations for managed care organizations as biologic drugs in the treatment of psoriasis continue to emerge on the market.

**Target audiences**

Managed health care professionals, including medical directors, pharmacy directors, and other senior managers in managed care organizations; primary care physicians; dermatologists; and pharmacists.

**Continuing medical education accreditation**

The Chatham Institute is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The Chatham Institute designates this educational activity for a maximum of 1.5 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. This CME activity has been planned and produced in accordance with the ACCME Essential Areas, Elements, and Policies.

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ACPE Universal Program Number (UPN): 812-000-03-013-H01.


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Psoriasis has not received widespread attention because, traditionally, dermatologists have not had effective treatments for moderate to severe manifestations of the disease. With a change in the understanding of the nature of psoriasis — from what had been thought to be a skin disease to what is now known to be an immune disorder — such therapies are now becoming available.

Disease prevalence and overview
Psoriasis affects more than 7 million Americans. The National Psoriasis Foundation (NPF) estimates that nearly 2 million individuals have moderate to severe disease. For these people, psoriasis is a painful, disfiguring, dispiriting chronic condition. The mean age of onset is 28 years, and 20,000 children under 10 years old are diagnosed with psoriasis each year. More than 1.5 million psoriatics seek help annually, generating overall treatment costs that may exceed $3 billion (NPF 2001). Table 1 (page 4) highlights the results of a 2001 NPF patient survey.

The most frequently experienced psoriasis symptoms include scaling (reported by 94 percent of NPF respondents), itching (79 percent), skin redness (71 percent), skin tightness (31 percent), bleeding (29 percent), burning sensation (21 percent), and fatigue (19 percent) (Krueger 2001).

Psoriasis is exceeded only by congestive heart failure in patient-reported physical disability scores on the Short Form (SF-36) Health Survey. This means that psoriatics experience greater physical disability than people with hypertension, myocardial infarction, diabetes, depression, arthritis, or cancer. Only depression exacts a higher toll than psoriasis, as indicated by scores on the mental health component of the SF-36 (Rapp 1999).

When psoriatic plaques overlie joints such as elbows or knees, bending the joints can crack the skin and cause bleeding. About 400 deaths related to psoriasis occur each year due to suicide, metabolic problems, and complications resulting from treatment (NPF 2001).

Most treatment-related complications have been attributed to methotrexate and cyclosporine, which, in recent years, have been the most widely prescribed systemic agents for psoriasis.

Systemic and phototherapies
Methotrexate. Methotrexate is approved by the U.S. Food and Drug Association (FDA) for psoriasis and rheumatoid arthritis (RA), and it has been used quite successfully in treating psoriasis. Twenty-six percent of psoriatics achieve PASI-75 (a 75-percent reduction in their Psoriasis Area and Severity Index scores; see accompanying article describing PASI, page 7) after 12 weeks on a methotrexate regimen (Callis 2002).

A chemotherapy agent at high doses, methotrexate is thought to act as an immunosuppressant at low doses. Adverse effects of methotrexate therapy include nausea and fatigue. It is also associated with rare cases of pneumonitis.

Psoriatics on methotrexate must be monitored with complete blood count and liver function tests monthly.
After every 1,500 mg (about 2 years, for average treatment regimens), patients must undergo a surveillance liver biopsy to check for early signs of cirrhosis (Spuls 1998).

**Cyclosporine.** Another immunosuppressant, cyclosporine, also has been highly effective and extremely fast-acting in treating psoriasis. More than three quarters of patients on cyclosporine achieve a 75-percent reduction in PASI scores, but only 10 to 15 percent of dermatologists prescribe it. Due to the nephrotoxicity associated with cyclosporine, the FDA limits its use to 1 year. This is problematic, as treatment for psoriasis is lifelong.

Side effects include hypertension, dysesthesia, tremors, gingival hyperplasia, and hirsutism. Laboratory abnormalities associated with use of cyclosporine include reduced creatinine clearance, elevated cholesterol and triglycerides, and decreased Mg²⁺ levels.

**Retinoids.** Oral retinoids, such as acitretin, have been effective against pustular and erythrodermic forms of psoriasis on the hands and feet. Nevertheless, cholesterol and triglyceride levels rise with these drugs, and many patients do not tolerate unpleasant side effects such as chilblains, xerosis, hair loss, skeletal hyperostoses, and calcification of ligaments and tendons. Because retinoids are teratogenic, this form of therapy is contraindicated in females of childbearing age.

Only 28 percent of patients with plaque psoriasis respond well to retinoid monotherapy, which is typically combined with phototherapy to boost its efficacy.

**Ultraviolet (UV) phototherapy.** Several factors have limited the usefulness of UV phototherapy, another treatment modality for psoriasis. The equipment (a UV-light booth in which the patient stands) costs between $13,000 and $17,000 and requires dedicated office space. Consequently, only one quarter of the 10,000 dermatologists in the United States offer phototherapy.

Access is problematic because patients must come to the dermatologist’s office two to three times weekly for phototherapy sessions, a regimen that is inconvenient and can compromise adherence to therapy. New narrow-band UVB light bulbs emit the wavelengths to which psoriasis responds best. All forms of UV therapy, however, are associated with photodamage and an increased risk of skin cancer.

Phototherapy also is understood poorly by payers, who sometimes authorize two or three treatments instead of the 40 or 50 treatments needed to clear patients of psoriasis and to prevent symptoms from returning. Treatment frequency usually is reduced after 2 months as tolerated. It also can be reduced further in summer months.

In an effort to control or reduce symptoms, avoid intolerable side effects, and minimize risk, some dermatologists switch from one therapy described here to another.

**Topical agents**

The challenges that persist with phototherapy and systemic oral medications may explain why topical treatments constitute 87 percent of current prescription treatments for severe psoriasis; phototherapy (21 percent) and systemic oral drugs (18 percent) are far less utilized (Krueger 2001). A recent survey of medical dermatologists (Molowa 2002) indicates that topical steroids constitute the most common therapy for treatment of severe psoriasis (prescribed in 45 percent of cases), followed by UVB phototherapy, calcipotriene, psoralen with ultraviolet A (PUVA), and methotrexate (Figure 1).

**Topical steroids.** These drugs retard the growth of skin cells and reduce inflammation. Some steroids are potent but can cause skin damage if used too frequently. They are available in many forms, including lotions, ointments, and sprays.

**Calcipotriene.** This form of Vitamin D₃ also slows the rate of cell growth. It is not as potent as some steroids, but is safer. Calcipotriene is applied as an ointment, cream, or scalp solution.

**Other topical agents.** Low utilization rates for other treatment modalities suggest that many available treatments for psoriasis are not well accepted by dermatologists. Tazarotene, a Vitamin A derivative, is a topical retinoid. Often, it causes skin irritation and makes the plaque bright red before it clears. Coal tar, also known as Goeckerman therapy, has been in use for a century. Applied to the skin, it is left to dry for two hours and gives the odor of hot pavement. Anthralin, a Vitamin E derivative, is another century-old treatment. It has no long-term side effects, but it can irritate the skin and stains most of whatever it comes into contact with.

**Biologic response modifiers**

Research during the last two decades has radically altered dermatology’s understanding of psoriasis. Pso
sis now is understood to be an immune system dysfunction rather than a primary skin disorder.

This understanding has led to the development of many new biologic agents that target the immune system. Four important agents in this category are alefacept and efalizumab, which target lymphocytes, and etanercept and infliximab, which target cytokines. Table 2 highlights the characteristics of the biologic drugs discussed here.

**Alefacept.** The FDA approved alefacept for use on Jan. 31, 2003, for treatment of adults with moderate to severe chronic plaque psoriasis.

Alefacept is a recombinant fusion glycoprotein that binds to leukocyte functional antigen number 3 (LFA-3) and has an IgG1 graft to promote stability. It binds to CD2 on T and NK cells, and inhibits secondary signaling. It kills lymphocytes, especially the so-called memory-effector (CD45R0+) cells, by inducing apoptosis. It is administered by intravenous (IV) push and by intramuscular (IM) injection.

Twenty-one percent of patients being treated with IM-alefacept achieved PASI-75 at their primary endpoint (week 14), compared to 5 percent on placebo. Of the patients who had achieved a PASI-75 reduction, the effect was long-lived. This subset of patients maintained a PASI-50 response for a median duration of 216 days (Biogen 2003).

Alefacept is slow-acting. An 8- to 12-week course is necessary to determine if this drug will be effective in a patient.

One of our patients entered the alefacept trial with a PASI score of 301 after having discontinued methotrexate. The patient received a weekly 15 mg IV dose of alefacept for 12 weeks, and his PASI score started to decline during the 12-week observation period. A second 12-

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**FIGURE 1 First-line therapies for moderate to severe patients**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2001</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>UVB light therapy</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Topical steroids</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Calcipotriene</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>PUVA</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Tazarotene</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Acitretine</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Coal tar</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>OTC moisturizers/emollients</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Hydroxyurea</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

**TABLE 2 Summary of leading biologic therapies**

<table>
<thead>
<tr>
<th></th>
<th>Alefacept</th>
<th>Efalizumab</th>
<th>Etanercept</th>
<th>Infliximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration</td>
<td>IM or IV push</td>
<td>SC</td>
<td>SC</td>
<td>SC</td>
</tr>
<tr>
<td>Response</td>
<td>Remittive</td>
<td>Suppressive</td>
<td>Suppressive</td>
<td>Remittive</td>
</tr>
<tr>
<td>Speed of onset</td>
<td>++++</td>
<td>+++</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>Durability</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Efficacy</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Safety</td>
<td>?</td>
<td>?</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>Pediatric use</td>
<td>?</td>
<td>?</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Weekly CD4+</td>
<td>None</td>
<td>PsA 1/2002</td>
<td>WBC</td>
</tr>
<tr>
<td>FDA status</td>
<td>FDA approval</td>
<td>Late 2002</td>
<td>Phase 3</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Intangibles</td>
<td>1st to market, remittive</td>
<td>Fast, convenient</td>
<td>Safety, PsA indication</td>
<td>Complex, last resort</td>
</tr>
</tbody>
</table>

**SOURCE:** COMPILED FROM PRESCRIBING INFORMATION AND/OR CLINICAL TRIAL DATA

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1PASI is determined on a scale of 0 to 72. The U.S. Food and Drug Administration considers a PASI score that exceeds 10 to be severe disease.
week course of therapy reduced his PASI score to 0, where it remained beyond the length of the study.

The adverse effects associated with alefacept during the trials were mild and well tolerated. Its adverse-event profile was comparable to placebo except for chills (1 percent among subjects receiving placebo versus 6 percent of subjects receiving alefacept), with CD4+ T-cell counts below 250 cells/µL and generally mild uncomplicated infections that responded to usual treatments. Alefacept was associated with no reports of disease rebound/flare on discontinuation of therapy. Because it depletes lymphocytes, CD4+ lymphocyte counts are monitored weekly during treatment (Ellis 2001).

Efalizumab. Efalizumab is a humanized monoclonal antibody against the CD11a chain of LFA-1 and is self-injected subcutaneously (SC) once per week. It does not deplete lymphocytes but does inhibit lymphocyte movement into the dermis and epidermis. It decreases epidermal hyperplasia, keratin-16 expression, and ICAM expression, all of which are features of active psoriasis.

Efalizumab is convenient to administer, has a rapid onset of action, and achieved statistical significance in all endpoints. Unlike alefacept, this is a quick-acting drug (with efalizumab, results began to differ from placebo after two doses). Twenty-nine percent of 1,095 patients with moderate to severe disease who received 1.0 mg/kg of efalizumab achieved a 75-percent reduction in PASI scores by week 12 (Koo 2002).

The manufacturer conducted a yearlong trial of the 82 percent of patients who achieved at least PASI-50 after 3 months of weekly injections. The percentage of patients achieving a PASI-75 has increased during the 12 months of therapy, demonstrating that efalizumab exerts tight control on psoriasis (Gottlieb 2002).

Two representative patients from phase 1 trials are illustrated in Figure 2. In response to one subcutaneous injection per week for 12 weeks, one patient’s PASI score declined from 59 to 10, while that of the other declined from nearly 17 to <2.

Figure 3 demonstrates the response of a representative patient during the longer-term trial. After 1 year, the prevalence of lesions dropped from 44 percent of his...
PASI: PSORIASIS AREA AND SEVERITY INDEX

A patient’s PASI score is calculated by observing, measuring, and recording the anterior and posterior body surface area of the head, trunk, upper limbs, and lower limbs affected by psoriasis, then determining the severity of the disease.

**Body surface area**

The patient’s palm, which is roughly equivalent to 1 percent of total body surface area (BSA), serves as the unit of measure. Thus, a “3” would mean that an area equivalent to three of the patient’s palms is affected by psoriasis.

Anterior plus posterior measurements are calculated for the head, trunk, upper limbs, and lower limbs, then each is divided by the percentage of BSA represented by those areas. The head represents 10 percent of BSA, the trunk 30 percent, upper limbs 20 percent, and lower limbs 40 percent. The results are then converted to area scores from 0 to 6, according to the following table:

<table>
<thead>
<tr>
<th>Score</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0% – 9%</td>
</tr>
<tr>
<td>1</td>
<td>10% – 29%</td>
</tr>
<tr>
<td>2</td>
<td>30% – 49%</td>
</tr>
<tr>
<td>3</td>
<td>50% – 69%</td>
</tr>
<tr>
<td>4</td>
<td>70% – 89%</td>
</tr>
<tr>
<td>5</td>
<td>90% – 100%</td>
</tr>
</tbody>
</table>

For example, an anterior trunk measure of 3 plus a posterior trunk measure of 4 equals 7, which is divided by 0.3 (because the trunk represents 30 percent of BSA), yielding a total BSA of 23.3 percent. Because 23.3 percent falls within the 10–29 percent range in the above table, it converts to an area score of 2.

**Severity scale**

Next, erythema, thickness, and scaling on head, trunk, upper limbs, and lower limbs are observed and ranked on a severity scale from 0 to 4:

- 0 = None
- 1 = Slight
- 2 = Moderate
- 3 = Severe
- 4 = Very severe

The severity total for each body area is multiplied by the corresponding area score, and the result is multiplied by the percentage of the total BSA represented by each of those areas (10 percent for the head, 30 percent for trunk, 20 percent for upper limbs, 40 percent for lower limbs). The results are added together to arrive at the PASI score.

For example, adding erythema severity of 2, thickness severity of 1, and scaling severity of 1 for the trunk totals 4, which is multiplied by the area score for the trunk of 2 (from above), yielding 8. Multiplying 8 by .30 (because the trunk represents 30 percent of total BSA) yields 2.4. This subtotal for the trunk is added to subtotals for the head, upper limbs, and lower limbs to arrive at the PASI score.

**Limitations**

Most dermatologists do not use the PASI in clinical practice. PASI scores are used mainly for research. In clinical trials, the U.S. Food and Drug Administration requires that a drug achieve PASI-75, which means a 75-percent reduction in one’s PASI score, for a certain percentage of patients over time.

The PASI is a measure of disease and clinical outcomes in the moderate ranges. Most of us who conduct clinical trials and who see many patients realize that PASI-75 is an extremely high bar that is unrealistic and unnecessary in clinical practice. It is not a tool that a managed care organization might consider using to determine outcomes, because most practicing dermatologists are neither trained nor required to use it.

Granted, the PASI is reproducible, semiquantitative, and takes into consideration “how much” and “how bad.” These are positive aspects of the index. The FDA, however, has encouraged the dermatological community and industry to develop a better scoring system that simplifies the process and would be meaningful to patients, physicians, and payers alike.
body surface area (BSA) to 3 percent and his PASI score declined from 18 to 7.

The mean time to recurrence of psoriasis (loss of 50 percent of improvement) is 9 weeks. The rebound rate (125 percent of baseline PASI after 12 weeks) is 3 percent. The disease came back quickly after treatment was stopped during the observation period and, therefore, efalizumab is likely to be used as continuous therapy. Efficacy and safety were shown through 15 months of continuous treatment in clinical trials (Genentech 2003). Continuous dosing appears safe and effective.

This agent is well tolerated. Adverse effects associated with efalizumab, which does not deplete lymphocytes, are mild to moderate flulike symptoms (e.g., headache, chills, myalgia) that occur after the first two injections. Rates are similar to placebo by the third dose.

A biologics license application (BLA) was submitted to the FDA for this agent in December 2002 and is under evaluation by the FDA for the treatment of moderate to severe plaque psoriasis. Phase 2 studies are underway for psoriatic arthritis (PsA) and RA.

**Infliximab.** Several characteristics link tumor necrosis factor (TNF) with the psoriasis disease process, making it likely to play an important role in psoriasis therapy. TNF is released by injured keratinocytes, and it is present in elevated levels in the psoriatic dermis and epidermis, where it regulates proinflammatory cytokines.

PASI scores correlate with TNF expression, and serum and lesional TNF levels decrease after effective therapy in relation to the degree of clinical improvement.

One of two TNF-α drugs, infliximab is indicated for Crohn’s disease and RA, but not for psoriasis or PsA. In Crohn’s disease, infliximab is indicated for reducing the signs and symptoms of moderate to severe disease, and for the closure of enterocutaneous fistulas in fistulizing Crohn’s disease. In RA, infliximab is indicated, in combination with methotrexate, for reducing signs and symptoms, and for inhibiting the progression of structural damage in patients with moderate to severe disease.

Infliximab is a chimeric (mouse/human) IgG1 monoclonal antibody with approximately 25 percent retained murine sequences, which makes it more antigenic. Administered intravenously, infliximab binds transmembrane-bound TNF-α, soluble TNF-α, and receptor-bound TNF-α with high specificity, high affinity, and high avidity (Knight 1993).

In a 33-patient study, infusions of infliximab were administered at week 0, week 2, and week 6. Eighty-two percent of patients achieved PASI-75 when results were measured at week 10 (Chaudhari 2001). In addition, 53 percent of patients maintained the response at the PASI-50 level after 8 months (Chaudhari 2001). The 5 mg/kg and 10 mg/kg doses of infliximab were equally effective. Multicenter studies are under way to confirm these results.
In clinical trials, approximately 10 percent of patients were antibody positive (Centocor 2003). The antibodies are generally low titer and do not crossreact with other approved monoclonal antibodies. Antibodies to infliximab are positive in approximately 10 percent of infusions and negative in approximately 3 percent of infusions. Infusion reactions are typically mild to moderate and are managed with acetaminophen or diphenhydramine HCl.

As of Aug. 23, 2001, 101 cases of tuberculosis worldwide were reported among the more than 170,000 patients treated with infliximab. The majority of cases have been pulmonary, and a third of all cases were disseminated. Fifteen deaths have been reported as a result of treatment with infliximab; of these, 11 were attributable to tuberculosis.

Infliximab is associated with impaired cell-mediated immunity, leaving patients vulnerable to opportunistic infections.

**Etanercept.** The second of the two TNF-α drugs, etanercept also is indicated not for psoriasis but for RA, PsA, and moderate to severe active polyarticular-course juvenile RA in patients who demonstrate an inadequate response to one or more disease-modifying antirheumatic drugs.

In its phase 2 trial, etanercept monotherapy achieved clinically meaningful and consistent efficacy in clearing psoriasis. Etanercept was given subcutaneously twice weekly to approximately 112 patients. Thirty percent of patients achieved a PASI-75 response at 12 weeks and 56 percent by week 24 (Amgen 2003).

While some patients treated with etanercept have developed tuberculosis, the incidence is similar to that expected in the population receiving treatment. The overall adverse-event profile was unremarkable.

**Discussion**

The immunologic nature of psoriasis will likely make biologic therapy the treatment of choice, replacing current topical, photo-, and systemic therapies. This important class of drugs will continue to be developed, with smaller molecules already being tested in trials. A goal of research in this area is development of an oral formulation of these medications.

Due to the convenience, safety, and efficacy of efalizumab and etanercept, it is conceivable that these subcutaneous drugs will dominate the market. These new therapies also offer the prospect of overall cost savings by arresting disease progression. Patients with PsA who take etanercept, for example, may be less likely to develop the more severe forms of disabling PsA than patients who do not. Alleviating the physical and mental burdens of chronic psoriasis also will pay dividends by lowering illicit drug use, alcoholism, and depression, and by liberating millions of Americans to live productive lives.

According to the 2001 NPF survey, approximately 2 million psoriatics report that their disease is severe. Nevertheless, estimates of the number of patients who will become candidates for these new treatments are low. Many psoriatics are disengaged from health care because dermatology has had little to offer them until now. When these individuals begin to see direct-to-consumer advertising for these biologic agents, they are likely to start seeking out these drugs to obtain relief from this disabling condition.

**References**


One way to measure the cost of a disease or condition is to look at a large retrospective database and examine treatment costs for that particular illness. This is what Medstat did, in conducting a study that quantified the burden of illness associated with psoriasis (Crown 2003). Yet in looking only at the primary illness, it’s easy to overlook the cost of comorbid conditions. Many psoriasis patients, for example, also suffer from obesity or depression and complain that they have trouble sleeping, have lost their interest in life, or are not as productive as they once were.

Beyond the direct medical cost of an illness, there are larger, indirect costs. Employers, for example, are interested in productivity. When an employee has psoriasis on the bottom of his feet and can’t go to work, or when the cream that must be spread all over a patient’s body keeps her distracted and less productive, the employer suffers as well.

Many of our employer clients have medical claims data, as well as administrative data on incidental absence, short-term disability, and workers’ compensation claims. The more forward-thinking of these employers are merging their data to try a new approach called health and productivity management. With Mark McClellan, MD, PhD — a physician and an economist — as the head of the U.S. Food and Drug Administration, I think this interest in managing productivity will grow.

Even so, relatively few large employers are thinking progressively about the cost of illness. It seems that many of our employer clients read in the business press that prescription drug expenditures are increasing roughly 20 percent each year and, instead of looking at the big picture, they just want to know what the drugs will cost and what the total cost of treating a patient will be.

In evaluating the burden of illness, it is important to consider quality-of-life issues for psoriasis patients who are undergoing treatment with current therapeutics. Quality-of-life issues are hard to quantify in economic terms, but there are ways to integrate them into the big-picture cost of an illness. Studies that have been completed document a functional impairment among psoriasis patients; the health-related quality of life for those with moderate or severe psoriasis and who are treated with current systemic therapeutics is, in general, relatively low when compared with the population at large.

The Medstat study

Objectives and methods

The objectives of our study were: (1) to compare the burden of moderate-to-severe psoriasis patients on the health care system to that of a randomly selected group of patients without psoriasis, extrapolating to the larger population; (2) to examine the prevalence of comorbid conditions in psoriasis patients; and (3) to identify the cost of serious adverse events, side effects, and monitoring.

Medstat pools data from large employer clients, such as General Electric, Navistar, and Chevron — in all, about 70 of the Fortune 200 companies; these employers are interested in benchmarking their health care experiences against those of other large employers, and so they give us permission to pool their data. The database on privately insured employees and their dependents holds information on 2.5 million covered lives per year and can typically track de-identified individuals over
several years; if they switch health plans, we can see them moving from plan to plan.

The database includes information about inpatient, outpatient, and pharmaceutical costs, as well as the types of health plans the employees are enrolled in and the designs of those plans. Claims data are valuable in that they show comorbid conditions, the various treatments a patient received, and side effects, especially in the case of systemic therapy. This is in contrast to survey data, which are not as detailed; when people are surveyed, they often find it difficult to remember the details of their treatments, office visits, and emergency room visits.

Our data consist of retrospective claims for employees with psoriasis or psoriatic arthritis (PsA) who were covered by commercial insurance from 1996 to 2000. Following the subjects for a minimum of 1 year and a maximum of 5 years, our intent was to identify long-term side effects of treatment. We annualized our measurements.

We divided the psoriasis patients into three categories (Figure 1):

- Patients whose psoriasis was mild and who received no treatment, monotherapy of a topical agent, or one or no prescriptions for topical agents. These subjects were classified as limited topicals.
- Patients who were treated with 1 to 4 topical agents and were given two or more refills of a topical agent. These were classified as more frequent topicals.
- Patients with moderate/severe psoriasis were those who had either PsA, any phototherapy, or any systemic therapy. Our focus was on this group, but we do present some initial data for the other patients.

We matched the moderate/severe group to a control group (nonpsoriasis group) comprising a random sample from the rest of the population; the groups were matched by age, gender, geographic region, and length of follow-up.

In the moderate/severe group, 45 percent had psoriasis alone, 28 percent had PsA as well as psoriasis, and another 28 percent had PsA alone. The patients’ ages ranged from about 47 to 52.

Results and discussion

We looked at the top 25 diagnoses for the moderate/severe psoriasis and the nonpsoriasis groups, focusing on those that are likely to be psoriasis-related side effects or comorbid conditions. The moderate/severe group had higher rates of carcinoma, hepatotoxicity, and nephrotoxicity than the nonpsoriasis group, as one might expect. We are particularly interested in the higher rates of anemia, gastrointestinal disorders, hypertension, and depression found in the moderate/severe group, as compared with the control group (Figure 2, page 12).

We used the Charlson Comorbidity Score, a tool commonly used to measure severe comorbidities associated with hospitalization (Charlson 1987). The moderate/severe psoriasis patients in our study had significantly higher scores than the control group. We also looked at the number of ICD-9 codes patients had, to see how many different body systems were involved in their illnesses.

Carcinoma, depression, diabetes, and thrombocytosis were the comorbid conditions that showed the greatest difference between the moderate/severe and the nonpsoriasis group in terms of cost. A large part of the cost associated with psoriasis patients is due to comorbidity rather than the psoriasis itself. If we could understand comorbidities better, we might have a more thorough understanding of how new treatments might affect patients. It appears that there is a clinical path between obesity, diabetes, hypertension, and psoriasis. What might the effect be of treating those comorbidities in a psoriasis patient? It is my belief that as the population
ages, this will become a greater issue. Body systems are complicated; sometimes, when treating a patient with comorbidities, improving one condition causes others to improve in response — thereby offsetting treatment costs of the other conditions. Other times, treating one condition makes the others worse, and thus the cost of treating those conditions also increases.

The most common treatments for moderate/severe psoriasis patients were methotrexate and psoralen with ultraviolet A (PUVA). In this study, we did not try to understand the timing of treatments — how many office visits, the average duration of treatment, or why patients went off treatments or switched to other ones. We simply followed them through the data for as long as we could, calculated the cost of the treatments they received and compared that to the treatments the controls received.

Not surprisingly, the moderate/severe psoriasis group had three times more lab tests and prescriptions than the control group. It also had twice as many outpatient services and four times as many psoriasis-related emergency room visits than the nonpsoriasis group. In the case of the moderate/severe group, inpatient costs were about a quarter of the total cost of treatment; the inpatient cost was $2,059 per psoriasis patient in the database, and the total cost of treatment was $7,639 per patient. These figures represent the direct cost of treatment only; a claims-based study such as this cannot calculate the additional indirect economic impact of illness, such as lost productivity.

A recent study estimated the total direct cost of care associated with psoriasis (not including comorbidities) at $649.6 million per year in the United States (Javitz 2002). If one considers indirect costs, such as lost productivity, the figures are much larger, ranging from $1.2 to $3.2 billion per year (Javitz 2002). Our figures are similar. Extrapolating to the entire United States population, using Javitz’s estimate of 1.4 million Americans with clinically significant psoriatic disease, we estimated the total cost of psoriasis to the health care system to be $705.6 million per year (Figure 3). The approximate $50 million difference between our estimate and that of Javitz is largely due to our different estimates of inpatient costs (primary diagnosis of psoriasis); ours was $74.2 million, while Javitz estimates $30.5 million (Javitz 2002).

Our study suffers from the same limitations as all claims-based studies — the lack of clinical data. A dermatologist who can actually examine a patient is much better able to determine the severity of the patient’s psoriasis than we, because we determine severity based only on a record of the treatments that a patient has received. We can see only the cost of the resources used, such as medical attention, drug use, etc. Claims data do not provide a complete patient history. For example, if a patient had received ultraviolet therapy at some point prior to the time frame we analyzed in the claims (1996–2000), our data would not reflect this. Claims data cannot capture many of the indirect cost dimensions of an illness, such as the effects of the illness and treatments on quality of life. On the other hand, claims are sometimes able to provide information on work loss and disability in certain settings with integrated medical claims, absenteeism, and disability systems. Finally — and importantly for psoriasis — claims cannot tell us about the cost to unsatisfied psoriasis patients who are undertreated or who do not seek treatment — a cost that is difficult to measure. Ironically, the benefits of new treatments, when they draw formerly undertreated patients back into the medical system, are generally neglected in the overall statistics regarding increased drug and medical expenditures.

**Market issues and biologics**

One important issue in the marketplace, particularly among large employers and MCOs, is concern about pharmacy costs.
scribing has been to try one therapy until there is physical evidence that a patient is not responding, then initiate new therapy. This approach adds expense to managed care organizations and the health care system in general; they are paying for care that results in no clinical benefit to patients. Although “personalized medicine” and biologics are relatively expensive, they may prove to be cost-effective if they can indeed eliminate the cost of treating patients who do not respond to treatment. This becomes especially true when considering quality of life as an element of cost.

Medstat has recently studied the cost-effectiveness of biologics in another therapeutic area. We have found that cost-effectiveness depends, in part, on the sensitivity of the test used to identify a condition and the cost of that test. It also depends on the probability of a response to a new therapy, the cost of treating with a new therapy, the response to existing therapy, and the cost of treating with existing therapy. Once these costs are considered, one can then answer the question, “Is this new treatment cost-effective compared with those already on the market?”

In the case of severe psoriasis, a diagnostic test may not be as important as it would be in other areas of biologics. For the practicing dermatologist, it is fairly easy to determine whether a patient is a good candidate for one of the new treatments. Because psoriasis is easily diagnosed, it may be a better candidate for biologics than other conditions from the perspective of payers. Perhaps most importantly, it is gratifying to see that, based on clinical trial data, there is a high probability that severe psoriasis patients will respond to biologics.

My impression is that, initially, the response of the health care system and managed care in particular was to try to keep a lid on costs by imposing restrictions on use. Recently, there has been a shift away from that approach, because it was not effective; instead, coverage of new therapies is permitted but employers and MCOs attempt to control their utilization through economic incentives, such as copayments, coinsurance, and deductibles. Under this scenario, moderate/severe psoriasis patients are given access to biologics as they become available but may have to pay substantial copayments to use them. Copayments can amount to 20 percent or more of the total cost of the drug. We don’t know how patients and the health care system will respond to higher copayments; it will be interesting to see the implications of this development on highly effective biologic therapies. If the trend toward shifting financial responsibility for care to consumers continues, then it is difficult, at this juncture, to predict consumer acceptance of biologic agents.

Personalized medicine and biologics create a new economic world, because the treatments are typically targeted to a narrow and often severely ill population. Whether managed care will be willing to pay for that might depend on practitioners’ and manufacturers’ ability to determine who will respond to treatment and who will not, which would eliminate the expense of treating patients who will not respond.

For many years, the standard approach toward pre-

References
Currently, we do not have step therapy in place for psoriasis because available therapies have been relatively inexpensive. The economics of therapy do not support the need, nor does step therapy make sense, clinically, for psoriasis. If effective new biologic response modifiers become first-line therapy, then step therapy would, as a matter of course, be unnecessary; the issue simply would be to make the drugs available. Managed care organizations will continue to use resources at their disposal, such as Milliman guidelines, but the MCO’s decision will be for the physician to proceed with effective treatments.

All of our medical policy information is available to the public on the Web. We have a national medical policy committee that looks at the literature and evaluates therapies for a disease or series of diseases. For psoriasis and this series of diseases, most clinics request ultraviolet light therapies. These requests are transferred to a nurse, who will say “yes” if she or he determines that the physician is calling about psoriasis and that the treatment is on the list of approved indications for psoriasis. The requirement that physicians call us is, in a sense, superfluous, in that we have the literature and data to support the request, but our decision is ultimately based on the physician’s diagnosis. We do not intervene beyond that point.

It is my opinion that the managed care industry will intervene even less in the future, given the rich database of treatment guidelines and information at its disposal. In the future, it is conceivable that there will be specialty disease management companies that will relieve managed care organizations of the responsibility for managing psoriasis. There are companies that do this with rheumatoid arthritis (RA), for example, where the literature demonstrates that biologics are an effective treatment for the disease. Although they are relatively costly, the biologic agents are effective; if you are a neurologist, rheumatologist, or dermatologist, you know that these therapies work. Once biologics become first-line therapy for psoriasis, there will be no need for traditional MCO management.
Effect of out-of-pocket payment

In recent years, MCOs have implemented tiered pharmacy benefits. In our system, older conventional therapies for psoriasis — including cyclosporine, methotrexate, calcipotriene, steroids, and tar preparations — are on the first tier. Contract language and a drug’s acquisition price influence the placement of drugs in certain tiers, and thus each health plan has its own system.

Anthem Blue Cross Blue Shield of Colorado has developed a four-tier system; the fourth-tier benefit provides coverage for higher-cost, self-administered injectable drugs, such as those to treat hepatitis and RA. There is a 30-percent member copayment for this tier, up to a per-claim maximum of $250. Among biologic therapies for psoriatic arthritis, etanercept is on the fourth tier.

Clearly, health plans are beginning to engage their members financially with an increasing number of therapies. While it will be the clinician’s decision as to whether the patient requires a drug, it will be the patient’s decision whether to comply with therapy. When the decision lies between the patient and the physician, the patient often will ask for the drug with the less-expensive copayment.

Most health plans, including HMOs, are now adding deductibles to copayments. The level of members’ financial responsibility per tier is reevaluated each year. Next year, for example, the member’s responsibility for fourth-tier products might be raised from 30 to 36 percent. Higher copayments or coinsurance may result in improved compliance, considering the increased patient investment in the product. An argument also can be made that higher copayments act as a barrier to compliance. This is the subject of great debate, and we do not yet know what effect changing these amounts will have on patients’ compliance with therapy.

Individuals are buying policies that not only exclude coverage for certain therapies, but also have $5,000 or $10,000 deductibles. Patients know that they have to pay up to a certain amount; they may be willing to accept less-expensive treatments until they reach their deductible, at which point they begin to request more-expensive therapies. The outcome of this behavior is an intangible that cannot be predicted.

Challenges facing insurers

Economic inequities involving specialty pharmacy products present health plans with an enormous series of challenges.

When these products are administered in a physician’s office, the issue of expense to the physician is raised. MCOs are looking at variable office copayments, including sharing the cost of clinician-administered injections with the member. The issue is complicated, in part because physicians do not always know how much to charge, but we are working on possible solutions. For example, we might be able to prohibit physicians’ keeping a drug supply in the office and require a patient copayment when a specialty pharmacy delivers the drug.

At-home injection by the patient adds to the difficulty of determining drug copayment amounts. There is no rationale for processing the cost of self-administered injections differently from those of clinician-administered injections, yet Medicare, for example, covers in-office injections but does not cover at-home injections. The variation among MCOs’ pharmacy benefit structures and between private and government systems creates an unequal coverage problem that must be addressed.

Another potentially complicating factor, in terms of drug coverage, is that the emerging therapies for psoriasis are effective for, and being made available to, middle-aged people. These are therapies that are useful to people who are 30 to 50 years old, who are or can be productive, and who are buying policies that require out-of-pocket payment. We do not know yet, from a policy point of view, what the effect will be when these middle-aged people turn 65 and suddenly realize that to continue with their therapy, it will cost them a certain amount per month.

An MCO would have strategies for when the middle-aged population begins to age. The use of biologics for RA is a good example. It took less than a year for RA biologics to start moving to first-line therapy, and although they are not all there yet, if a patient needs a drug, a patient gets it. Managed care will do what is appropriate to support such decisions.

Disease and case management are big issues in managed care now, but disease management is most logical for only seven or eight chronic conditions and does not include psoriasis. Case management is provided for any extreme illness, but again, probably not psoriasis; in psoriasis, and dermatology in general, the diagnosis and treatment occur quickly.

Coverage in the future

We have been able to cover a wide range of dermatologic therapies because they are relatively inexpensive. When we put a new drug in the fourth tier, the challenge will be for the clinician to explain to the patient that a fourth-tier drug is worth the coinsurance. The clinician knows that only one third of patients takes a drug cor-
Following Sullivan’s presentation, several of those in attendance discussed the issue of therapy administration in the physician’s office versus in the patient’s home. Michael J. Boskello, RPh, William H. Crown, PhD, David M. Pariser, MD, Craig L. Leonard, MD, and Pamela D. Thomas, MD, MPH, contributed the following points to this discussion:

Increasing a patient’s copayment — his or her financial stake in therapy — may lead to improved compliance, but the physician can be certain of compliance only when patients receive therapy in the office. At home, patients could potentially take it upon themselves to reduce their amount of therapy to a level where they are willing to live with some psoriasis to save money. In the medical office, if nurses or physician assistants give injections, physicians save time and increase revenue, yet the amount of revenue from a new therapy cannot be determined until a number of patients are receiving it. Complicating this scenario, until a product is well established under coverage policies, a physician might not purchase and stock the product, even without having to obtain prior authorization. Some patients do not want to go to the physician’s office on a weekly basis to receive therapy; physicians have to “chase down” some patients to make sure they come in.

The patient’s point of view should be considered, including how often she or he wants to come in, and whether she or he would prefer to self-administer therapy at home. During subcutaneous therapy trials in a particular office, more than 90 percent of patients chose at-home self-injection. Of the remaining 10 percent, some patients chose in-clinic administration for social reasons — to be with other people who shared their problems — even though they were physically able to self-administer the drug.

### TABLE 1  Anthem Blue Cross Blue Shield of Colorado’s policy position and rationale

<table>
<thead>
<tr>
<th>Policy position</th>
<th>Rationale</th>
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<tbody>
<tr>
<td>Medically necessary:</td>
<td>Psoralen with Ultraviolet A (PUVA) is considered medically necessary in the treatment of the following: psoriasis, mycosis fungoides (cutaneous T-cell lymphoma), atopic dermatitis, atopic eczema, lichen, vitiligo, and acute/chronic pityriasis lichenoides. Actinotherapy (UVA or UVB) is considered medically necessary in the treatment of the following conditions: psoriasis, chronic urticaria, pruritus of renal failure, mycosis fungoides (cutaneous T-cell lymphoma), eczema, pityriasis rosea, lichen, and pityriasis lichenoides. Goeckerman therapy is considered medically necessary in the treatment of psoriasis.</td>
</tr>
<tr>
<td>Not medically necessary:</td>
<td>Ultraviolet light therapy (PUVA, UVA, or UVB) is not medically necessary as a home therapy.</td>
</tr>
<tr>
<td>Investigational:</td>
<td>The use of laser therapy (e.g., xenon-chloride, excimer) for the treatment of psoriasis or vitiligo is considered investigational.</td>
</tr>
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</table>

Ultraviolet light (with and without the introduction of psoralen) is widely used for the treatment of skin conditions. Evidence in the peer-reviewed medical literature suggests that this treatment can provide efficacious therapy for individuals affected by various types of skin conditions (listed above in the “medically necessary” statement). This use of ultraviolet light as a home therapy is not supported in the literature, as routine clinical evaluations are necessary to ensure that the exposure dose of radiation is kept to the minimum level compatible with adequate control of disease and the prevention of complications. While laser therapy emits ultraviolet light, there is currently insufficient evidence to support the use of this technology in individuals with skin conditions. Additional evidence is needed to determine the efficacy of laser therapy before it can be considered a standard method of treatment in individuals with specific skin conditions.

SOURCE: ANTHEM BLUE CROSS BLUE SHIELD OF COLORADO, UPDATED OCT. 21, 2002. REPRINTED WITH PERMISSION.
rectly, another third incorrectly, and the final third not at all.

An interesting consideration is whether the pharmaceutical industry should be dealing primarily with managed care companies or with patients. It is my belief that in the future, drug manufacturers will work more directly with patients. Direct-to-consumer advertising is an example of that. Direct-to-consumer advertising is an important element in getting the patient involved, and if certain economics exist, the managed care company is left out. Thus, the managing of these products is reduced to manipulating consumer economic factors.

For example, a manufacturer might offer a coupon for the first 3 weeks of therapy, until the drug begins to take effect. Or, if the health plan has a $250 deductible, the manufacturer might offer consumers a $100 coupon to get them to try its product over a competitive product in the same class, as opposed to contracting with a pharmacy benefit manager for a discount. Those are the dynamics that we will see — in essence, who gets the economic benefit? If the clinician has three or four competing drugs that can be used appropriately for a patient’s treatment, the question becomes whether the manufacturer should approach the clinician or the patient. Increasingly, manufacturers are deciding that they should approach the patient instead of managed care.

Yet managed care plays many important roles in the health care system that benefit consumers and physicians, and it should be a part of the decision-making process. Managed care tries to improve the public’s health literacy in an effort to prevent illness and unnecessary health care expenditures, and we have had some success with this through the help of funding from the pharmaceutical industry. The true value of managed care is better quality for the patient. Patients receive access to better-quality treatment, in part because MCOs can provide data to physicians who otherwise might not be able to obtain that information without having certain data capabilities. These are good services that managed care provides.
Currently, one third of dermatologists in the United States use systemic therapy for patients who have moderate to severe psoriasis. Of the other two thirds, some are surgeons or physicians whose practices deal only with cosmetic dermatology. However, the majority of dermatologists who do not prescribe systemic agents do not do so because they are concerned about the risk of toxicity associated with systemic drugs for treating psoriasis. The development of new biologic response modifiers for treating psoriasis is likely to change the current paradigm.

The American Academy of Dermatology (AAD) considers it important to educate dermatologists on this new frontier of treatment, so it convened a consensus conference to address the use of the new biologic and other, nonbiologic, treatments for psoriasis. The AAD Consensus Statement on Psoriasis Therapies will be published soon in the *Journal of the American Academy of Dermatology*. The following summarizes the major points within the AAD statement.

**Diagnosing psoriasis and psoriatic arthritis**

The standard of care for diagnosing psoriasis and psoriatic arthritis (PsA), as stated by the AAD, is that psoriasis should be diagnosed
by a dermatologist, after obtaining a patient history and performing a physical examination. Skin biopsy is sometimes, but not always, necessary to establish a diagnosis of psoriasis, and when possible, precipitating causes such as drugs, stress, environment, and concomitant disease should be considered. While no laboratory test is available to screen for psoriasis, one of the hallmarks of PsA is seronegative arthritis.

**Selecting therapy**

When deciding what therapy to use for the treatment of psoriasis, the AAD recommends that physicians consider whether the disease is regular plaque-type psoriasis or another form of psoriasis (such as guttate, pustular, erythrodermic, palmoplantar, PsA, scalp psoriasis, nail psoriasis, or inverse psoriasis). Choice of therapy not only depends on the type of psoriasis being treated, but also on the severity and locations of the psoriatic lesions. The age of the patient and his or her ability to be accessible for in-office treatment should also be considered.

Economics are an important factor in the selection of treatment. Because relatively few dermatologists have been prescribing systemic therapy, these treatments for psoriasis have generally not had extensive scrutiny from managed care organizations. Yet now that drugs that have been shown to be successful in treating moderate to severe psoriasis are available — though at greater cost than traditional therapies — dermatologists must become more involved in determining cost-benefit ratios and third-party coverage.

When selecting a therapy for psoriasis, the AAD also recommends that physicians consider patients’ quality of life. Some issues related to quality of life include employability and interpersonal relationships.

Finally, patients’ comorbid diseases or state of illness are important considerations to take into account, lest the treatment interfere with their care or patients find themselves unable to follow through with a psoriasis-treatment regimen.

**Categorizing disease**

The severity of psoriasis is a qualitative measure and has little to do with the extent of skin surface involved. For example, if psoriatic lesions manifest themselves on 1 percent of a patient’s body, this may be considered treatable with topical therapy. If the 1 percent is on the soles of a patient’s feet, however, making it difficult for the patient to walk or work, systemic therapy may be warranted.

Severity hinges on measures of disease activity, resistance to prior therapy, and psychosocial considerations. Thus, it is important for physicians and managed care professionals to move away from the classic categorization of psoriasis as mild, moderate, or severe. Rather, psoriasis should be classified as limited — which, usually, can be treated with topical therapy — and moderate to severe, which requires systemic therapy. Limited disease may also warrant phototherapy or systemic therapy, if it is not responsive to topical therapies or if there is disruption in the patient’s daily activities and/or employment.

Patients with PsA may have limited skin disease but require more aggressive systemic therapies. The final version of the AAD consensus document includes the statement that psoriasis involving the hands, feet, head and neck, genitalia, or covering more than 5 percent of the skin surface may be considered severe disease warranting systemic therapy.

**Available therapies**

For treatment of limited psoriasis, there are many topical agents available for treatment, including corticosteroids, retinoids, and tar preparations. Topical immunomodulators, which are commonly used to treat atopic dermatitis, are also being investigated for their efficacy in treating limited psoriasis.

The currently available treatments for moderate to severe psoriasis include phototherapy, which can be used with or without topical agents. Home phototherapy units are available, and, while they present an initial cost to those who use them, patients who respond to this treatment will find an overall cost benefit in contrast with visiting the dermatologist’s office three times a week for the same treatment. Photochemotherapy also can be used to treat moderate to severe psoriasis. This treatment, which must be performed in the office, is being used far less frequently than in the past, however.

Older therapies for moderate to severe psoriasis, including methotrexate, oral cyclosporine, and oral retinoids, are discussed in detail in this publication in the article by Leonardi.

The four biologic agents listed in the AAD consensus statement are acceptable as first-line agents for those patients who require systemic treatment for plaque-type psoriasis. These four agents are etanercept, alefacept, efalizumab, and infliximab. While not all these biologic agents have been approved by the U.S. Food and Drug Administration for use in the treatment of psoriasis, the AAD has chosen to recommend these agents as first-line therapies based on clinical experience that has been gathered to date.

For forms of psoriasis other than plaque types, there are fewer data on treatment with biologic agents; therefore, the AAD is not prepared to list them as first-line treatment options for pustular, guttate, or erythrodermic psoriasis. Clinical experience with real-world use of biologic agents will determine the usefulness of such agents in these forms of psoriasis.
Goals of therapy

When selecting a treatment for plaque-type psoriasis, the goal should be long-term control of the disease. Complete clearing may be possible with available therapies.

Currently, success of therapy is often expressed in terms of a patient’s improvement on the psoriasis area and severity index (PASI), under which the aim of therapy is to achieve a 75-percent reduction in severity. PASI, however, is an imperfect proxy for clinical outcomes measurement; PASI is a tool designed for use in clinical trials, mandated by the FDA, and is not part of routine clinical care. While successful treatment roughly correlates to the degree of PASI improvement, a 75-percent improvement from baseline is often an unrealistic objective when considering treatment to improve a patient’s health. In actuality, effectiveness of care is judged independently by both the patient and the physician, whose definitions of successful therapy are framed by different parameters. Therefore, it is widely recognized that dermatology requires a better scoring system to measure the success of treatment for psoriasis.

The AAD will provide updates on biologic therapy and indications for its uses. As the body of evidence supporting the efficacy of these new therapies for psoriasis and PsA grows, it is expected that a large number of dermatologists will accept these agents into their practices.

Sources


ROUNDTABLE DISCUSSION

David M. Pariser, MD: How would managed care professionals prefer that dermatologists document or evaluate psoriasis?

Humberto Guerra-Garcia, MD, MPH: Some managed care organizations maintain a separate injectables program, using evidence-based guidelines to ensure optimal utilization and to control high cost. Many times, specific guidelines are not available, making accurate information from the practitioner crucial. The expert assessment of a specialist, such as a dermatologist with experience in treating psoriasis, may frequently be the only justification needed for prior authorization. At the population level, psoriasis patients who qualify for treatment with biologics may vary in number; therefore, the impact on usage of these injectables may be different across MCOs.

Pariser: In thinking about how biologics might become accepted, how do you decide, for example, whether it is appropriate to treat rheumatoid arthritis with the use of existing biologics? Do you have algorithmic guidelines to help you make these decisions?

Guerra-Garcia: Most cases of rheumatoid arthritis are cleared for step therapy based on current standards of practice; we have not seen many rheumatologists requesting biologics as first-line therapy. Most requests for biologics include an evaluation of treatments that have been used, as well as FDA indications. However, we research applications beyond FDA indications, and in certain individual cases we may authorize use of any medication beyond an FDA indication if it is clinically appropriate and in collaboration with the prescriber.

Craig L. Leonardi, MD: In my experience, the majority of the patients who enroll in clinical trials for biologics have become disconnected from the health care system. We run a large clinical trial center. Sixty percent of those who come to us do so because they have been unable to find somebody who is interested in their disease
or who could offer them treatment or advice that works to improve their condition. It is encouraging to have new choices for psoriatic patients. This is a group of patients who have been neglected for a long time.

William H. Crown, PhD: Will the availability of new biologic treatments cause dermatologists to forgo the use of standard treatments, considering the safety and side-effect profiles and the quality-of-life issues associated with the older therapies?

Leonard: In my opinion, the safety profiles of biologic therapy, even in a trial setting, are better than those of currently available treatments.

Leonard: The cost of monitoring the side effects of older therapies, such as performing liver biopsies or monitoring renal toxicity, should be considered when talking about the overall cost of a treatment.

Adelaide H. Hebert, MD: I concur. The cost of monitoring the side effects of older therapies, such as performing liver biopsies or monitoring renal toxicity, should be considered when talking about the overall cost of a treatment.

Terry J. Sullivan, MD, MPH: The bottom line is that biologics will evolve the same way that drugs for rheumatoid arthritis have. They will become first-line therapy. I do not see cost as an issue with biologics; the system will absorb the extra cost and will accommodate biologics because these drugs are effective.

Leonard: There is a need for some kind of objective measure to automatically qualify a patient for a biologic agent. Creating such a measure would save patients the torture of having to go through step therapy with topical steroids and other therapies when it is clear they will not work.

Pariser: If there is some concern about the AAD consensus statement because it’s not an algorithmic guideline, then you might consider the National Psoriasis Foundation, which does have a more formal guideline.

Sullivan: But I think you made the point earlier, when discussing PASI, that this does not lend itself to a guideline easily, because of the nature of the condition and they way it is scored. As an evaluative tool, the PASI may not be the best clinical approach. Nor does the available research support a benefit to developing rigid measures of disease severity as might be done for some other medical conditions.

Kirck: However, every time dermatologists ask managed care for preauthorization for a treatment, they are asked to present their notes proving that the patient has undergone therapy. Perhaps the AAD consensus statement will be enough to prevent this.

Crown: Do you think that biologics will be used in combination with older therapies to treat patients with severe cases?

Leonard: The early adopters will be dermatologists who are using the current systemic treatments. I would expect to see combinations of methotrexate and alefacept being used, crossing patients over into new therapy. I have difficulty with mixing and matching biologic therapies because in some cases, combinations of prednisone, cyclosporine, and infliximab resulted in high-grade immunosuppression.

Crown: I was not thinking so much in terms of the development of a new compound that combined various properties of drugs; I was thinking more about how physicians would practice now that they have broader choices in treating patients.

Leonard: Because I chose dermatology as my profession, I have always wanted to find ways to bring relief to patients with bad skin disease. I have been frustrated by not having the right tools to do this, so the availability of biologics to treat psoriasis is exciting to me. Biologics are not subtle; they have a major impact on patients who are in desperate need.

Pariser: It exciting for us as medical dermatologists to be able to provide care in a way that we have never before. Patients are picking up on this.

Hebert: I think dermatologists will begin to see more patients with psoriasis simply because, for the first time, we have a good treatment to offer. This is a wonderful time to practice dermatology, because of our new capacity to help these patients with biologics.

Guerra-Garcia: The development of these biologic agents will provide managed care with an opportunity to partner with dermatologists to develop guidelines for appropriate treatment of plaque psoriasis. Working closely with physicians who treat patients with this condition will produce the best results.

Pariser: I’m pleased that we didn’t get tremendous resistance from our managed care colleagues about this, and I hope we can figure out a way to provide these agents to the people who will benefit from them.
CONTINUING EDUCATION QUESTIONS
Managed Care Best Practices in the Treatment and Management of Psoriasis

Please tear out the combined answer sheet/evaluation form on page 23 (physicians) or page 24 (pharmacists). On the answer sheet, 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 affects more than 7 million Americans. According to the National Psoriasis Foundation, how many psoriatic patients consider their disease to be moderate to severe?
   a. 200,000
   b. 500,000
   c. 1 million
   d. 2 million

2. Medstat estimated the total cost of psoriasis (as a primary diagnosis only) to the national health care system to be:
   a. $74.2 million per year.
   b. $649.2 million per year.
   c. $705.6 million per year.
   d. $3 billion per year.

3. Which of the following therapies is most commonly used in the management of moderate to severe psoriasis?
   a. Phototherapy.
   b. Systemic therapy with methotrexate.
   c. Systemic therapy with cyclosporine.
   d. Systemic therapy with retinoids.
   e. Topical therapy with steroids.

4. According to the AAD, in choosing psoriasis therapy, physicians should consider the:
   a. Form of psoriasis, patients' quality of life, and comorbid conditions.
   b. Severity and locations of lesions and patient's state of health.
   c. Patient's access to office for treatment.
   d. Answers “a” and “b.”
   e. All the above.

5. Contract language and a drug’s acquisition price:
   a. Help to shape a health plan's unique system.
   b. Contribute toward uniform standards among plans.
   c. Influence the placement of drugs in certain tiers.
   d. Answers “a” and “c.”

6. Because cyclosporine is nephrotoxic, the FDA limits its use in treatment of psoriasis to:
   a. 6 months.
   b. 9 months.
   c. 1 year.
   d. 18 months.

7. The cost-effectiveness of personalized medicine and biologic drugs could potentially be realized if these therapies can reduce or eliminate the expense of treating patients who are unresponsive to treatment.
   a. True
   b. False

8. In the AAD consensus statement, four biologic agents have been listed as first-line agents for patients requiring systemic treatment for plaque-type psoriasis based on:
   a. Long-term studies.
   b. Patient demand.
   c. Clinical experience.
   d. FDA indications.

9. Medstat found that cost-effectiveness depends, in part, on the:
   a. Cost of drugs currently under development for a condition.
   b. Cumulative cost of prior therapy.
   c. Sensitivity and cost of the test used to identify a condition.
   d. All of the above.

10. Many health plans are now changing the level of patients' financial responsibility for health care services by:
    a. Adding deductibles to copayments.
    b. Reevaluating member responsibility per tier yearly.
    c. Abandoning management of drug therapy.
    d. Answers “a” and “b.”
    e. Answers “b” and “c.”
CONTINUING EDUCATION ANSWER SHEET/CERTIFICATE REQUEST
Managed Care Best Practices in the Treatment and Management of Psoriasis

CME CREDIT FOR PHYSICIANS
Sponsored by The Chatham Institute

See page 24 for answer sheet for pharmacists

I certify that I have completed this educational activity and post-test and claim ______ number of credits.

Signature: _______________________________________
First name, MI ____________________________________
Last name, degree ________________________________
Title ___________________________________________
Affiliation _______________________________________
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Complete answer sheet/evaluation form and mail to:
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The Chatham Institute
26 Main Street, 3rd Floor
Chatham, NJ 07928

Credit will be awarded upon successful completion of assessment questions (80 percent or better) and completion of program evaluation. If a score of 80 percent or better is not achieved, no credit will be awarded and the registrant will be notified.

Please allow up to 6 weeks for processing.

The cost of this activity is provided at no charge to the participant through an unrestricted educational grant by Genentech.

EXAMINATION: Place an X through the box of the letter that represents the best answer to each question on page 22. There is only ONE answer per question. Place all answers on this answer form:

A B C D E
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PROGRAM EVALUATION
So that we may assess the value of this self-study program, we ask that you please fill out this evaluation form.

Have the activity’s objectives been met?
Objective no. (see page 2) Yes No
1. A B C D E
2. A B C D E
3. A B C D E
4. A B C D E
5. A B C D E
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Was this publication fair, balanced, and free of commercial bias? Yes _____ No _____
If no, please explain: __________________________________________________
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This educational activity has contributed to my personal effectiveness and should improve my ability to:

Treat/manage patients Strongly agree Strongly disagree
Strongly agree
5 4 3 2 1 n/a
Communicate with patients 5 4 3 2 1 n/a
Manage my medical practice 5 4 3 2 1 n/a
Other __________________ Strongly agree Strongly disagree

Effectiveness of this method of presentation:

Excellent Very good Good Fair Poor

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Time spent reading this publication: H _____ M _____

What other topics would you like to see addressed?
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Comments: ______________________________________
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CONTINUING EDUCATION ANSWER SHEET/REQUEST FOR STATEMENT OF CREDIT
Managed Care Best Practices in the Treatment and Management of Psoriasis

CPE CREDIT FOR PHARMACISTS
Sponsored by The Chatham Institute

See page 23 for answer sheet for physicians

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Pharmacist — This program is approved for 1.5 contact hours (0.15 CEU).

ACPE program number: 812-000-03-013-H01
Release date: May 12, 2003
Expiration date: May 11, 2004

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H ______  M _______

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Did you detect any bias in this presentation?
Yes _____ No _______

If yes, please explain:
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