

New Treatments and Management of the Psoriasis Patient

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Summary

Psoriasis can be a devastating disease both physically and emotionally. Treatments are available to help many patients with psoriasis. Unfortunately, there are no guidelines to define severe disease or preferred treatments. Additionally, there is no way to predict which patients will respond to which treatments. Biologics are transforming the treatment of this disease.

Key Points

- Psoriasis has a similar impact in physical and mental functioning as that seen in cancer, arthritis, hypertension, heart disease, diabetes, and depression.
- There are no uniform guidelines for determining degree of disease or appropriate treatment.
- Moderate to severe disease requires systemic therapy.
- New biologic agents have the ability to interrupt the disease pathway through the modulation of T-cell response and cytokine levels and may, therefore, slow or halt disease progression.
- Biologics can be managed with a prior authorization policy requiring one prior systemic therapy failure.

PSORIASIS IS A NON-CONTAGIOUS, lifelong skin disease. According to the National Institutes of Health, as many as 7.5 million Americans have psoriasis. The most common form, plaque psoriasis, appears as raised, red patches or lesions covered with a silvery white buildup of dead skin cells, called scale (Exhibit 1).

Psoriasis is not just a cosmetic problem. Studies show that about 60 percent of patients report their disease to be a large problem in their everyday life. Psoriasis has similar impact in physical and mental functioning as that seen in cancer, arthritis, hypertension, heart disease, diabetes, and depression (Exhibit 2).¹

Psoriasis can be a very severe disease. About one-quarter of patients have moderate to severe psoriasis. There is a big difference between a person with mild disease and those with severe psoriasis. Most mild disease can be treated with topical agents. When patients have extensive or severe disease, topical therapy is not possible because the disease is too widespread. Psoriasis morbidity includes skin symptoms of itching, burning, and open areas of skin; psoriatic arthritis; cosmetic disfigurement; pustular flares; and erythrodermic flares.

Psoriasis affects about 2 percent of the U.S. population, and psoriatic arthritis, about 0.2 percent.² One and half million people seek physician care for this disease annually. The total annual costs of psoriasis have been estimated at \$1.6 billion to \$3.2 billion. The average cost per patient is \$1,400 to \$6,600. About 50 percent of the annual cost is medication.³ Patients with moderate to severe disease have 2.5 times the annual cost of those with mild disease. The higher cost for the patients with severe psoriasis is related to co-morbid factors and the toxicity of treatment.

People who have severe psoriasis are more likely to smoke, be obese, have cardiovascular issues, have metabolic syndrome, and have a heart attack. All of these factors have been recently identified. The same way that systemic inflammation in rheumatoid arthritis leads to cardiovascular morbidity occurs in psoriasis. This is a systemic disease, which has to be taken into account in people with severe disease.

Patients perceive their disease differently from physicians. In one study, physicians assessed approximately 22 percent of patients as having marked or severe psoriasis.⁴ This assessment was based on the percentage of patients who had a baseline score of

Exhibit 1: (pix of psoriasis)



4 (“marked”) or 5 (“severe”) on the Physician’s Static Global Assessment of Psoriasis. Scores were recorded on a scale of 0 to 5, with 0 indicating no evidence of disease and 5 indicating severe induration, erythema, and scaling.

The perception of disease severity was different for patients, with approximately 75 percent assessing themselves as having marked or severe psoriasis on the Patient’s Global Assessment of Psoriasis.⁴

Degree of disease is somewhat difficult to define. There are no uniform, universally agreed upon guidelines. Many want to use affected percentage of body surface area. The problem is a patient with psoriasis of the feet may only have two percent of the body surface area affected but is unable to walk and is disabled from psoriasis. Medication studies use Psoriasis Area and Severity Index (PASI) scores, but physicians in the community do not. Most managed-care companies use body surface area to define severity. Another divider that marks moderate to severe disease versus mild is the ability of topical therapy to manage the disease versus the need for systemic therapy. For example, a person who had significant involvement of their hands and feet, but a small body surface area, needs systemic therapy. Unfortunately, many patients with moderate or severe disease are not treated systemically.

For patients who need systemic therapy, the toolbox contains many more agents than in the past (Exhibit 3). Phototherapy is an effective treatment for many patients. Narrow band, ultraviolet B light (NB-UVB) is now the gold standard for therapy. Phototherapy requires proper equipment and visits two to three times per week. An example of before and after phototherapy is shown in Exhibit 4. Because of low reimbursements, many physicians have stopped using phototherapy. Phototherapy units are not available in many areas of the United States.

Exhibit 2: Disability Associated with Psoriasis vs Other Major Medical Diseases (N=317)

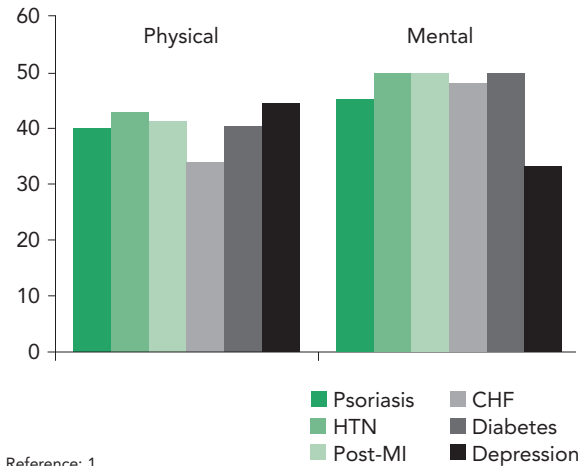
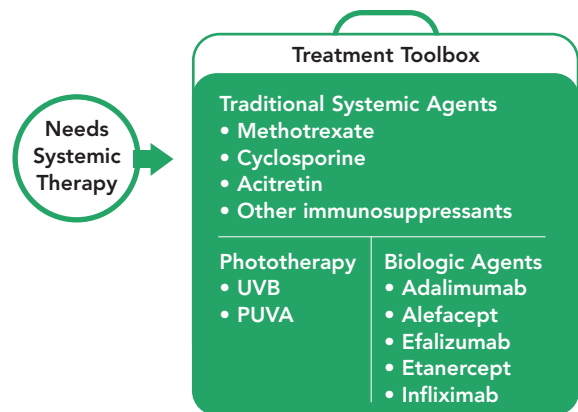


Exhibit 3: Psoriasis Therapy



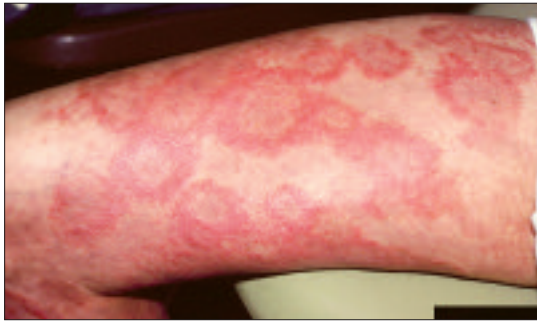
Additionally, the managed care requirement of a co-pay for each treatment makes phototherapy excessively costly for many patients.

Oral systemic therapies include methotrexate, cyclosporine, and acitretin. Methotrexate is used as a once per week therapy. It has not been studied to the same standards as biologic therapy. Methotrexate does have some significant acute and chronic side effects, especially liver toxicity.

Cyclosporine (Neoral[®]) is a very effective therapy that is a quick fix. Given as daily dosing, it works very rapidly for most patients. The problem is in the FDA labeling; its use is restricted to one year of therapy. In many cases, cyclosporine is used as a bridge between agents when patients have a significant flare. Cyclosporine does cause significant adverse effects including kidney toxicity.

Acitretin (Soriatane[®]) is a retinoid derived from

Exhibit 4: Before and After Phototherapy



Before



After

Vitamin A. It is not a cytotoxic or immunosuppressive agent. It is not very helpful as monotherapy but is very effective when combined with phototherapy. This agent is an excellent maintenance medication with typical retinoid dose related side effects. One of the problems is that acitretin cannot be used in a woman of childbearing potential because of teratogenicity.

Advances in understanding the immunological basis of psoriasis have resulted in a shift in therapeutic focus toward agents that interfere with the psoriatic disease process at the cellular level. These new biologic agents have the ability to interrupt the disease pathway through the modulation of T-cell response and cytokine levels and may, therefore, slow or halt disease progression. There is evidence that early intervention with the tumor necrosis factor (TNF) blocking agents may prevent disability from psoriatic arthritis. The trouble is identifying which patients will develop arthritis.

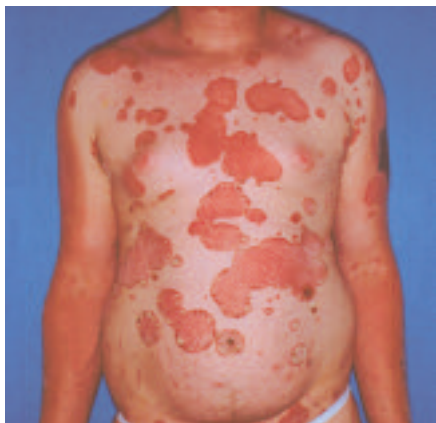
Biologic agents are shifting the treatment paradigm in psoriasis, offering long-term safety and efficacy to a patient population that has long been underserved. Biologics may become the treatment of choice, especially for patients for whom current therapies are no longer effective or cause unacceptable side effects.

There are five biologics for treatment of psoriasis. Three are TNF blocking agents—adalimumab (Humira®), etanercept (Enbrel®), and infliximab (Remicade®). Alefacept (Amevive®) and efalizumab (Raptiva®) affect T-cells. Infliximab and alefacept are intravenous agents administered in doctor's offices and typically covered by managed care as a medical benefit. The others are given a subcutaneous injection and are typically covered as a pharmacy benefit. The choice of biologic medication many times depends on the patient's insurance coverage.

Etanercept is self-injected one or two times a week. It is FDA approved for psoriasis, psoriatic

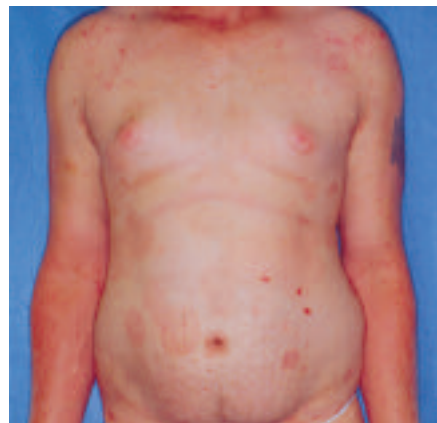
Exhibit 5: Infliximab (Remicade) Therapy

Week 0



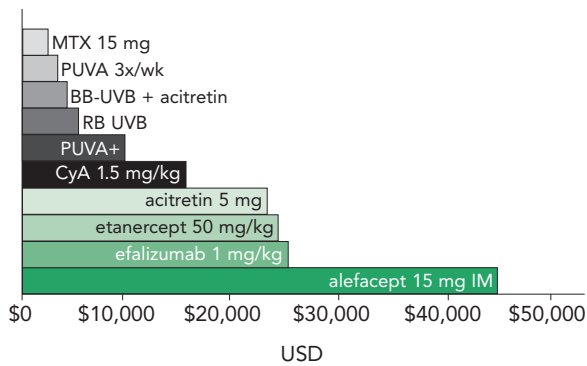
PASI 42

Week 10



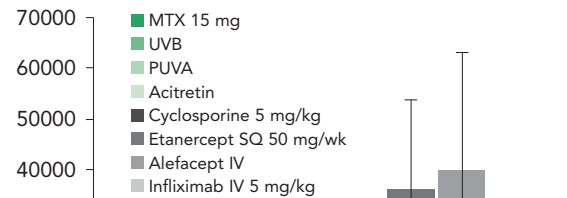
PASI 1.8

Exhibit 6: Annualized Costs to Achieve 75% PASI Improvement (USD)



Reference: 5, 6

Exhibit 7: Annual Cost Per Success



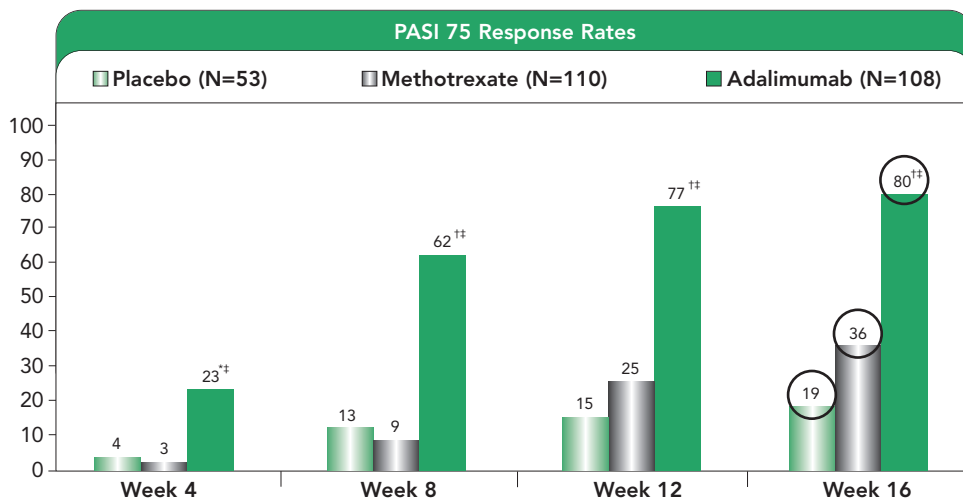
Reference: 5, 6

arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, and ankylosing spondylitis. In psoriasis, it can be given as a double dose the first 12 weeks of therapy. Adalimumab is self-injected every other week and is approved for psoriatic arthritis and rheumatoid arthritis. The company has submitted an application to the FDA for psoriasis approval. Efalizumab also is self-injected once a week and is approved for psoriasis. It does not have a beneficial effect in psoriatic arthritis and many patients with severe psoriasis have psoriatic arthritis. Another issue with this agent is that it is important not to stop abruptly because patients can flare quickly.

Infliximab is given as an intermittent intravenous infusion. After an induction period, patients usually receive infusions every six to eight weeks. It is approved

for psoriasis, psoriatic arthritis, rheumatoid arthritis, Crohn's disease, and ankylosing spondylitis. Of all the biologic agents, it is probably the most effective for the skin lesions, but even in dermatology a lot of physicians do not use it because of the intravenous infusion issue. Exhibit 5 shows a before and after with infliximab as an example of the efficacy of the biologic agents. Alefacept is given as weekly IM injections in the physician's office over the course of 12 weeks. This agent, which is only approved for psoriasis, results in a significant remission in about 17 percent of patients. In patients who have a response, it can last seven or more months after the end of the injection cycle. There is a slow response to this agent, so the 12 doses are completed before any response is

Exhibit 8: Adalimumab 40 mg Qeow vs. MTX vs. Placebo: PASI-75 Over Time



*p=0.001, †p<0.001, both †p<0.001 vs. MTX
Intention-to-treat (ITT), patients with missing PASI scores were considered non-responders.

Reference: 7

seen. Because of this and the low response rate, dermatologists do not frequently use alefacept.

In the treatment of psoriasis, there are issues with therapy access. Most managed-care programs require prior authorization for biologics but the requirements differ greatly from plan to plan.

In some areas, there is no prior authorization allowing dermatologists to write for a biologic, yet the patient has had no other prior treatment. Some plans have onerous policies to approve biologic use. One example is that patients had to fail two phototherapy treatments or two systemic agents and phototherapy, and have 30 percent body surface areas affected before a biologic would be approved.

Under the United Kingdom's biologic guidelines, patients may receive a biologic if they have a PASI score greater than 10, an affected body surface area greater than 10 percent, or a disease quality life index (DLQI) score greater than 10 and fulfill certain clinical criteria. These include failure of conventional therapy, side effects with conventional therapy, unstable disease, other significant co-morbidities, or psoriatic arthritis. Although some managed care plans have similar criteria, there is much variability in prior authorization policies for biologics among plans in the United States.

Biologic agents cost \$20,000 to \$25,000 annually for usual doses. At least two cost comparisons have been published looking at total costs of caring for patients with psoriasis versus the clinical outcome.⁵⁻⁶ These publications tried to determine the cost of a clinically meaningful improvement. Exhibits 5 and 6 show the annualized costs to achieve a 75 percent PASI response. Although the cost estimates used in these studies are relatively accurate, the efficacy rates are based on non-comparable studies but it is the best available information. There are few head-to-head comparisons with any of the treatments and response rates are based on short-term studies. The authors of one of these publications concluded, when considering cost-effectiveness in addition to safety and efficacy, ultraviolet Type B phototherapy appears to be the best first-line agent for the control of moderate-to-severe psoriasis, despite a small potential for cumulative toxicity.⁵ Additionally, they concluded that the biologics should be considered as second-line agents alongside the traditional systemic treatments when phototherapy proves to be ineffective or is otherwise contraindicated, such as in patients with psoriatic arthritis.⁵

One small head-to-head study done in Europe compared placebo, methotrexate, and adalimumab.⁷ This is the first placebo-controlled trial of methotrexate in psoriasis using current methods of evaluation. As shown in Exhibit 8, the authors

concluded that adalimumab demonstrated significantly superior efficacy and more rapid improvements in psoriasis compared with either methotrexate or placebo.

The next-generation biologics for psoriasis are interleukin 2 and interleukin 3 antibodies. It is very likely that these medications will be approved for use every three months. Based on small studies presented at international meetings, these agents appear quite effective.

To maximize access while controlling costs, managed-care plans should eliminate phototherapy co-payments. Additionally, they should place no restrictions or prior authorizations for conventional systemic therapy (methotrexate, cyclosporine, acitretin, or oxsoresalen ultra). Biologics can be managed with a prior authorization policy. A reasonable restriction on biologic use is that patients should have one prior systemic therapy failure before trying a biologic.

Conclusion

Psoriasis can be a devastating disease. At this time, response to treatment cannot be predicted nor are there guidelines for treatment. According to the available data, the biologic treatments are more effective and probably safer in the long term than conventional systemic agents. Because of their cost, use can be limited to those patients who have failed at least one systemic agent. **JMCM**

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