A new or relatively new class of medications always poses both challenges and opportunities. So it is with biologics for psoriasis. Biologics generally provide an efficacy that roughly mirrors that of the immunosuppressive drugs methotrexate and cyclosporine, yet they appear to be considerably safer than the older drugs. Patients can receive biologics without worrying about the potential serious toxicities associated with older systemic therapies.

The combined safety and efficacy of biologics continue to make a big difference in the way dermatologists approach psoriasis treatment, as an increasing number of physicians adopt biologics into their practices. These medications are expensive, but for those individuals with severe psoriasis wishing for a safe and effective treatment, the biologics may well be worth the cost. The long-term effects of some of these agents are being actively studied. While etanercept has about 12 years of data, some of the agents are considerably newer.
Although the biologics share much in common, the agents are not necessarily interchangeable. With several injectables already approved for psoriasis and more on the horizon, many dermatologists wonder when and how to choose one agent over another to treat a particular patient. To aid therapy selection, it’s worth reviewing some of the criteria by which dermatologists might select a medication best suited for the case at hand.

**Safety and Efficacy**
When considering the safety of biologics, it’s important to realize that some psoriasis patients are simply poor candidates for these potent agents. These generally include, among others, individuals with serious co-morbidities such as congestive heart failure, multiple sclerosis, diabetes mellitus, recent active cancer treatment, or active systemic infection.

In these patients, for example, you would not want to use an anti-tumor necrosis factor (TNF)-α agent such as etanercept (Enbrel, Amgen/Wyeth) or infliximab (Remicade, Centocor). (The latter is widely used but not yet approved for psoriasis.) “Those in my mind would be contraindicated,” says Abby S. Van Voorhees, MD, Assistant Professor at the University of Pennsylvania School of Medicine, and Director of the Psoriasis and Phototherapy Treatment Center in Philadelphia. “In those patients I might choose one of the other biologics. Sometimes patients are shunted toward or away from drugs because of other concurrent diseases they may have.”

Coming down the pipeline and still awaiting FDA approval for psoriasis is adalimumab (Humira, Abbott),...
which is likewise a TNF-α blocking agent and therefore is not advisable for use in patients with congestive heart failure, multiple sclerosis, or diabetes mellitus. Otherwise, biologic medications are generally well-tolerated, without the toxicity risks associated with commonly-used immunosuppressive agents, such as methotrexate (which is potentially hepatotoxic) and cyclosporine (which is potentially nephrotoxic). These agents have been used safely by dermatologists, but there are reported cases of major toxicity with each of them.

“I look at it from the perspective of safety first,” says Jerry Bagel, MD, Director of the Psoriasis Treatment Center of Central New Jersey in East Windsor, NJ. “I still believe Amevive (alefacept, Biogen-Idec) is the safest. I think then Enbrel and Raptiva (efalizumab, Genentech/Xoma) are a little less safe. Amevive for some people is a reasonably good initial choice.” Dr. Bagel tempers his enthusiasm for alefacept by noting that only about 35 percent of patients do well after 12 weeks of alefacept alone. Coupling it with narrow-band UVB phototherapy, however, his success rate with alefacept climbs to 65 percent. Other physicians effectively utilize phototherapy either alone—which may on its own be sufficiently efficacious—or in tandem with medical therapy.

One drawback of alefacept is that its efficacy doesn’t manifest until after eight to 12 weeks, its peak efficacy coming at the 12-week mark, says Mark Lebwohl, MD, professor and chairman of the Department of Dermatology at Mt. Sinai School of Medicine in New York and Chairman of the Medical Board of the Psoriasis Foundation. Another drawback is that alefacept lowers the CD-4 count, which means you must monitor the patient’s blood count weekly. Even so, patients for whom the medication is effective are generally happy with its use.

Concomitant Disease
Concomitant arthritis is not uncommon with psoriasis. “It boils down to, if people have psoriatic arthritis, I might jump to Enbrel,” Dr. Bagel says. Etanercept currently is the only biologic agent approved to treat both psoriasis and psoriatic arthritis (PSA). “And obviously I would not use Raptiva for psoriatic arthritis. On the other hand, I tell people there are certain risk factors. There may be certain issues with Enbrel, such as increased risk of infection, slight increase in the frequency of multiple sclerosis.” Trials of efalizumab in PSA failed to demonstrate statistical superiority over placebo.

Since etanercept requires two injections a week, some patients prefer the once-weekly efalizumab. Efalizumab is preferable to alefacept in those with a history of congestive heart failure. Those with severe diabetes mellitus are better off receiving efalizumab rather than etanercept, Dr. Bagel says.

Ten percent of patients with psoriasis have erosive arthritis, while one-third of patients complain of joint pain, says Joseph L. Jorizzo, MD, Professor and Former and Founding Chairman of the Department of Dermatology at the Wake Forest University School of Medicine. About half of those with joint pain will develop arthritic erosions within 10 years. “If they have arthritis, you have FDA approval for psoriatic arthritis with etanercept,” Dr. Jorizzo says. Etanercept prevents progression of the disabling erosions, while methotrexate and other drugs do not, he notes.

Other clinical scenarios may require a cautious approach to biologics. A psoriasis patient who has had a thick melanoma removed this year, for example, should not receive any treatment that affects the immune system—including methotrexate, cyclosporine, and the biologics. For that patient, Dr. Jorizzo would likely use the retinoid acitretin (Soriatane, Connetics).

Consider other scenarios. If a patient had cancer five years ago, for example, Dr. Jorizzo would first obtain the assent of the
patient’s oncologist before prescribing etanercept. A patient with multiple sclerosis, however, would not be a good candidate for etanercept. Even though it was originally used to treat that disease, the package insert advises against its use in that setting. A patient with a history of a seizure disorder or headache, however, could receive the drug. Dr. Jorizzo always notifies the neurologist in that setting. Those with a history of congestive heart failure should check with their cardiologists before starting etanercept, but such patients can use TNF-α drugs Dr. Jorizzo likes to notify the cardiologist in these instances.

The primary advantage of biologics lies in efficacy and safety. “The biologics are safer than some of the traditional drugs we have used because they are not metabolized in the kidney or the liver,” Dr. Jorizzo says. Biologics do not have FDA package inserts with the same level of warnings as do drugs used to treat cancer, such as methotrexate, or drugs used in transplant patients, such as cyclosporine or mycophenolate. The latter are highly effective medications, but biologics have not been linked with the kinds of liver, kidney, or bone marrow side effects that are seen with these more potent agents. Long-term, no one knows the side effects of protracted use of biologics, some of which have been available only for two to three years. Etanercept and infliximab have now been studied for more than 10 years.

**The Switch**

When should you consider switching the patient from one biologic agent to another? It depends on the drug. “For the most part, I think a reasonable time is between 12 and 24 weeks,” Dr. Van Voorhees says. “If a drug is not showing signs that it’s working in that timeline, then that’s when, in my hands, patients get switched.” We have yet to accumulate a body of literature on the safety and efficacy of combining one biologic with another. At any rate, given the expense of biologics, dermatologists would prefer to keep the patient on monotherapy if possible.

Dr. Jorizzo gauges a treatment’s efficacy as defined by the FDA standard. This measure is represented by the so-called PASI score, which takes into account surface area affected and the thickness of the lesions, scaliness, and redness. According to the FDA primary efficacy endpoint, psoriasis patients must be clear or almost clear after 12 weeks of treatment; this correlates with a PASI score of 75. When etanercept is used according to the FDA-approved regimen—a loading dose of 50mg twice weekly then tapered to 50mg per week at 12 weeks—49 percent of patients achieve a PASI score of 75 at 12 weeks. At six months, the score rises to 55 percent. “It is nice to know that you can load and then come down to a lower dose (and still achieve greater efficacy),” Dr. Jorizzo says.

The other two drugs approved for psoriasis—alefacept and

**Mechanisms of Action**

All biologics are similar in that they all promote better regulation of the immune system. Otherwise their mechanisms of action differ significantly. “Some of these drugs are working directly on the T-cells, trying to turn them off,” Dr. Van Voorhees says. “Some of the drugs prevent those activated T-cells from coming back from the lymph nodes where they get activated.” It’s a matter of preventing migration of activated T-cells—which secrete TNF-α—from the lymph nodes back to the skin.

Infliximab and adalimumab block the cytokine TNF-α. The other two—alefacept and efalizumab—block T-cell activation and the movement of T-cells and their activation,” Dr. Lebwohl says. “Afacept blocks T-cell activation, and [rids the site] of a selected group of T-cells that may have a lot to do with psoriasis.”

“I think of [anti-TNF-α agents] as sort of the mop-up drugs,” Dr. Van Voorhees says. “These are drugs where you’re not preventing the activation of T-cells, you’re not preventing them from getting back into the skin, you’re just preventing that activated product from causing the downhill cascade. [Biologics] all work on the immune system, but at different places.”
efalizumab—fall short of etanercept’s FDA-based efficacy standard (alefacept achieves a 75 PASI in 23 percent of patients at 12 weeks, and efalizumab in 22-27 percent of patients.) “I have not been really anxious to use those two drugs based on their low efficacy,” Dr. Jorizzo says.

**Routes of Administration**

The route of administration is a key clinical concern. Alefacept is administered intramuscularly, while efalizumab and etanercept are given subcutaneously. Adalimumab is also administered subcutaneously, while infliximab involves an IV infusion.

Most patients are willing to learn how to do a subcutaneous injection, often finding it less daunting than they had anticipated, Dr. Van Voorhees says. On the other hand, there are some patients who simply don’t want to learn the skill, perhaps feeling more comfortable with alefacept administered by a nurse in the physician’s office. Others have vision problems and have concerns about being able to mix the compound or reading the units on a syringe. Others lack dexterity of the hands. For some people, an IV infusion may be the best drug-delivery avenue. The patient’s lifestyle and personality may direct you to one mode of administration over another.

Infliximab, generally regarded as the most effective biologic agent, is also the most burdensome and time-consuming to administer, requiring a slow three-hour infusion. Doctors without an infusion center may not likely prescribe infliximab, or they may refer out for it. Infusion reaction is one of the drug’s side effects. “It’s the drug that I use first for patients with really awful psoriasis, because it works when everything else fails,” says Dr. Lebwohl.

Efalizumab is administered once a week. Only a small proportion of patients will respond early on, but as they stay on the
drug longer, larger numbers of patients will find it beneficial. “The main problem is that if you stop it, it can be a very bad rebound,” Dr. Lebwohl says. “Patients have to be very, very wary. If they stop it, they need to transition onto another treatment so they don’t rebound.”

**Cost of Treatment**

No doubt cost is a key consideration for many patients. Biologics are expensive medications. “Insurance dictates to a large degree which agents we’ll use,” Dr. Lebwohl says. “If a patient doesn’t have a prescription plan, they will probably get one of the agents that is most easily administered in the office—alefacept or infliximab—because that’s paid for with their regular insurance.” Unfortunately, alefacept only works well 40 percent of the time, at most. Patients saddled with a high co-pay are likely to feel ill-served if the drug confers little benefit. “That’s why a lot of dermatologists don’t use [alefacept] as often as they otherwise might,” Dr. Lebwohl says.

The cost of biologics, along with unknown long-term consequences, are keeping some physicians from prescribing these agents. Nonetheless, their popularity is growing. “Etanercept is being used by more and more dermatologists,” Dr. Lebwohl says. “I think at last count it was (approximately) 2,000 dermatologists. So it really has caught on.”

**Weighing the Options**

A broad range of considerations come into play when deciding whether to start a psoriasis patient on a biologic agent, and if so, which one. As we accumulate more clinical data on their safety and efficacy, dermatologists will likely prescribe these agents with greater confidence. Even so, the literature to date suggests that biologics have earned a prominent place among the treatment options for patients with severe psoriasis. 

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**Biologic Therapy for Psoriasis**

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