

The Role of Biologic Therapies in Dermatology



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KEYWORDS

- Biologics • Dermatology • Etanercept • Adalimumab • Infliximab • Ustekinumab
- Secukinumab • IVIG

KEY POINTS

- Biologic therapies are molecules that target specific proteins implicated in immune-mediated disease and are frequently encountered in dermatology.
- Common biologic therapies encountered include tumor necrosis factor alpha inhibitors, interleukin (IL)-12/IL-23 inhibition, IL-17 inhibitors, rituximab, and intravenous immunoglobulin.
- Psoriasis is the most common indication for which biologics are used currently but several other dermatologic diseases seem to be responsive to biologic therapy.
- Understanding the mechanisms of action, labeled and off-label uses in dermatology, common adverse effects, and cost limitations helps to inform clinical decision making and improve patient outcomes.

INTRODUCTION

Advances in the understanding of disease pathophysiology for inflammatory skin diseases and in drug development have ushered in biologic therapies in dermatology. Biologic therapies are molecules that target specific proteins implicated in immune-mediated disease. In dermatology, the approved and emerging biologic therapies work extracellularly to alter T-cell activation and differentiation, block cytokines, or eliminate pathogenic B cells.¹ Biologic agents can be divided into 3 main groups: monoclonal antibodies, fusion proteins, and cytokines.² Depending on their mechanism of action, biologic medications have been used for different dermatologic indications. Notably, psoriasis is the skin disease for which biologics have been used most extensively.³ However, biologics have also been used in, or are in development for, other inflammatory skin diseases. This article discusses the following biologic agents

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used in dermatology with regard to their mechanism of action, clinical use, and adverse effects: tumor necrosis factor (TNF) alpha inhibitors, interleukin (IL)-12/IL-23 inhibition, IL-17 inhibitors, rituximab, and intravenous immunoglobulin (IVIG).

TUMOR NECROSIS FACTOR INHIBITORS

TNF plays a key role in chronic inflammatory diseases such as psoriasis and psoriatic arthritis. Biologic agents that inhibit TNF include a fusion protein, etanercept, and monoclonal antibodies such as infliximab and adalimumab.⁴

Differences exist in the mechanisms of action of various TNF inhibitors. Etanercept is a fully human fusion protein that is composed of a dimeric soluble p75 TNF receptor and a human immunoglobulin (Ig) G Fc fragment.² Infliximab is a chimeric IgG1- κ monoclonal antibody with human constant and murine variable regions that bind specifically to TNF- α .² Adalimumab is a fully human monoclonal IgG1 antibody that targets TNF- α .²

Etanercept, infliximab, and adalimumab are currently US Food and Drug Administration (FDA) approved in dermatology for plaque psoriasis and psoriatic arthritis.^{2,5} The FDA-approved dose of etanercept for psoriasis is 50 mg twice weekly for 3 months, followed by 50 mg weekly for an unspecified amount of time.^{5,6} Infliximab is an infusion dosed at 5 mg/kg at weeks 0, 2, and 6, then every 8 weeks.⁶ The FDA-approved dose for adalimumab is an initial dose of 80 mg at week 0 that is followed by 40 mg every other week starting at week 1.⁶

The TNF inhibitors are used off label for several dermatologic conditions. Etanercept, infliximab, and adalimumab have been used for neutrophilic dermatoses (eg, aphthous stomatitis, Behçet disease, pyoderma gangrenosum), bullous dermatoses (eg, bullous pemphigoid, pemphigus vulgaris, cicatricial pemphigoid), granulomatous dermatoses (eg, generalized granuloma annulare, sarcoidosis), autoimmune connective tissue diseases (eg, dermatomyositis, scleroderma), and other disease (eg, graft-versus-host disease [GVHD], hidradenitis suppurativa, and pityriasis rubra pilaris).⁵

In general, when starting a patient on a TNF inhibitor, the following tests are ordered in our clinic: initial tuberculosis screening with a Purified protein derivative (PPD) or Quantiferon Gold test (but not both), complete blood count (rare cases of anemia and pancytopenia have been reported), comprehensive metabolic panel (liver function test abnormalities have been reported), hepatitis B surface antigen, hepatitis C virus (HCV) antibody, and possibly a human immunodeficiency virus (HIV) test. These tests are summarized in [Table 1](#).

Absolute contraindications for the TNF inhibitors include a known hypersensitivity to the medication, concurrent use of anakinra (IL-1 receptor antagonist), and various infections.⁵ These infections are described by the American College of Rheumatology as active bacterial infections or bacterial infections requiring antibiotic therapy, active tuberculosis or untreated latent tuberculosis, active herpes zoster infection, active life-threatening fungal infections, severe bacterial or viral upper respiratory tract infections, nonhealed infected skin ulcers, acute infection with hepatitis B virus (HBV) or HCV, untreated chronic HBV infection, or chronic HBV or HCV infection with significant liver injury (defined as Child-Pugh classes B or C).⁷ In addition, infliximab should be avoided in patients who have a known hypersensitivity to murine proteins because it is a chimeric antibody.⁵ Infliximab is also unique in that it is dosed intravenously, which can be inconvenient for patients.⁴ A relative contraindication common to TNF inhibitors includes a family history of demyelinating disease. Infliximab is also relatively contraindicated in patients with high-grade congestive heart failure.⁵

Table 1 Biologics used in dermatology for FDA-approved indications			
Biologic	FDA-approved Dermatologic Indication	Dosage	Monitoring Requirement
Etanercept	Plaque psoriasis Psoriatic arthritis	50 mg SC injection twice weekly for 3 mo; 50 mg weekly SC injection thereafter	Baseline tests: <ul style="list-style-type: none"> • CBC (repeat at 2–3 mo then every 6–12 mo) • CMP (repeat at 2–3 mo then every 6–12 mo) • PPD or Quantiferon gold (repeat yearly) • Hepatitis B surface antigen and core IgM antibody (repeat yearly) • HCV antibody • ±HIV and ANA
Infliximab	Plaque psoriasis Psoriatic arthritis	3–5 mg/kg per infusion at weeks 0, 2, and 6, then every 8 wk	Same as etanercept
Adalimumab	Plaque psoriasis Psoriatic arthritis	80 mg SC injection day 0, 40 mg SC injection day 7, then 40 mg SC injection every 14 d	Same as etanercept
Ustekinumab	Moderate to severe plaque psoriasis	45 mg (≤ 100 kg) or 90 mg (>100 kg) by SC injection at weeks 0 and 4, then every 12 wk thereafter	Same as etanercept
Secukinumab	Moderate to severe plaque psoriasis	150 mg or 300 mg SC injection weekly for 5 consecutive weeks followed by SC injection once every 4 wk	Same as etanercept
Rituximab	Granulomatosis with polyangiitis Microscopic polyangiitis	<ul style="list-style-type: none"> • Rheumatoid arthritis dosing: 1000 mg every 2 wk \times 2 doses • Lymphoma dosing: 375 mg/m² per week \times 4 doses⁵ 	<ul style="list-style-type: none"> • CBC every 2 wk during treatment and every 1–3 mo thereafter⁵ • Initial HBsAg and anti-HBc
IVIg ⁵	GVHD Kawasaki disease	2 g/kg/cycle, divided into 3–5 equal doses, given over 3–5 consecutive days	<ul style="list-style-type: none"> • CBC • CMP • Immunoglobulin levels (in particular to exclude IgA deficiency) • Screen for rheumatoid factor and cryoglobulins because these patients are at increased risk for renal failure • Consider screening for hepatitis B and C as well as HIV

Abbreviations: ANA, antinuclear antibody; CBC, complete blood count; CMP, comprehensive metabolic panel; HBc, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; SC, subcutaneous.

Several special issues deserve extra mention. The first includes a history of malignancy. Limited studies have failed to provide evidence for increased risk of recurrent or new cancer in patients treated with a TNF inhibitor who have a history of a prior malignancy. The paucity of data stems from exclusion of these patients from clinical trials. However, data from the British Society for Rheumatology Biologics Registry identified 177 patients treated with anti-TNF for rheumatoid arthritis (RA) with a prior malignancy and compared them with 117 patients with RA with prior malignancy being treated with traditional disease-modifying antirheumatic drugs (DMARDs). The rates of incident malignancy were 25.3 events/1000 person-years in the anti-TNF cohort compared with 38.3/1000 person-years in the DMARD cohort. Even with these data, the investigators recommended that these results should not be interpreted as indicating that it is safe to treat all patients with RA with prior malignancy with anti-TNF therapy.⁸

Screening for latent tuberculosis infection is another special issue and should be performed before the initiation of TNF-inhibitor therapy. Patients who have evidence of latent tuberculosis should initiate treatment of latent tuberculosis before starting a TNF inhibitor. Isoniazid for 9 months is the typical treatment. Although the duration of latent tuberculosis infection therapy before starting a TNF inhibitor has not been well established, most authorities suggest that patients receive at least 1 month of treatment before starting TNF-inhibitor therapy.⁹

HCV infection is also an issue commonly seen when starting a TNF inhibitor. Although HCV antibody is a commonly drawn laboratory test before the therapy, few data exist relating to the use of TNF inhibitors in patients infected with HCV. For example, one study examined 9 patients with RA infected with HCV who were treated with etanercept. At 3 months, no patient had evidence of increased hepatic inflammation. In addition, no significant viral load increases were observed in those with detectable HCV RNA. In addition, no reactivation was observed in those with undetectable HCV RNA.¹⁰

HIV is another issue commonly encountered with TNF inhibitors, especially considering that it is a risk factor for psoriasis. In general, anecdotal data suggest that TNF inhibition can be tolerated well by patients infected with HIV, provided that the patient is on an effective antiretroviral regimen before starting a TNF inhibitor.¹¹

Several adverse effects are noted with the TNF inhibitors. Collectively, postmarketing case reports of the TNF inhibitors have reported rare adverse effects of nonmelanoma skin cancer, infections (specifically tuberculosis reactivation, invasive fungal infections, and hepatitis B reactivation), neurologic disease, congestive heart failure, autoimmune conditions, and hematologic toxicity (eg, leukopenia, neutropenia, thrombocytopenia, and pancytopenia).⁵ The most common side effects associated with etanercept and adalimumab are injection site reactions. For patients receiving infliximab, infusion reaction needs to be monitored. Theoretically with all TNF inhibitors there is also an increased risk of developing neutralizing antidrug antibodies, but this risk seems to be highest with infliximab because it is a chimeric antibody.⁵

The risk of developing hematologic malignancies is a commonly discussed topic with the use of biologics. A black box warning for lymphoma and other malignancies accompanies the TNF inhibitors. TNF inhibitors have been used commercially for nearly 20 years. For example, etanercept was released for commercial use in late 1998. Since that time, numerous conflicting studies have discussed the risk of lymphoma associated their use. However, because TNF-inhibitor therapies are often reserved for patients with the most severe disease, there is likely to be a higher intrinsic risk of lymphoma in patients who require treatment with TNF inhibitors. Numerous large studies have found no increased risk of lymphoma in patients treated with TNF inhibitors compared with similar disease-equivalent cohorts.¹²⁻¹⁴

Although monotherapy with biologic agents is effective for many patients with psoriasis, some patients require combination therapy. Many trials have evaluated the efficacy and safety of combination therapies in moderate to severe psoriasis.¹⁵ For example, etanercept or adalimumab with phototherapy may result in a greater reduction of disease severity than either alone. Etanercept and methotrexate in combination are more effective than monotherapy with either medication. Acitretin has been used to decrease the dosing of etanercept while maintaining similar levels of efficacy. Short-term cyclosporine has also been combined with etanercept or adalimumab to control psoriasis flares.¹⁵

INTERLEUKIN-12/INTERLEUKIN-23 INHIBITION

Ustekinumab is a fully human monoclonal antibody that binds the p40 subunit of IL-12 and IL-23.⁴ IL-12 and IL-23 are implicated in the pathogenicity of psoriasis and other autoimmune inflammatory conditions. These key cytokines are secreted by antigen-presenting cells and are important mediators of the differentiation of naive T cells into T-helper (Th) 1 and Th17 cells. Th17 cells produce distinct cytokines that have essential functions in host defense, inflammation, and keratinocyte proliferation.⁵

Ustekinumab is approved for the treatment of moderate to severe psoriasis and psoriatic arthritis. It is administered based on weight at 45 mg (≤ 100 kg) or 90 mg (>100 kg) by subcutaneous (SC) injection at weeks 0 and 4, then every 12 weeks thereafter.⁶ The same screening tests that were mentioned previously for initiation of TNF inhibitors are typically ordered for patients who are to start ustekinumab.

The safety and tolerability of ustekinumab have been studied extensively in clinical trials, and postmarketing studies are underway to further determine the long-term safety profile of the medication.⁵ The most common adverse effects associated with ustekinumab are injection site reaction, headache, nasopharyngitis, and upper respiratory tract infections.¹⁶ Ustekinumab has not been shown to increase the risk for serious infections, internal malignancy, or adverse cardiovascular events. A meta-analysis of the safety profile of ustekinumab showed no significant difference in serious infections or internal malignancies compared with placebo.¹⁷ Recently, a multicenter, longitudinal, disease-based registry (Psoriasis Longitudinal Assessment and Registry [PSOLAR]) at dermatology centers examined 9154 patients treated with biologic agents and indicated that adalimumab and infliximab carry a higher risk of serious infection compared with nonbiologic therapies, whereas etanercept and ustekinumab do not.¹⁸ In addition, at 5-years, there are no significant differences in rates of major adverse cardiovascular events between patients on ustekinumab and those in the general population.

When examining the efficacy of ustekinumab with a TNF inhibitor, a randomized controlled trial of 903 patients with moderate to severe psoriasis compared either 45 or 90 mg of ustekinumab (at weeks 0 and 4) with high-dose etanercept (50 mg twice weekly for 12 weeks) and found that the efficacy of ustekinumab was superior to etanercept over a 12-week period.¹⁹ The primary end point was the proportion of patients with at least 75% improvement in the Psoriasis Area and Severity Index (PASI) at week 12. The efficacy and safety of a crossover from etanercept to ustekinumab were evaluated after week 12. There was at least 75% improvement in the PASI at week 12 in 67.5% of patients who received 45 mg of ustekinumab and 73.8% of patients who received 90 mg, compared with 56.8% of those who received etanercept ($P = .01$ and $P < .001$, respectively). Similarly, 65.1% of patients who received 45 mg of ustekinumab and 70.6% of patients who received 90 mg of ustekinumab had cleared or

minimal disease according to the physician's global assessment, compared with 49.0% of patients who received etanercept ($P < .001$ for both comparisons). Among patients who did not have a response to etanercept, 48.9% had at least 75% improvement in the PASI within 12 weeks after crossover to ustekinumab.

INTERLEUKIN-17 INHIBITORS

The Th17 pathway is central to the pathogenesis of psoriasis, and the IL-17 molecule is key to the Th17 pathway. IL-17 consists of a class of cytokines that are important in activating the innate immune response and is considered the main driver against extracellular bacteria. Six cytokines belong to the IL-17 family, classified as IL-17A to IL-17F, with IL-17A and IL-17F possessing the greatest amino acid sequence similarity (55%) and similar biological properties. Because of their pleiotropic activity on various tissue cells and innate immune cells, IL-17A is considered crucial in tissue inflammation. Increasing evidence suggests that IL-17A plays a key role in a large number of immune-mediated disorders, including psoriasis and psoriatic arthritis.³

At present, there are 3 biologic agents used to target IL-17A: secukinumab, brodalumab, and ixekizumab.³ Secukinumab is a human IgG1(kappa) that neutralizes IL-17A. In January 2015, the FDA approved secukinumab to treat moderate to severe plaque psoriasis in adults who do not respond well to medication applied directly to the skin.^{17,20} Secukinumab is given as an injection once a week for 5 consecutive weeks followed by an injection once every 4 weeks. It is approved at both 150-mg and 300-mg dosages.¹⁷

Ixekizumab is a humanized IgG4 monoclonal antibody (mAb) neutralizing IL-17A, a mechanism of action that is similar to secukinumab. Brodalumab is a human mAb blocking IL-17RA, the receptor subunit that is shared by IL-17A and IL-17F. Brodalumab and ixekizumab are currently being tested for the treatment of moderate to severe psoriasis in phase III clinical trials as of April 2015.^{21,22}

At this time, initial laboratory work-up before initiating treatment with IL-17 inhibitors is similar to that for TNF inhibitors, and it is summarized in **Table 2**. The physiologic impact of long-term IL-17 antagonism needs to be shown in larger and longer clinical trials. There is a need for a better understanding of how IL-17 antagonism affects psoriatic arthritis. In addition, clinical implications of targeting the IL-17 versus IL-17 receptor needs to be better characterized.³

To date, the safety profile for secukinumab is acceptable. Nasopharyngitis is the most common adverse effect. Serious infection rates were not significantly different between those treated with secukinumab and those treated with placebo. Oral candidiasis has been noted in several subjects on secukinumab, and the effect seems to be dose dependent.²³ Findings from postmarketing studies will help inform clinicians and patients regarding long-term safety and rare adverse events. At this time, clinical studies for ixekizumab and brodalumab also showed acceptable safety profiles, and these biologics are pending FDA approval for use in patients with moderate to severe psoriasis.

RITUXIMAB

Rituximab is a chimeric murine-human IgG1 monoclonal antibody to CD20 that induces depletion of B cells. CD20 is a B cell-specific antigen expressed on the surface of B lymphocytes during differentiation from the pre-B-cell to the mature B-cell stage. CD20 is not found on plasma cells or stem cells. As a result, treatment with rituximab does not result in dramatic decreases of immunoglobulin levels. Rituximab's mechanisms of action include antibody-dependent cellular cytotoxicity, complement-mediated lysis,

Table 2
Biologics used in dermatology for selected non-FDA-approved indications

Biologic	Off-label Use	Dosage	Special Considerations
Etanercept	Pyoderma gangrenosum ³³	25–50 mg twice weekly	Effective in several case reports
Infliximab	Sarcoidosis ³⁴	3–10 mg/kg/dose at 0, 2, 6, and every 8–19 wk subsequently	9 of 10 patients reported subjective improvement of skin lesions; all 10 had objective improvement
	Pyoderma gangrenosum ³⁵ Hidradenitis suppuritiva ³⁶	5 mg/kg/dose 5 mg/kg/dose	Effective in placebo-controlled trial with 30 subjects Randomized, double-blind, placebo-controlled crossover trial
Adalimumab	Sarcoidosis ³⁷	80 mg initial loading dose followed by 40 mg once weekly	12-wk, double-blind placebo-controlled trial showed improvement in several cutaneous findings in the adalimumab-treated patients relative to placebo recipients
	Pyoderma gangrenosum ³⁸	80 mg initial loading dose, followed by 40 mg wk 1, then 40 mg every other week	May be effective after failure of other systemic therapies
	Hidradenitis suppuritiva ³⁹	160 mg initial loading dose followed by 40 mg once weekly	Higher doses needed than for psoriasis; large studies are pending
Ustekinumab	Subacute cutaneous lupus erythematosus ⁴⁰	45 mg (≤ 100 kg) or 90 mg (> 100 kg) by SC injection at weeks 0 and 4, then every 12 wk thereafter	Multiple case reports showed efficacy in recalcitrant disease
Rituximab	Pemphigus vulgaris ^{26,41}	Lymphoma or RA dosing have been used. See Table 1	Several case reports and small series of efficacy. Recent report of improvement with combined anti-CD20 and IVIG. Needs controlled trials. Recent systematic review highlights clinical response within 6 wk of treatment
	Dermatomyositis ⁴²		Large, randomized, multicenter controlled trial sponsored by NIH showed efficacy
IVIG	Pyoderma gangrenosum ⁴³ Pemphigus vulgaris Dermatomyositis ⁴⁵ Toxic epidermal necrolysis ^{46,47}	2 g/kg/cycle over 3–5 consecutive days	Found effective in combination with systemic steroids and other immunosuppressant drugs in series of 7 cases Has been combined with rituximab for recalcitrant disease ⁴⁴ Double-blind, placebo-controlled trial showed efficacy Differing reports on efficacy of IVIG exist. Interpretation of literature is limited by lack of treatment regimen uniformity, lack of adequate control data, and size of studies performed

Abbreviation: NIH, US National Institutes of Health.

and direct disruption of signaling pathways and triggering of apoptosis. The contribution of each mechanism remains unclear, and different mechanisms may predominate in the treatment of different diseases.²⁴ However, within 6 months of therapy it is hoped that new B cells that do not produce the pathogenic antibodies will return to circulation.²⁵

At present, rituximab is FDA approved for non-Hodgkin lymphoma, chronic lymphocytic leukemia, RA, granulomatosis with polyangiitis (Wegener granulomatosis), and microscopic polyangiitis.¹⁷ Rituximab can be dosed in 2 different ways: lymphoma dosing (375 mg/m² per week for 4 doses) or RA dosing (1000 mg every 2 weeks for 2 doses).⁵

Rituximab is currently used off label for many conditions in dermatology. These conditions include pemphigus vulgaris, paraneoplastic pemphigus, epidermolysis bullosa acquisita, bullous pemphigoid, primary cutaneous B-cell lymphoma, dermatomyositis, acute and chronic GVHD, and systemic lupus erythematosus.²⁴ The use of rituximab for the pemphigus group of blistering diseases is worth extra discussion as it is currently the most common use of this drug in dermatology.²⁶ A large systematic review of patients receiving either the lymphoma or RA dosing showed that patients seem to experience an initial clinical response within 6 weeks of treatment. Most investigators also treat with conventional immunosuppressive therapies during and after rituximab therapy. However, relapse rates are 50% or more and many investigators conclude that additional rituximab or systemic therapies may be needed to maintain remission.²⁶

In treatments with rituximab, infusion reactions are the most common adverse event. These reactions can be pretreated with acetaminophen, diphenhydramine, or methylprednisolone.²⁴ The incidence of serious adverse effects is low. In a study of rituximab for the treatment of RA, infections occurred in 35% of patients compared with 28% of the placebo group. Serious infections occurred in 2% of the rituximab group compared with 1% in the placebo group.²⁷ Because rituximab is a chimeric antibody, human antichimeric antibodies (HACA) can theoretically develop. One study showed that HACAs developed in less than 1% of patients treated for lymphoma, although the incidence may be higher in patients with autoimmune disorders.^{28,29}

In addition, there is a risk of reactivation of the HBV infection. Reactivation of HBV can be idiopathic, asymptomatic, and rapid; rigorous reactivations can lead to fulminant liver failure and even death. The FDA issued a recommendation that all health care professionals screen patients on rituximab for HBV infection by measuring hepatitis B surface antigen and hepatitis B core antibody. In addition, patients with evidence of prior HBV infection should be monitored for clinical and laboratory signs of HBV reactivation during and for several months after completing rituximab therapy because reactivations may occur several months following completion of rituximab therapy.¹⁷

INTRAVENOUS IMMUNOGLOBULIN

IVIg is a fractionated blood product consisting of IgG antibodies that was first used in antibody deficiency disorders. It is increasingly being used for several inflammatory and autoimmune conditions.³⁰ IVIg is currently FDA approved in dermatology for GVHD and Kawasaki syndrome.³¹ IVIg is also currently being used to treat a wide range of difficult-to-treat dermatologic diseases, including dermatomyositis, autoimmune bullous skin diseases, and toxic epidermal necrolysis.^{30,31}

Before starting IVIg, a complete history and physical with emphasis on cardiopulmonary and renal status should be performed to assess patients at risk for fluid overload. Laboratory tests include a complete blood count and chemistries to assess liver

and renal function. Immunoglobulin levels should be assessed, in particular IgA, because some patients have an increased risk of anaphylaxis. Screening for rheumatoid factor and cryoglobulins can be considered because patients with positive values are at increased risk for renal failure from IVIG. Consider screening for hepatitis B and C, along with HIV.⁵

Adverse effects of IVIG include infusion reactions that are generally mild and self-limiting, often occurring 30 to 60 minutes after onset of the infusion.³¹ They include flushing, myalgia, headaches, fever, chills, lower backache, nausea or vomiting, chest tightness, wheezing, changes in blood pressure, and tachycardia. Rare episodes of anaphylaxis have occurred, particularly in IgA-deficient patients with anti-IgA antibodies.³¹ Coombs-positive hemolysis and transient neutropenia have also been reported. Acute renal failure has also been reported and is thought to be related to an injury to the proximal tubule induced by high solute load. In addition, rare neurologic complications such as aseptic meningitis are seen 10 hours to 7 days after high-dose IVIG.³¹

SUMMARY

Biologic therapy has dramatically changed the way medicine, and specifically dermatology, is practiced today. The use of biologic agents in dermatology is evolving, with psoriasis being the most common indication for which biologics are used currently. However, several other dermatologic diseases seem to be responsive to biologic therapy, and continuing research and development efforts are elucidating the benefit-risk profiles of various biologic medications in these dermatologic conditions.¹⁵

Although biologic agents have revolutionized the management of dermatologic conditions, cost must also be considered when evaluating management options, especially compared with traditional agents. For example, the cost of 1 year of induction and maintenance treatment of psoriasis in 2014 was estimated to be \$53,909 for ustekinumab, \$46,395 for etanercept, and \$39,041 for adalimumab.³² Nonetheless, because of their efficacy, the cost of a biologic may be offset by significant reductions in the number of hospital stays, reduction in use of other systemic therapies, and increased satisfaction by patients.³² Thus, understanding their mechanisms of action, labeled and off-label uses in dermatology, and common adverse effects helps to inform clinical decision making and improve patient outcomes.

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