Psoriasis is a frustrating and often debilitating inflammatory skin disease that affects 0.6% to 4.8% of people worldwide.\(^1\) Classically characterized by discrete erythematous plaques covered by a silvery white scale in characteristic locations, psoriasis may also present with pustular, guttate, and erythrodermic variants that share different features from the classic form. Patients who have psoriasis may initially present to their primary care office with no diagnosis but concerned about the cosmetic changes of their psoriatic lesions and the itching and pain often associated with these lesions.

Although the underlying cause of psoriasis is incompletely understood, recent evidence has linked psoriasis with atherosclerotic cardiovascular disease and the metabolic syndrome.\(^2\) The relatively high prevalence of psoriasis mandates that primary care physicians be able to manage localized or mild disease and also be knowledgeable about treatment of moderate and severe disease to ensure appropriate dermatologic collaboration.
Psoriasis is ubiquitous throughout the world. It affects approximately 2.5% of the Caucasian population and 1.3% of the African American population in the United States, with approximately 150,000 newly diagnosed cases every year. The incidence of psoriasis is somewhat lower in Asians (0.4%). Generally, it is more common in individuals living at higher latitudes or in colder locales, and less common in individuals who have greater sun exposure.

Psoriasis is equally common in men and women. It usually presents itself in a bimodal age distribution, with the earlier peak incidence between 15 and 30 years of age, and the later peak incidence between 50 and 60 years of age. The earlier peak is associated with more severe disease. This bimodal presentation has led to the definition of two forms of psoriasis: type I, often HLA-Cw6–associated, with age of onset before 40 years; and type II, which is not HLA-associated, with age of onset after 40 years. No current evidence shows that type I and type II psoriasis respond differently to different therapies.

Genetic and environmental factors have been shown to predispose individuals to developing psoriasis. Based on population studies, the risk for psoriasis in children is estimated to be 41% if both parents are affected, 14% if one parent is affected, and 6% if one sibling is affected. Similarly, a family history can be found in 5% to 10% of patients who have psoriasis. Recent evidence from HLA studies suggests a polygenic mode of inheritance, with certain class I major histocompatibility complex (MHC) antigens, particularly B13, B17, B39, and Cw6, and the class II MHC antigen DR7 occurring with increased frequency in relatives of patients who have psoriasis. The HLA antigens B27 and B38 are also associated with psoriatic arthritis.

In some families, variation at a single non–HLA genetic locus on chromosome 17q is linked to psoriasis susceptibility. In other more recent studies, the psoriasis susceptibility 1 locus, which is located in the MHC on chromosome 6p and is linked to the aforementioned HLA antigens, has been estimated to account for only one third to one half of the variation in genetic liability to psoriasis, suggesting that additional non-MHC genes are involved.

As would be expected in a genetic disease, a higher concordance for psoriasis is seen in monozygotic versus dizygotic twins. However, the reported concordance for monozygotic twins has ranged from 35% to 73% in different studies, variability that points to nongenetic influences also playing a role in the pathogenesis of psoriasis. Accordingly, several environmental triggers have been identified. Patients living in colder climates are at greater risk for developing the disease, probably because they are exposed to less ultraviolet radiation, which has been shown to be protective against psoriatic lesions (see later discussion on phototherapy). Smoking is associated with an increased risk for psoriasis and increased severity of the disease. Psoriasis may also be exacerbated by streptococcal infection and certain drugs, particularly interferon-α, lithium, antimalarials, abrupt cessation of systemic corticosteroids, and β-blockers. Psoriasis can also be the presenting sign of HIV infection, and HIV-associated psoriasis is classically more severe than the common form. An association has also been seen between psoriasis and obesity and alcohol consumption, but whether these factors may actually cause the disease or are a result of having psoriasis is unclear.

The Koebner phenomenon, also known as the isomorphic response, is the occurrence of psoriasis in areas of trauma. It usually occurs 1 to 2 weeks after injury in an
all-or-none pattern, with psoriatic lesions appearing at either all or no sites of injury. Approximately 25% of patients report a history of the Koebner phenomenon at some point in their lives, and estimates of lifetime prevalence rise as high as 76% when coupled with infection and stress.4

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Psoriasis is diagnosed through physical examination. Psoriasis usually presents with symmetric, well-demarcated, erythematous plaques with overlying silvery scales, often with accompanying pruritus (Fig. 1A–D). Single lesions may become confluent, extend laterally, or develop partial central clearing. Removing the silvery scales induces trauma to the underlying dilated capillaries and results in pinpoint bleeding in the site of the lesion, a finding known as the Auspitz sign. Although psoriasis may affect almost any part of the body, it most commonly appears on the elbows, knees, scalp, gluteal cleft, umbilicus, and lower back. The Koebner phenomenon may explain why the knees and elbows are common sites for psoriatic lesions, because chronic trauma is often experienced in these regions. Nail involvement, particularly pitting, onycholysis, and red-brown discoloration resembling drops of oil, more often in fingers than toes, can occur in up to 50% of patients. Geographic tongue, which presents as asymptomatic erythematous patches on the tongue correlating with loss of filiform papillae, may also be seen, although it is nonspecific. A seronegative inflammatory arthritis is seen in approximately 25% of patients, and these patients who have psoriatic arthritis (PsA) are more likely to also have nail abnormalities. In PsA, skin disease usually precedes joint disease by an average of 12 years in 84% of patients (Fig. 1F).11

This pattern of psoriasis represents the most common form of the disease—plaque-type psoriasis or psoriasis vulgaris—seen in approximately 90% of patients. Approximately one third of patients who have psoriasis vulgaris are reported to have moderate-to-severe disease based on their extensively involved body surface area or the significant impact on their quality of life.12

In addition to psoriasis vulgaris, the disease has four other variants: guttate, inverse, pustular, and erythrodermic. Guttate ("drop-like") psoriasis, which is most associated with HLA-Cw6,4 consists of numerous 0.5- to 1.5-cm papules over the trunk and proximal extremities, and often erupts suddenly. Inverse psoriasis is characterized by sharply demarcated erythema without scale, localized to intertriginous areas such as the axillae, genital folds, or neck. Inverse psoriasis must therefore be distinguished from fungal infections.

The pustular and erythrodermic psoriatic variants are potentially more severe and life-threatening. In pustular psoriasis, pustules develop either in a rim around plaques, on the palmoplantar surfaces, or throughout the body. The latter form may be accompanied by high fevers, leukocytosis, and hepatotoxicity, and often requires inpatient systemic therapy. Similar widespread involvement is observed in the erythrodermic psoriatic variant, characterized by generalized erythema and scaling from head to toe (Fig. 1E). These patients, like those who have sustained burns, are at increased risk for infection, severe dehydration, and electrolyte loss and must also be treated aggressively in the inpatient setting.13

Once the diagnosis of psoriasis is suggested through physical examination, a careful history is important in defining the nature of the disease and determining appropriate treatment. Physicians should document the age of onset, family history, and prior course of the disease. Of important prognostic implication is the history of relapse, because patients who frequently experience relapse tend to develop more severe
disease, with rapidly enlarging lesions covering significant parts of the body, and may require more aggressive therapy. Physicians should also inquire about current medications, joint complaints, and previous response to therapy.

Psoriatic plaques may occasionally resemble atopic dermatitis, or eczema, but will usually be thicker, redder, and more sharply demarcated than eczematous lesions. Furthermore, psoriasis usually affects the extensor surfaces on the knees and elbows, whereas eczema typically involved the flexor surfaces. Psoriatic plaques may occasionally resemble seborrheic dermatitis, tinea infections, cutaneous T-cell lymphoma,
ichthyosis, secondary syphilis, and Reiter’s syndrome. In the few cases in which physical examination and clinical history are not diagnostic, skin biopsy may be indicated to make the diagnosis. Classic histopathologic features of psoriasis include epidermal hyperplasia with parakeratosis (retention of nuclei in the stratum corneum), a neutrophil-rich stratum corneum (Munro’s abscess), thinning of the granular layer of the epidermis, and a mononuclear dermal and epidermal infiltrate. Infiltration of T cells and dendritic cells in plaques and dysregulated angiogenesis of dermal blood vessels have also been described (Fig. 2).

PATHOGENESIS

Psoriatic immunopathogenesis consists of the complex interplay among innate and acquired immune cell types and among immune factors produced by dendritic cells, T cells, and keratinocytes in the psoriatic plaque. Effector cells of innate immunity in psoriatic lesions include neutrophils and dendritic cells. In psoriatic lesions and arthritic joints, dendritic cells express tumor necrosis factor α (TNFα), an inflammatory cytokine that up-regulates nuclear factor-κB (NF-κB) and can thereby induce inflammatory molecules such as interleukin (IL)-1, IL-8, IL-6, and inducible nitric oxide synthase (iNOS). iNOS, in turn, may facilitate nitric oxide production, thereby causing capillary vasodilatation. TNFα could also promote emigration of leukocytes into the skin, induce adhesion molecule expression, and up-regulate vascular endothelial growth factor (VEGF), further facilitating inflammation and angiogenesis in the psoriatic plaque.

In addition to expressing TNFα, dendritic cells produce the cytokine IL-23. IL-23 is known to be a critical player in psoriatic immunopathogenesis through its effects on Th17 T-cell development and production of cytokines such as IL-17 and IL-22.

COMORBIDITIES

Although primarily a disease of the skin, psoriasis is now known to be inextricably linked to several other diseases. Recent evidence has even suggested an increased overall risk for mortality with a hazard ratio of 1.5 (95% CI, 1.3–1.7) in especially young patients who have severe psoriasis. An average of 25% of patients who have psoriasis also develop the inflammatory seronegative spondyloarthropathy PsA, characterized by stiffness, pain, swelling, and tenderness of the joints and surrounding ligaments and tendons (dactylitis and enthesitis). In addition to digital involvement, enthesitis in PsA commonly involves insertion sites of the plantar fascia, the Achilles’ tendons, and ligamentous attachments to the ribs, spine, and pelvis. Nail disease is frequently seen in PsA, especially in patients who have distal interphalangeal (DIP) joint involvement. If untreated, PsA can develop into debilitating, erosive arthropathy characterized by persistent inflammation, progressive joint damage, physical disability, and increased mortality.

In addition to their risk for developing PsA, patients who have psoriasis are believed to have a genetic susceptibility to autoimmune disease and dysregulation of TNFα, and therefore are more likely to develop Crohn’s disease than individuals who do not have psoriasis. Psoriasis has also been shown to occur more commonly in families of patients who have multiple sclerosis compared with controls, although it is unclear whether patients who have psoriasis are at higher risk for developing multiple sclerosis.

Patients who have psoriasis also have an increased risk for metabolic syndrome and cardiovascular disease, suggesting that the chronic inflammation of psoriasis may be a risk factor for cardiometabolic pathology, perhaps for the same reason that
Fig. 2. Histopathologic changes in psoriatic skin. (A) normal skin. (B) Epidermis in psoriatic skin, characterized by acanthosis (thickening of the viable cell layers), elongation of epidermal rete ridges (arrowheads), hyperkeratosis (thickening of the cornified layer), loss of the granular layer, parakeratosis (nuclei in the stratum corneum), dilated dermal blood vessels that nearly reach the epidermis (arrows), and a mixed leukocytic infiltrate seen in both dermis and epidermis. (C) Neutrophilic granulocytes have transmigrated through the epidermis (arrow) and have formed a Munro microabscess underneath the stratum corneum (arrowhead). As the lesions progress, these microabscesses are transported to the upper layers of the stratum corneum, where they slough off (D, arrow). Focal expression of epidermal intercellular adhesion molecule 1 (ICAM-1) indicates keratinocyte activation (E), and immunostaining of CD3 (a T-cell receptor–associated antigen) indicates the abundance of T cells within dermis and epidermis (F). In addition, immunostaining of the ε(CD103) integrin, an adhesion receptor that binds to epidermal E-cadherin, reveals almost exclusive expression by intraepidermal T cells (G). ICAM-1 and the ε(CD103) integrin contribute to the recruitment of pathogenic lymphocytes to psoriatic skin. (From Schön MP, Boehncke WH. Psoriasis. N Engl J Med 2005;352:1899–912; with permission.)
C-reactive protein is used as a biomarker for coronary disease. In a hospital-based case-control study on 338 adult patients who had chronic plaque psoriasis, Gisondi and colleagues observed that the metabolic syndrome was significantly more common in patients who had psoriasis than in controls (30.1% versus. 20.6%; odds ratio, 1.65; \( P < .005 \)) after the age of 40 years, independent of the incidence of smoking. This association showed a time-course relationship, with patients experiencing psoriasis for the longest time also having the highest prevalence of metabolic syndrome. In this study, patients who had psoriasis also had a higher prevalence of hypertriglyceridemia and abdominal obesity.

Similarly, evidence from the United Kingdom General Practice Database, which contains data on more than 130,000 patients who have psoriasis aged 20 to 90 years, has shown that patients who have psoriasis have a higher-than-normal incidence of myocardial infarction, even after correcting for classic atherosclerotic risk factors, such as smoking, diabetes, obesity, hypertension, and hyperlipidemia. To what extent immunobiologic and other anti-inflammatory therapies may also reduce the risk for cardiovascular disease in patients who have psoriasis remains to be determined.

Some evidence shows that patients who have psoriasis have an increased lifetime risk for also developing lymphoma. In a retrospective cohort study of 2718 patients who had psoriasis in the United Kingdom, Gelfand and colleagues found that patients who had psoriasis had a 2.95 relative rate of developing lymphoma compared with the general population, independent of age, gender, and methotrexate therapy.

In addition to their higher risk for developing medical comorbidities, patients who have psoriasis are more prone to mood disorders, including depression, which occurs in as many as 60% of patients, and a substantial proportion of these patients may actively contemplate suicide. Importantly, a recent multicenter randomized phase III trial comparing twice-weekly etanercept therapy with placebo in more than 600 adults who had moderate-to-severe plaque psoriasis found that patients treated with etanercept had a significant decrease in their Hamilton rating scale for depression scores (suggesting that they had fewer symptoms of depression) compared with control subjects.

**TREATMENT**

Patients who have psoriasis report an impaired quality of life to a degree that rivals that caused by other major illnesses such as diabetes and cancer. At the same time, treatment of the disease presents many challenges for patients and health care providers. The goal of treatment is long-term, safe, and effective clearance of psoriatic lesions. Part of the challenge in treating psoriasis is that traditional psoriatic treatments are only somewhat effective (eg, topical agents), inconvenient (eg, phototherapy), or toxic (eg, methotrexate); these attributes lead to poor patient compliance and increase the tendency for psoriatic flares.

Over the past 10 years, targeted immunobiologic therapies have been and are being developed aimed at creating the ideal therapy to clear psoriasis and that can be safely and effectively used on a chronic basis. These therapies, which incorporate current understanding of psoriatic immunopathogenesis, are rapidly transforming the management of moderate-to-severe psoriasis for patients and providers alike. This section focuses on treatment of patients who have psoriasis; discussion of PsA therapy is beyond the scope of this review.

Current treatments for psoriasis can be compartmentalized into five categories: topical applications, phototherapy, traditional systemic treatments, immunobiologics,
and experimental approaches. As with many diseases that can present with increasing degrees of severity, treatment modalities for psoriasis are selected based on extent of disease, patient preference, comorbidities, and individual patient response. The traditional approach to treatment of psoriasis categorizes patients into two groups. The first group, which encompasses 75% of patients and includes individuals who have mild or localized disease that does not significantly impact quality of life, are generally managed with topical therapy as the first line of treatment. The second traditional treatment group includes the remaining 25% of patients who have moderate-to-severe psoriasis that affects quality of life, and these patients often require more aggressive systemic therapy. Of course, even in the first group, location of lesions (eg, genitals or face), previous failure of topical therapy, excessive inconvenience, history of frequent relapsing disease, or presence of psoriatic arthritis may also prompt the consideration of systemic therapy.

Topical therapies include emollients, corticosteroids, vitamin D analogs, the vitamin A analog tazarotene, topical immunosuppressants, tars, and anthralin. Emollients are important to maintain skin hydration, minimize itching, and avoid Koebnerization. Topical corticosteroids are at once anti-inflammatory, antiproliferative, and immunosuppressive and are the mainstay of topical psoriatic therapy because of their short-term efficacy and broad range of potency. In choosing a topical corticosteroid, physicians must consider the anatomic site, thickness of the psoriatic plaque, extent of involvement, and relative contraindications (eg, preexisting skin atrophy). Although the typical corticosteroid regimen consists of twice-daily topical applications, some regimens that involve especially potent corticosteroid preparations recommend infrequent applications (eg, every weekend), a schedule known as pulse therapy.

The vitamin D analogs, calcipotriene and tacalcitol, and the vitamin A analog tazarotene, are somewhat effective in reversing keratinocyte hyperproliferation and thereby reducing the severity of psoriatic plaques. Several recent trials found that combined use of daily calcipotriene and superpotent corticosteroids, either halobetasol in a pulse therapy pattern or daily betamethasone, may actually be more efficacious and better tolerated than either agent alone. The calcineurin inhibitors tacrolimus and pimecrolimus have been studied as steroid-sparing agents in patients who have plaque psoriasis, but a recent FDA warning linking these medications with certain types of lymphoma has curtailed their use of late. Keratolytics are used to decrease scale. Finally, topical coal tar preparations and anthralin are traditional modalities that have been historically tedious to use; these therapies have largely fallen out of favor by the medical community in light of the newer corticosteroid and vitamin D analog preparations.

Patients who have more sun exposure have a lower risk for developing psoriasis because of the antiproliferative and anti-inflammatory effects of ultraviolet light on psoriatic plaques. Therefore, phototherapy with ultraviolet B (UVB) radiation and the more potent photochemotherapy with psoralen plus ultraviolet A radiation (PUVA) are still occasionally used in patients who have moderate-to-severe psoriasis. PUVA penetrates deeper into the dermis and is usually used when UVB fails. However, because of the highly technical nature of these treatment modalities, and because several recent studies have highlighted a worrisome link between prolonged PUVA phototherapy and squamous cell carcinoma and melanoma, these treatments should be reserved for specially trained dermatologists.

When psoriasis is moderate-to-severe, the physician should consider systemic therapy. Specific indications for systemic therapy include moderate-to-severe plaque psoriasis, usually involving at least 10% of the body surface area; failure of topical treatment; incapacitating disease affecting quality of life; PsA; or generalized pustular
or erythrodermic psoriasis. Traditional therapies in this category include methotrexate (MTX), cyclosporine, and acitretin.

In addition to preventing epidermal hyperproliferation by inhibiting dihydrofolate reductase (DHFR), MTX is believed to prevent the proliferation of T cells by also inhibiting aminopterin, an enzyme involved in purine metabolism. It is administered orally, intramuscularly, or subcutaneously, usually in once-weekly (7.5–25 mg) regimens. Although effective, MTX has many side effects, including hepatotoxicity, bone marrow suppression, pneumonitis, abortion, and teratogenicity. These side effects can be observed even with concomitant administration of folic acid. As a result of the potential for hepatotoxicity, prior guidelines suggest a liver biopsy after a 1.5-g cumulative dose.

Cyclosporine (CsA) is another immunosuppressive medication that works rapidly and is effective in most patients. In psoriasis, CsA inhibits keratinocyte hyperproliferation and prevents production of IL-2, thereby impairing helper T-cell activation. In a large randomized control trial published in 1991, Ellis and colleagues found that 8 weeks of CsA dose-dependently cleared the plaques of patients who had moderate-to-severe psoriasis, compared with no clearance of plaques in patients treated with placebo. At the same time, significant side effects can be observed, including nephrotoxicity, hypertension, hypercholesterolemia, increased infection, hirsutism, gum hypertrophy, headache and tremor, and a potential increase in cutaneous and internal malignancies.

The final FDA-approved traditional systemic therapy for psoriasis is acitretin, a systemic retinoid indicated for patients who have severe plaque psoriasis and for pustular and erythrodermic forms of the disease. When used to treat severe plaque psoriasis, acitretin is often combined with UVB or PUVA phototherapy as a dose-sparing approach. However, acitretin is teratogenic, and has been associated with mucocutaneous side effects, hypertriglyceridemia, and hepatotoxicity.

Recent advances in understanding the immunopathogenesis of psoriasis has led to the development of a promising class of immunomodulatory medications known as biologics. The biologics are recombinant proteins (either monoclonal antibodies or fusion proteins) extracted from animal tissue that target activated T cells, adhesion molecules, or chemokines that play a role in psoriasis. These medications are revolutionizing the management of psoriasis because they are highly effective and well tolerated by patients. In clinical trials, medication efficacy is recorded with the Psoriasis Area and Severity Index (PASI) score, a measure of overall psoriasis severity and coverage that assesses body surface area and erythema, induration, and scaling. A 75% improvement in the PASI score (PASI-75) is usually used to document the effectiveness of specific therapies in clinical trials. Some trials used the Physicians Global Assessment (PGA), which requires the investigator to assign a single estimate of the patient’s overall severity of disease on a 5- to 6-point scale.

Five biologic agents are currently approved by the FDA: alefacept (Amevive) and efalizumab (Raptiva), which target pathogenic T cells, and adalimumab (Humira), etanercept (Enbrel), and infliximab (Remicade), which target TNFα. Newer agents are also currently being tested in clinical trials.

As a general rule, the National Psoriasis Foundation recommends that psoriasis patients taking biologics should be monitored with baseline and periodic blood work, including chemistry screen with liver function tests, complete blood count, hepatitis panel, and tuberculosis testing. Specific medications may require additional monitoring based on side effect profiles. Because the biologics are immunosuppressive, patients on these medications and methotrexate and cyclosporine must avoid live attenuated vaccinations and must be carefully monitored for signs or symptoms of infection.
The recombinant dimeric fusion protein alefacept binds to CD2 on memory effector T lymphocytes, thereby inhibiting the number of these cells in psoriatic plaques. It is FDA-approved as a 12-week, 15-mg intramuscular injection for the treatment of adult patients who have moderate-to-severe chronic plaque psoriasis who are candidates for systemic agents or phototherapy. Phase III trials showed that 21% of patients achieved a PASI75 score 2 weeks after the twelfth injection of alefacept. A recent study found that patients may benefit from up to two additional 12-week therapeutic courses of alefacept, with the greatest clinical responses seen with concomitant UVB therapy. Because of alefacept’s inhibitory effect on T cells, patients taking this medication should have their CD4 counts checked before treatment and every other week on treatment. Patients infected with HIV who have psoriasis are not candidates for alefacept therapy.

Efalizumab is a recombinant monoclonal antibody directed against the CD11a subunit of the integrin (LFA-1) responsible for T-cell adhesion. It is FDA-approved for adults who have chronic moderate-to-severe plaque psoriasis and is administered weekly as a subcutaneous injection: 0.7 mg/kg for the initiation dose followed by 1-mg/kg weekly doses thereafter. In a phase III randomized, placebo-controlled, double-blind study of nearly 600 patients who had psoriasis treated with efalizumab or placebo, Lebwohl and colleagues found that 22% of the patients treated with efalizumab, 1 mg/kg per week, and 28% of the patients treated with efalizumab, 2 mg/kg per week, had achieved PASI-75 at week 12, compared with only 5% of patients treated with placebo. A similar trend was observed at week 24 of efalizumab versus placebo treatment. Even after the discontinuation of efalizumab at week 24, in fact, an improvement of 50% or more in the PASI was maintained in approximately 30% of patients during 12 weeks of follow-up. Despite this encouraging data, efalizumab is not effective against PsA; it has also been associated with psoriatic arthritis flares during therapy, psoriasis rebound, flu-like symptoms, hemolytic anemia, thrombocytopenia, peripheral demyelination, and progressive multifocal leukoencephalopathy.

The second group of FDA-approved biologics encompasses the TNF inhibitors, three of which are approved for use in both psoriasis and psoriatic arthritis. Adalimumab, a fully human anti-TNFα monoclonal antibody, is effective against moderate-to-severe plaque psoriasis and PsA, and also may be effective long-term. A recent 52-week, multicenter study of 1212 patients who had psoriasis randomized to either adalimumab or placebo every other week found that 71% of those treated with adalimumab achieved PASI-75 at week 16, compared with 7% of those treated with placebo. This study also observed that when the patients who had achieved PASI-75 after 33 weeks of continuous adalimumab therapy were re-randomized in a double-blind manner to either continued adalimumab or placebo, only 5% of those re-randomized to adalimumab lost adequate response (defined as <50% improvement in the PASI response relative to baseline and at least a six-point increase in PASI score from week 33), compared with 28% of patients re-randomized to placebo. Adalimumab is currently approved for moderate to severe psoriasis treatment in a dosing regimen of 80 mg subcutaneously the first week, followed by 40 mg subcutaneously the next week and then every 2 weeks thereafter.

Etanercept, a recombinant human TNFα receptor protein fused with the Fc portion of IgG1, is FDA-approved when given in dosing regimens of 50 mg subcutaneously twice weekly for the first 12 weeks followed by 50 mg weekly thereafter for moderate-to-severe plaque psoriasis and for PsA. A randomized trial of etanercept in 652 adult patients who had plaque psoriasis noted an improvement from baseline of PASI-75 or more in 34% of the etanercept group receiving 25 mg twice weekly and 49% of the etanercept group receiving 50 mg twice weekly, compared with 4%
of the patients in the placebo group. In fact, the clinical responses continued to improve with 24-week treatment.\textsuperscript{30,49} Etanercept is FDA-approved for treating moderate to severe psoriasis as follows: 50 mg subcutaneously twice weekly for 12 weeks followed by step-down to 50 mg once-weekly dosing.

Infliximab is a chimeric antibody that binds to and inhibits TNF$_\alpha$; it is now FDA-approved for severe psoriasis and PsA. In phase III trials, 75.5\% to 80\% of patients who had psoriasis experienced a PASI-75 response after induction therapy (5 mg/kg intravenous infusions at weeks 0, 2, and 6). After adding maintenance dosing of infliximab every 8 weeks through 46 weeks, 61\% of patients had at least a 75\% improvement at week 50.\textsuperscript{23,43,50,51}

Because TNF$_\alpha$ inhibitors have been used for nearly 10 years as part of the treatment armamentarium for rheumatoid arthritis and inflammatory bowel disease, the potential toxicities of these medications are now well understood. TNF$_\alpha$ inhibitors carry the potential for increased risk for serious infections, including opportunistic infections; demyelinating disorders; hepatotoxicity; lupus-like syndromes; pancytopenias; lymphoma; and non-melanoma skin cancers.\textsuperscript{30} However, TNF$_\alpha$ inhibitors are usually given as monotherapy for psoriasis but are often prescribed alongside additional immunosuppressive therapy for rheumatoid arthritis and inflammatory bowel disease, so the side effects observed with TNF$_\alpha$ inhibitor therapy for rheumatoid arthritis and inflammatory bowel disease may overestimate the expected side effects of TNF$_\alpha$ inhibitor therapy for psoriasis.\textsuperscript{30}

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