TABLE 71-3 FDA-APPROVED SYSTEMIC THERAPY FOR PSORIASIS

		Administration		
Agent	Medication Class	Route	Frequency	Adverse Events (Selected)
Methotrexate	Antimetabolite	Oral	Weekly	Hepatotoxicity, pulmonary toxicity, pancytopenia, potential for increased malignancies, ulcerative stomatitis, nausea, diarrhea, teratogenicity
Acitretin	Retinoid	Oral	Daily	Teratogenicity, hepatotoxicity, hyperostosis, hyperlipidemia/pancreatitis, depression, ophthalmologic effects, pseudotumor cerebri
Cyclosporine	Calcineurin inhibitor	Oral	Twice daily	Renal dysfunction, hypertension, hyperkalemia, hyperuricemia, hypomagnesemia, hyperlipidemia, increased risk of malignancies

Fingernail involvement, appearing as punctate pitting, onycholysis, nail thickening, or subungual hyperkeratosis, may be a clue to the diagnosis of psoriasis when the clinical presentation is not classic.

According to the National Psoriasis Foundation, up to 30% of patients with psoriasis have psoriatic arthritis (PsA). There are five subtypes of PsA: symmetric, asymmetric, distal interphalangeal predominant (DIP), spondylitis, and arthritis mutilans. Symmetric arthritis resembles rheumatoid arthritis, but is usually milder. Asymmetric arthritis can involve any joint and may present as "sausage digits." DIP is the classic form, but occurs in only about 5% of patients with PsA. It may involve fingers and toes. Spondylitis also occurs in about 5% of patients with PsA. Arthritis mutilans is severe and deforming. It affects primarily the small joints of the hands and feet. It accounts for fewer than 5% of PsA cases.

An increased risk of metabolic syndrome, including increased morbidity and mortality from cardiovascular events, has been demonstrated in psoriasis patients. Appropriate screening tests should be performed. The etiology of psoriasis is still poorly understood, but there is clearly a genetic component to the disease. In various studies, 30–50% of patients with psoriasis report a positive family history. Psoriatic lesions contain infiltrates of activated T cells that are thought to elaborate cytokines responsible for keratinocyte hyperproliferation, which results in the characteristic clinical findings. Agents inhibiting T cell activation, clonal expansion, or release of proinflammatory cytokines are often effective for the treatment of severe psoriasis (see below).

TREATMENT PSORIASIS

Treatment of psoriasis depends on the type, location, and extent of disease. All patients should be instructed to avoid excess drying or irritation of their skin and to maintain adequate cutaneous hydration. Most cases of localized, plaque-type psoriasis can be managed with mid-potency topical glucocorticoids, although their long-term use is often accompanied by loss of effectiveness (tachyphylaxis) and atrophy of the skin. A topical vitamin D analogue (calcipotriene) and a retinoid (tazarotene) are also efficacious in the treatment of limited psoriasis and have largely replaced other topical agents such as coal tar, salicylic acid, and anthralin.

Ultraviolet (UV) light, natural or artificial, is an effective therapy for many patients with widespread psoriasis. Ultraviolet B (UVB), narrowband UVB, and ultraviolet A (UVA) light with either oral or topical psoralens (PUVA) is used clinically. UV light's immunosuppressive properties are thought to be responsible for its therapeutic activity in psoriasis. It is also mutagenic, potentially leading to an increased incidence of nonmelanoma and melanoma skin cancer. UV-light therapy is contraindicated in patients receiving cyclosporine and should be used with great care in all immunocompromised patients due to the increased risk of skin cancer.

Various systemic agents can be used for severe, widespread psoriatic disease **(Table 71-3)**. Oral glucocorticoids should not be used for the treatment of psoriasis due to the potential for development of life-threatening pustular psoriasis when therapy is discontinued. Methotrexate is an effective agent, especially in patients with psoriatic arthritis. The synthetic retinoid acitretin is useful, especially when immunosuppression must be avoided; however, teratogenicity limits its use.

The evidence implicating psoriasis as a T cell–mediated disorder has directed therapeutic efforts to immunoregulation. Cyclosporine and other immunosuppressive agents can be very effective in the treatment of psoriasis, and much attention is currently directed toward the development of biologic agents with more selective immunosuppressive properties and better safety profiles **(Table 71-4)**. Experience with these biologic agents is limited, and information regarding combination therapy and adverse events continues to emerge. Use of tumor necrosis factor (TNF-α) inhibitors may worsen congestive heart failure (CHF), and they should be used with caution in patients at risk for or known to have CHF. Further, none of the immunosuppressive agents used in the treatment of psoriasis should be initiated if the patient has a severe infection; patients on such therapy should be routinely screened for tuberculosis. There have been reports of progressive multifocal leukoencephalopathy in association with treatment with the TNF-α inhibitors. Malignancies, including a risk or history of certain malignancies, may limit the use of these systemic agents.

TABLE 71-4 BIOLOGICS APPROVED FOR PSORIASIS OR PSORIATIC ARTHRITIS

		Administration			
Agent	Mechanism of Action	Indication	Route	Frequency	Warnings
Etanercept	Anti-TNF-α	Ps, PsA	SC	Once or twice weekly	Serious infections, hepatotoxicity, CHF, hematologic events, hypersensitivity reactions, neurologic events, potential for increased malignancies
Adalimumab	Anti-TNF-α	Ps, PsA	SC	Every other week	Serious infections, hepatotoxicity, CHF, hematologic events, hypersensitivity reactions, neurologic events, potential for increased malignancies
Infliximab	Anti-TNF-α	Ps, PsA	IV	Initial infusion followed by infusions at weeks 2 and 6, then every 8 weeks	Serious infections, hepatotoxicity, CHF, hematologic events, hypersensitivity reactions, neurologic events, potential for increased malignancies
Golimumab	Anti-TNF-α	PsA	SC	Monthly	Serious infections, hepatotoxicity, CHF, hypersensitivity reactions, neurologic events, potential for increased malignancies
Ustekinumab	Anti-IL-12 and anti-IL-23	Ps	SC	2 doses 4 weeks apart, then every 12 weeks	Serious infections, neurologic events, potential for increased malignancies

Abbreviations: CHF, congestive heart failure; IL, interleukin; IM, intramuscular; Ps, psoriasis; PsA, psoriatic arthritis; SC, subcutaneous; TNF, tumor necrosis factor.