Chapter 17: Psoriasis

INTRODUCTION

- *Psoriasis* is a chronic T-lymphocyte–mediated systemic inflammatory disease characterized by recurrent exacerbations and remissions of thickened, erythematous, and scaling plaques and multiple comorbidities, including psoriatic arthritis.

PATHOPHYSIOLOGY

- Genetic predisposition coupled with an unknown precipitating factor triggers an abnormal immune response mediated via T-lymphocytes, resulting in keratinocyte proliferation and the initial psoriatic skin lesions. Precipitating factors implicated in the development of psoriasis include skin injury, infection, drugs, smoking, alcohol consumption, obesity, and psychogenic stress.
- Psoriasis susceptibility genes and variants reside on various chromosomes. The psoriasis susceptibility locus 1 (*PSORS1*) on chromosome 6p is a key gene locus, accounting for up to 50% of disease heritability. The major histocompatibility complex antigen HLA-Cw6 and tumor necrosis factor (TNF)-α are major psoriasis susceptibility genes, along with interleukin (IL)-23 and many other loci. There appears to be a general role for T lymphocytes and a specific role for TH17 lymphocytes in psoriasis pathogenesis and as indicators of psoriasis risk.
- Interactions between dermal dendritic cells and activated Th-1 and Th-17 cells in concert with numerous growth factors and cytokines (eg, TNF-α, interferon gamma, IL-1) cause epidermal hyperplasia and dermal inflammation.

CLINICAL PRESENTATION

- Skin lesions in plaque psoriasis (psoriasis vulgaris) are erythematous, red-violet in color, at least 0.5 cm in diameter, well demarcated, and typically covered with silver flaking scales. They may appear as single lesions on predisposed areas (eg, knees and elbows) or generalized over a wide body surface area (BSA).
- Pruritus may be severe and require treatment to minimize excoriations from frequent scratching. Lesions may be physically debilitating or socially isolating.
- Preexisting psoriasis can be exacerbated by drugs (eg, lithium, nonsteroidal anti-inflammatory drugs [NSAIDs], antimalarials, β-adrenergic blockers, fluoxetine, and withdrawal of corticosteroids), times of stress, and seasonal changes.
- Potential comorbidities include psoriatic arthritis, depression, anxiety, hypertension, obesity, diabetes mellitus, Crohn disease, and alcoholism.
- Psoriatic arthritis develops in about 30% of patients with plaque psoriasis. It most commonly presents as polyarticular peripheral arthritis but can vary widely with peripheral and/or axial, monoarticular, or polyarticular patterns.

DIAGNOSIS

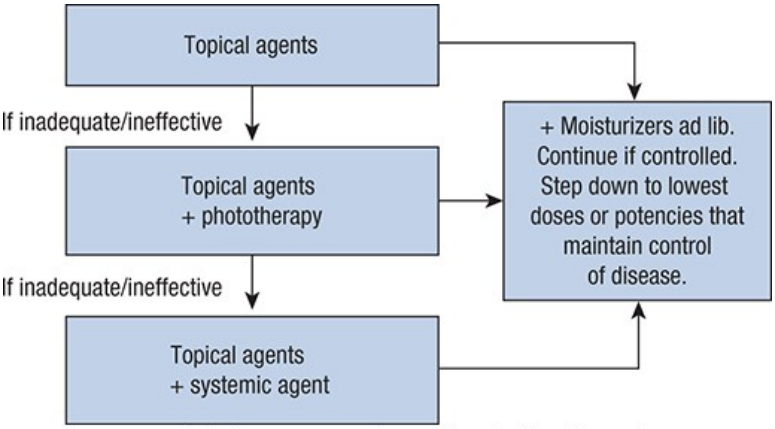
- Diagnosis is based on physical examination findings of characteristic lesions. Skin biopsies are not diagnostic of psoriasis.
- Classification of psoriasis as mild, moderate, or severe is based on BSA and Psoriasis Area and Severity Index (PASI) measurements. A 2011 European classification system defines severity of plaque psoriasis as either mild or moderate-to-severe.

TREATMENT

- Goals of Treatment: Minimize or eliminate skin lesions, alleviate pruritus, reduce frequency of flare-ups, treat comorbid conditions, screen for and manage lifestyle factors that may trigger exacerbations, avoid adverse treatment effects, provide cost-effective treatment, provide appropriate counseling (eg, stress reduction), and maintain or improve quality of life.
- See **Figures 17-1** and **17-2** for psoriasis treatment algorithms based on disease severity.

FIGURE 17-1

Treatment algorithm for mild-to-moderate psoriasis.

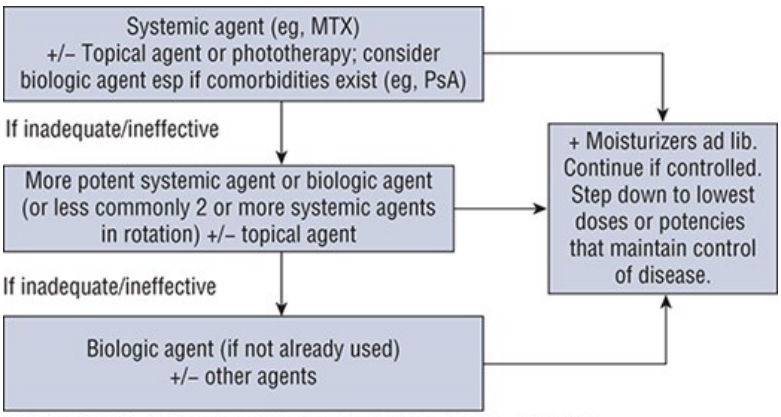


Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

FIGURE 17-2

Treatment algorithm for moderate-to-severe psoriasis.

(MTX, methotrexate; PsA, psoriatic arthritis.)



Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

Nonpharmacologic Therapy

- Nonmedicated moisturizers help maintain skin moisture, reduce skin shedding, control scaling, and reduce pruritus.
- Oatmeal baths further reduce pruritus, and regular use may decrease need for systemic antipruritic drugs. Harsh soaps and detergents should be avoided. Cleansing should involve tepid water, preferably with lipid- and fragrance-free cleansers.

- Sunscreens (preferably sun protection factor [SPF] 30 or higher) should be used when outdoors.
- Stress management can improve extent and severity of psoriasis.

Pharmacologic Therapy

Topical Therapies

- **Corticosteroids** (**Table 17-1**) have anti-inflammatory, antiproliferative, immunosuppressive, and vasoconstrictive effects. They are recommended in U.S. treatment guidelines as first-line treatment for limited psoriasis either as monotherapy or with nonsteroidal topical agents; potency can be enhanced with different vehicles, and as needed by occlusion.

  ✔ Lower-potency products should be used for infants and for lesions on the face, intertriginous areas, and areas with thin skin. Mid- to high-potency agents are recommended as initial therapy for other body areas in adults. Reserve the highest potency corticosteroids for patients with very thick plaques or recalcitrant disease, such as plaques on the palms and soles. Use potency class I corticosteroids for only 2–4 weeks.

  ✔ Ointments are the most occlusive and most potent formulations because of enhanced penetration into the dermis. Patients may prefer the less greasy creams or lotions for daytime use.

  ✔ Cutaneous adverse effects include skin atrophy, acne, contact dermatitis, hypertrichosis, folliculitis, hypopigmentation, perioral dermatitis, striae, telangiectasias, and traumatic purpura. Systemic adverse effects may occur with superpotent agents or with extended or widespread use of midpotency agents. Such effects include hypothalamic–pituitary–adrenal axis suppression and less commonly Cushing syndrome, osteonecrosis of the femoral head, cataracts, and glaucoma.

- **Calcipotriene** (Dovonex) and **calcitriol** (Vectical) are vitamin D_3 analogs that bind to vitamin D receptors, which inhibit keratinocyte proliferation and enhance keratinocyte differentiation. They also inhibit T-lymphocyte activity. These agents can be used as first-line monotherapy or in combination with a topical corticosteroid for mild plaque psoriasis. Calcipotriene 0.005% cream, ointment, foam, or gel is applied to affected areas twice daily. Calcitriol ointment 3 mcg/g is applied to affected areas twice daily. Adverse effects include mild irritant contact dermatitis, burning, pruritus, edema, peeling, dryness, and erythema.

- **Tazarotene** (Tazorac) is a topical retinoid that normalizes keratinocyte differentiation, diminishes keratinocyte hyperproliferation, and clears the inflammatory infiltrate in psoriatic plaques. It is available as a 0.05% or 0.1% gel and cream and is applied once daily (usually in the evening). It may be combined with a topical corticosteroid to enhance efficacy and reduce irritation. Adverse effects of tazarotene include a high incidence of dose-dependent irritation at application sites, resulting in burning, stinging, and erythema. Irritation may be reduced by using the cream formulation, lower concentration, alternate-day applications, or short-contact (30–60 minutes) treatment. Tazarotene is contraindicated in pregnancy and should not be used in women of childbearing potential unless effective contraception is being used.

- **Anthralin** has a direct antiproliferative effect on epidermal keratinocytes, normalizing keratinocyte differentiation. Short-contact anthralin therapy (SCAT) is the preferred regimen, with ointment applied only to the thick plaque lesions for 2 hours or less and then wiped off. Zinc oxide ointment or nonmedicated stiff paste should be applied to the surrounding normal skin to protect it from irritation. Use anthralin with caution, if at all, on the face and intertriginous areas due to potential for severe irritation. Anthralin concentrations for SCAT range from 1% to 4% or as tolerated. Concentrations for continuous therapy vary from 0.05% to 0.4%. Anthralin may cause severe skin irritation, folliculitis, and allergic contact dermatitis.

- **Coal tar** is keratolytic and may have antiproliferative and anti-inflammatory effects. Formulations include crude coal tar and tar distillates (liquor carbonis detergens) in ointments, creams, and shampoos. Coal tar is used infrequently due to limited efficacy and poor patient adherence and acceptance. It has a slower onset of action than calcipotriene, has an unpleasant odor, and stains clothing. Adverse effects include folliculitis, acne, local irritation, and phototoxicity. Risk of teratogenicity is low when used in pregnancy.

- **Salicylic acid** has keratolytic properties and has been used in shampoos or bath oils for scalp psoriasis. It enhances penetration of topical corticosteroids, thereby increasing corticosteroid efficacy. Systemic absorption and toxicity can occur, especially when applied to >20% BSA or in patients with renal impairment. Salicylic acid should not be used in children. It may be used for limited and localized plaque psoriasis in

pregnancy.

- **Pimecrolimus** 1% cream (Elidel) is a calcineurin inhibitor shown to be effective for plaque psoriasis when used under occlusion and for patients with moderate-to-severe inverse psoriasis (involving intertriginous areas). It may be a useful alternative for patients with intertriginous or facial lesions because it is less irritating than calcipotriene and does not have the topical adverse effects of corticosteroids (eg, skin atrophy).

TABLE 17-1

Topical Corticosteroid Potency Chart

Potency Rating	Topical Corticosteroid
Class 1: Superpotent	Betamethasone dipropionate 0.05% ointment (Diprolene and Diprosone ointment) Clobetasol propionate 0.05% lotion/spray/shampoo/foam (Clobex lotion/spray/shampoo, OLUX and OLUX-E foam) Clobetasol propionate 0.05% cream, gel, solution (scalp), ointment (Cormax, Temovate, Dermovate) Diflorasone diacetate 0.05% ointment (Florone, Psorcon, ApexiCon) Flurandrenolide tape 4 mcg/cm^2 (Cordran) Halobetasol propionate 0.05% cream, lotion, ointment (Ultravate)
Class 2: Potent	Amcinonide 0.1% ointment (Cyclocort, Amcort) Betamethasone dipropionate 0.05% cream/gel (Diprolene cream, gel, and Diprosone cream) Desoximetasone 0.25% cream, gel, ointment (Topicort) Diflorasone diacetate 0.05% ointment (ApexiCon, Florone, Psorcon) Fluocinonide 0.05% cream, gel, ointment (Lidex) Halcinonide 0.1% cream (Halog)
Class 3: Upper mid-strength	Amcinonide 0.1% cream (Cyclocort) Betamethasone valerate 0.1% ointment (Betnovate/Valisone) Diflorasone diacetate 0.05% cream (Psorcon, Florone, ApexiCon) Fluticasone propionate 0.005% ointment (Cutivate) Mometasone furoate 0.1% ointment (Elocon) Triamcinolone acetonide 0.5% cream and ointment (Aristocort)
Class 4: Mid-strength	Betamethasone dipropionate 0.05% spray (Sernivo) Betamethasone valerate 0.12% foam (Luxiq) Clocortolone pivalate 0.1% cream (Cloderm) Desoximetasone 0.05% cream and gel (Topicort LP) Fluocinolone acetonide 0.025% ointment (Synalar) Fluocinolone acetonide 0.2% cream (Synalar-HP) Hydrocortisone valerate 0.2% ointment (Westcort) Mometasone furoate 0.1% cream, lotion, solution (Elocon) Triamcinolone acetonide 0.1% ointment (Kenalog)
Class 5: Lower mid-strength	Betamethasone dipropionate 0.05% lotion (Diprosone) Betamethasone valerate 0.1% cream and lotion (Betnovate/Valisone) Desonide 0.05% lotion, ointment, gel (DesOwen, Tridesilon) Fluocinolone acetonide 0.01% shampoo (Capex) Fluocinolone acetonide 0.01%, 0.025%, 0.03% cream (Synalar) Flurandrenolide 0.05% cream and lotion (Cordran) Fluticasone propionate 0.05% cream and lotion (Cutivate) Hydrocortisone butyrate 0.1% ointment, lotion, cream (Locoid, Locoid Lipocream)

	Hydrocortisone probutate 0.1% cream (Pandel) Hydrocortisone valerate 0.2% cream (Westcort) Prednicarbate 0.1% cream and ointment (Dermatop) Triamcinolone acetonide 0.1% cream, ointment and lotion (Kenalog)
Class 6: Mild (low potency)	Alclometasone dipropionate 0.05% cream and ointment (Aclovate) Betamethasone valerate 0.05% cream and ointment (Valisone) Desonide 0.05% cream, ointment, gel (DesOwen, Desonate, Tridesilon) Desonide 0.05% foam (Verdeso) Fluocinonide acetonide 0.01% cream and solution (Synalar) Fluocinonide acetonide 0.01% FS oil (Derma-Smoothe)
Class 7: Least Potent	Hydrocortisone 0.5%, 1%, 2%, 2.5% cream, lotion, spray, and ointment (various brands)

Phototherapy and Photochemotherapy

- Phototherapy consists of nonionizing electromagnetic radiation, either ultraviolet A (UVA) or ultraviolet B (UVB), as light therapy for psoriatic lesions. UVB is given alone as either broadband or narrowband (NB-UVB). UVB is also given as photochemotherapy with topical agents such as crude coal tar (Goeckerman regimen) or anthralin (Ingram regimen) for enhanced efficacy. UVA is generally given with a photosensitizer such as an oral psoralen to enhance efficacy; this regimen is called PUVA (psoralen + UVA treatment). Adverse effects of phototherapy include erythema, pruritus, xerosis, hyperpigmentation, and blistering. Patients must be provided with eye protection during and for 24 hours after PUVA treatments. PUVA therapy may also cause nausea or vomiting, which may be minimized by taking the oral psoralens with food or milk. Long-term PUVA use can lead to photoaging and cataracts. PUVA is also associated with a dose-related risk of carcinogenesis.

Systemic Nonbiologic Agents

- **Acitretin** (Soriatane) is a retinoic acid derivative and the active metabolite of etretinate. Retinoids may be less effective than methotrexate or cyclosporine when used as monotherapy. Acitretin is more commonly used in combination with topical calcipotriene or phototherapy. Although low-dose acitretin (25 mg/day) is safer and better tolerated than higher-dose (50 mg/day) therapy, low-dose acitretin is not recommended as monotherapy. Therapy is continued until lesions have resolved. It is better tolerated when taken with meals. Adverse effects include hypertriglyceridemia and mucocutaneous effects such as dryness of the eyes, nasal and oral mucosa; chapped lips; cheilitis; epistaxis; xerosis; brittle nails; and burning skin. Ophthalmologic changes include photosensitivity, decreased color vision, and impaired night vision. Hepatitis and jaundice are rare and liver enzyme elevations are usually transient. All retinoids are teratogenic and are contraindicated in pregnancy. Acitretin should not be used in women of childbearing potential unless they use effective contraception for the duration of therapy and for at least 2 years after drug discontinuation. Blood donation (men and women) is not permitted during and for at least 1 year after treatment.

- **Cyclosporine** is a systemic calcineurin inhibitor that is effective for inducing remission and for maintenance therapy of moderate-to-severe plaque psoriasis. Intermittent short-course therapy (<12 weeks) is preferable to continuous therapy because it appears to reduce the risk of nephrotoxicity. Cyclosporine is significantly more effective than etretinate and has similar or slightly better efficacy than methotrexate. The usual oral dose is 2.5–5 mg/kg/day given in two divided doses. After inducing remission, maintenance therapy using low doses (1.25–3 mg/kg/day) may prevent relapse. When discontinuing cyclosporine, a gradual taper of 1 mg/kg/day each week may prolong the time before relapse compared to abrupt discontinuation. Because more than half of patients stopping cyclosporine relapse within 4 months, patients should be given appropriate alternative treatments shortly before or after discontinuing cyclosporine. Adverse effects include nephrotoxicity, hypertension, hypomagnesemia, hyperkalemia, hypertriglyceridemia, hypertrichosis, and gingival hyperplasia. The risk of skin cancer increases with the duration of treatment and with prior PUVA treatments.

- **Methotrexate** has anti-inflammatory effects due to its effects on T-cell gene expression and also has cytostatic effects. It is more effective than acitretin and has similar or slightly less efficacy than cyclosporine. Methotrexate can be administered orally, subcutaneously (SC), or intramuscularly. The starting dose is 7.5–15 mg once weekly, increased incrementally by 2.5 mg every 2–4 weeks until response; maximal doses

are 25 mg weekly. Adverse effects include nausea, vomiting, stomatitis, macrocytic anemia, and hepatic and pulmonary toxicity. Nausea and macrocytic anemia may be reduced by giving oral folic acid 1–5 mg daily. It is an abortifacient and teratogenic and is contraindicated in pregnancy.

- **Tofacitinib** (Xeljanz, Xeljanz XR) is a small-molecule Janus Kinase (JAK) inhibitor that blocks signaling through common receptors for cytokines including IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21. It is indicated for the treatment of adults with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other disease-modifying antirheumatic drugs (DMARDs). The recommended dose (in combination with nonbiologic DMARDs) is 5 mg orally twice daily or 11 mg (extended-release) once daily. The recommended dose is 5 mg once daily in patients with moderate-to-severe renal impairment or moderate hepatic impairment. Tofacitinib should not be used in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine.

- **Apremilast** (Otezla) is a small-molecule inhibitor of phosphodiesterase 4 (PDE4), which increases intracellular cyclic AMP (cAMP) and reduces production of proinflammatory mediators. It is indicated for treatment of adults with active psoriatic arthritis and patients with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Recommended dosing is 10 mg orally on day 1, 10 mg twice daily on day 2, 10 mg in the morning and 20 mg in the evening on day 3, 20 mg twice daily on day 4, 20 mg in the morning and 30 mg in the evening on day 5, then 30 mg twice daily thereafter. The dosage regimen should be reduced in severe renal impairment. The most common adverse reactions (≥5%) are diarrhea, nausea, and headache.

Systemic Biologic Agents

- Biologic agents are considered for moderate-to-severe psoriasis when other systemic agents are inadequate or contraindicated or when comorbidities exist. Cost considerations tend to limit their use as first-line therapy.

TNF Inhibitors

- **Adalimumab** (Humira) is a monoclonal TNF-α antibody that provides rapid control of psoriasis. It is indicated for psoriatic arthritis and treatment of adults with moderate-to-severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy. The recommended dose for psoriatic arthritis is 40 mg SC every other week. The recommended dose for adults with plaque psoriasis is an initial dose of 80 mg SC, followed by 40 mg every other week starting 1 week after the initial dose. The most common adverse reactions are infections (eg, upper respiratory and sinusitis), injection site reactions, headache, and rash.

- **Etanercept** (Enbrel) is a fusion protein that binds TNF-α, competitively interfering with its interaction with cell-bound receptors. Unlike the chimeric infliximab, etanercept is fully humanized, minimizing the risk of immunogenicity. Etanercept is FDA approved for reducing signs and symptoms and inhibiting the progression of joint damage in patients with psoriatic arthritis; it can be used alone or in combination with methotrexate. It is also indicated for patients 4 years or older with chronic moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The recommended dose for psoriatic arthritis is 50 mg SC once weekly. For plaque psoriasis, the dose is 50 mg SC twice weekly (administered 3 or 4 days apart) for 3 months, followed by a maintenance dose of 50 mg once weekly. Adverse effects include local reactions at the injection site (20% of patients), respiratory tract and GI infections, abdominal pain, nausea and vomiting, headaches, and rash.

- **Infliximab** (Remicade) is a chimeric monoclonal antibody directed against TNF-α. It is indicated for psoriatic arthritis and chronic severe plaque psoriasis. The recommended dose is 5 mg/kg by IV infusion at weeks 0, 2, and 6, then every 8 weeks thereafter. For psoriatic arthritis, it may be used with or without methotrexate. Adverse effects include headaches, fever, chills, fatigue, diarrhea, pharyngitis, and upper respiratory and urinary tract infections. Hypersensitivity reactions (urticaria, dyspnea, and hypotension) and lymphoproliferative disorders have been reported.

- **Certolizumab pegol** (Cimzia) is a humanized antigen-binding fragment of a monoclonal antibody that is further conjugated with a polyethylene glycol moiety. This binds to TNF-α, blocking its interaction with TNF receptors. It is indicated for treatment of adults with psoriatic arthritis or moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Recommended dosing is 400 mg (as 2 × 200-mg SC injections) every 2 weeks, with a dose-reduced regimen for patients <90 kg: 400 mg (as 2 × 200-mg SC injections) initially and at weeks 2 and 4, followed by 200 mg SC every other week.

Interleukin-12/23 Inhibitors

- **Ustekinumab** (Stelara) is an IL-12/23 monoclonal antibody approved for the treatment of psoriasis in adults 18 years or older with moderate-to-

severe plaque psoriasis. The recommended dose for patients weighing ≤100 kg is 45 mg SC initially and 4 weeks later, followed by 45 mg SC every 12 weeks. For patients weighing >100 kg, the dose is 90 mg SC initially and 4 weeks later, followed by 90 mg SC every 12 weeks. Common adverse effects include upper respiratory infections, headache, and tiredness. Serious adverse effects include those seen with other biologics, including tubercular, fungal, and viral infections and cancers. Reversible posterior leukoencephalopathy syndrome (RPLS) has also been reported.

Interleukin-17A Inhibitors

- **Secukinumab** (Cosentyx), **ixekizumab** (Taltz), and **brodalumab** (Siliq) are monoclonal antibodies that inhibit IL-17A, a proinflammatory cytokine that binds to receptors on keratinocytes, leading to inflammation and recruitment of inflammatory cell types, resulting in psoriatic plaques. These agents have comparable efficacy and similar adverse effects (eg, nasopharyngitis, upper respiratory tract infections, injection site reactions).

  ✔ Secukinumab is a fully human IgG1κ monoclonal antibody that selectively binds and inhibits IL-17A. Recommended dosing for plaque psoriasis is 300 mg SC at weeks 0, 1, 2, 3, and 4 followed by 300 mg SC every 4 weeks.

  ✔ Ixekizumab is a humanized IgG4 monoclonal antibody that neutralizes IL-17A. Recommended dosing is an initial dose of 160 mg SC followed by 80 mg every 2 weeks until week 12, followed by a maintenance phase of 80 mg SC every 4 weeks thereafter. Neutralizing anti-ixekizumab antibodies develop over time and are associated with reduced drug concentrations and loss of efficacy.

  ✔ Brodalumab is a fully human IgG2 anti-IL-17RA monoclonal antibody that binds to the IL-17 receptor A and blocks the biologic activities of multiple IL-17 subtypes. The recommended dose is 210 mg SC on weeks 0, 1, and 2, then 210 mg every 2 weeks thereafter.

Interleukin-23 Inhibitors

- **Guselkumab** (Tremfya), **tildrakizumab** (Ilumya), and **risankizumab** (Skyrizi) inhibit IL-23, which induces a population of T-helper cells (TH17 cells) with a unique inflammatory gene signature important in the pathogenesis of psoriasis and other autoimmune diseases. Neutralizing antibodies to specific IL-17 inhibitors have been reported that may be associated with lower biologic serum concentrations and reduced efficacy.

  ✔ Guselkumab is a fully human IgG1 lambda monoclonal antibody that blocks the p19 subunit of IL-23. The recommended dose is 100 mg SC at weeks 0 and 4, and then every 8 weeks thereafter.

  ✔ Tildrakizumab is a humanized IgG1 monoclonal antibody designed to selectively block IL-23 by binding to the p19 subunit. The recommended dose is 100 mg SC administered only by a healthcare provider at weeks 0 and 4, and then every 12 weeks thereafter.

  ✔ Risankizumab is a humanized IgG1 monoclonal antibody that selectively inhibits IL-23 by binding to the p19 subunit. The recommended dose is 150 mg (two 75-mg SC injections) at weeks 0 and 4 and then every 12 weeks thereafter.

Combination Therapies

- Combination therapy may be used to enhance efficacy or minimize toxicity. Combinations can include two topical agents, a topical agent plus phototherapy, a systemic agent plus topical therapy, a systemic agent plus phototherapy, two systemic agents used in rotation, or a biologic agent with either a nonbiologic systemic or topical agent (see **Figs. 17-1** and **17-2**).

- The combination of a topical corticosteroid and a topical vitamin D_3 analogue is effective and safe with less skin irritation than monotherapy with either agent. The combination product containing calcipotriene and betamethasone dipropionate ointment (Taclonex) is effective for relatively severe psoriasis and may also be steroid sparing.

- The combination of retinoids with phototherapy (eg, tazarotene plus broadband UVB, acitretin plus broadband UVB or NB-UVB) also increases efficacy. Because retinoids may be photosensitizing and increase the risk of burning after UV exposure, doses of phototherapy should be reduced to minimize adverse effects. The combination of acitretin and PUVA (RE-PUVA) may be more effective than monotherapy with either treatment.

- Phototherapy has also been used with other topical agents, such as UVB with coal tar (Goeckerman regimen) to increase treatment response, because coal tar is also photosensitizing.

- Cyclosporine in combination with calcipotriene/betamethasone dipropionate is superior to cyclosporine alone. Cyclosporine may also be used with SCAT, but it should not be used with PUVA due to reduced efficacy and an increased risk of cutaneous malignancies.
- The combination of methotrexate and UVB appears to be synergistic. Low-dose methotrexate (eg, 7.5–10 mg once weekly) in combination with a biologic agent may be beneficial.

Alternative Drug Treatments

- **Mycophenolate mofetil** (CellCept) inhibits DNA and RNA synthesis and may have a lymphocyte antiproliferative effect. Although not FDA approved for psoriasis indications, oral mycophenolate mofetil may be effective in some cases of moderate-to-severe plaque psoriasis.
- **Hydroxyurea** inhibits cell synthesis in the S phase of the DNA cycle. It is occasionally used off-label for patients with recalcitrant severe psoriasis, but biologic agents may be a better option in these patients.

EVALUATION OF THERAPEUTIC OUTCOMES

- Help patients understand the general principles of therapy and the importance of medication adherence.
- A positive response involves normalization of involved areas of skin, as measured by reduced erythema and scaling, as well as reduction of plaque elevation.
- Successful management also includes control of itching and comorbid conditions such as dyslipidemia, hypertension, psoriatic arthritis, and depression.
- PASI is a uniform method to determine the extent of BSA affected, along with the degree of erythema, induration, and scaling. In the United States, severity of psoriasis is classified as mild, moderate, or severe:
    - ✔ Mild: ≤5% BSA involvement
    - ✔ Moderate: PASI ≥8 (higher in trials of biologics)
    - ✔ Severe: PASI ≥10 or Dermatology Life Quality Index (DLQI) ≥10 or BSA ≥10%
- The Physician Global Assessment can also be used to summarize erythema, induration, scaling, and extent of plaques relative to baseline assessment.
- Achievement of efficacy by any therapeutic regimen requires days to weeks. Initial dramatic response may be achieved with some agents, such as corticosteroids. However, sustained benefit with pharmacologically specific antipsoriatic therapy may require 2–8 weeks or longer for clinically meaningful response.

See Chapter 114, Psoriasis, authored by Rebecca M. Law and Wayne P. Gulliver, for a more detailed discussion of this topic.