Psoriasis is the most common autoimmune condition in the US, affecting 7.5 million people. It is a complex, genetically linked disease; 1 in every 3 patients with psoriasis has a relative with the condition. The human and economic tolls are significa-nt. Patients with psoriasis have lower quality of life scores, along with increased occurrences of depression, anxiety and suicidal ideation. In the US, more than $63 million is spent annually in direct healthcare costs for psoriasis.

Currently, there is no cure; however, a variety of treatments (topical, systemic, phototherapy) are available to manage symptoms, minimize disease progression, and improve quality of life. Since the early 2000s, research into the immunopathogenesis of psoriasis has led to the development of biologic agents that target specific components of the immune system. Despite the availability of multiple treatments, patients with psoriasis in the US are often under treated, or untreated. Untreated or under treated psoriasis leads to disseminated disease and poten-tially, to joint impairment in the form of psoriatic arthritis (PsA), which causes pain and stiffness of affected joints.

While psoriasis treatment guidelines recommend that trained specialty providers prescribe systemic therapies for patients with this disease, community practitioners should have a sufficient knowledge base to monitor treatment. Frequent patient interactions allow community practitioners, including pharmacists and nurse practitioners, to play an important role in psoriasis management. This issue will review basic information about cutaneous psoriasis and summarize various treatments, so practitioners can better manage and educate patients.

Learning Objectives

Pharmacist

1. Describe psoriasis symptoms and how body surface area and the Psoriasis Area Severity Index (PASI) are used in assessing psoriasis severity.

2. List commonly used topical treatments. Counsel patients regarding administration, side effects, and precautions.

3. Discuss the epidemiology and contributing factors for the development of psoriasis.

4. Compare and contrast systemic treatments used for psoriasis, including effectiveness, side effects, and precautions.
Accreditation

PharmCon, Inc. is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

PharmCon, Inc. reports CPE credits to CPE Monitor automatically after credit is earned. Your NABP ePID and birthdate must be in your online profile for successful credit submission.

PharmCon, Inc. reports CPE credits to CE Broker automatically after credit is earned. Your license number must be in your online professional profile for successful credit submission.

Universal Activity Number
Pharmacist
0798-9999-18-248-H01-P

Credit Hours
1.5 Hours

Activity Type
Knowledge-Based

CE Broker Tracking Number
20-686912

Activity Offline Date
May 16, 2021

Activity Release Date
March 1, 2020

ACPE Expiration Date
June 16, 2021

Educational Support Provided By
Pharmaceutical Education Consultants, Inc.

All opinions expressed by the author(s) are strictly their own and not necessarily approved or endorsed by PharmCon, Inc.

Consult full prescribing information on any drugs or devices discussed.
CE-PRN is a division of PharmCon, Inc.

© 2019 PharmCon, Inc.
All rights reserved.
None of the contents of this publication may be reproduced in any form without the written permission of the publisher.
Introduction

Psoriasis is the most common autoimmune condition in the US, affecting 7.5 million people.\(^1\) It is a complex, genetically linked disease; 1 in every 3 patients with psoriasis has a relative with the condition.\(^2\) The human and economic tolls are significant. Patients with psoriasis have lower quality of life scores, along with increased occurrences of depression, anxiety and suicidal ideation.\(^3\) In the US, more than $63 million is spent annually in direct healthcare costs for psoriasis.\(^4\) Currently, there is no cure; however, a variety of treatments (topical, systemic, phototherapy) are available to manage symptoms, minimize disease progression, and improve quality of life.\(^5-7\) Since the early 2000s, research into the immunopathogenesis of psoriasis has led to the development of biologic agents that target specific components of the immune system. Despite the availability of multiple treatments, patients with psoriasis in the US are often under treated, or untreated.\(^8\) Untreated or under treated psoriasis leads to disseminated disease and potentially, to joint impairment in the form of psoriatic arthritis (PsA), which causes pain and stiffness of affected joints.\(^8\) While psoriasis treatment guidelines recommend that trained specialty providers prescribe systemic therapies for patients with this disease, community practitioners should have a sufficient knowledge base to monitor treatment. Frequent patient interactions allow community practitioners, including pharmacists and nurse practitioners, to play an important role in psoriasis management. This issue will review basic information about cutaneous psoriasis and summarize various treatments, so practitioners can better manage and educate patients.

The Bottom Line

- Psoriasis is recognized as an immune-mediated, chronic, systemic inflammatory condition. It is believed that abnormal T-cell activity contributes to overproduction of epidermal cells, leading to the cutaneous (skin) symptoms of psoriasis. The inflammatory process leads to the production of various cytokines, such as tumor necrosis factor-α (TNFα), interferon gamma, and interleukins (IL-12, IL-17A, and IL-23).

- There are 5 clinical subtypes of cutaneous psoriasis, the most common of which is plaque psoriasis (up to 90% of patients). Severity is often defined by the percentage of body surface area involved; severe disease usually involves more than 10%.

- About 80% of patients with mild to moderate psoriasis can be managed well with topical medications. Topical therapy is used along with systemic therapies for patients with moderate to severe disease, who need more aggressive treatment.

- Corticosteroids are the cornerstone of topical therapy. Other agents include emollients, moisturizers, keratolytics, coal tar and anthralin, topical vitamin D analogs (eg, calcipotriene, calcitriol), and tazarotene.

- As many as 20-30% of people with psoriasis have moderate to severe disease, requiring treatment with phototherapy and immunosuppressive or immunomodulatory drugs such as methotrexate, cyclosporine, retinoids, apremilast, and biologic agents.

- Biologics carry a small but significant risk of opportunistic infections such as influenza, upper respiratory tract infections including tuberculosis, and candidiasis. Biologics are contraindicated in patients with active, serious infections.

Background

Psoriasis is no longer thought of as a skin disorder; instead, it is recognized as an immune-mediated, chronic, systemic inflammatory condition. It is also considered a multisystem disease because it is linked with several other disorders including: inflammatory bowel disease
(eg, Crohn’s, ulcerative colitis)\(^9,10\), cardiovascular disease, and metabolic syndrome or components of the syndrome (eg, obesity, diabetes).\(^11,12\) The typical age at onset is bimodal (two peak age ranges) at 16 to 22 years and 57 to 60 years – 75% of cases are diagnosed before 46 years of age. Women and men are equally affected. Psoriasis is more common among Caucasians (3.6%), but is also seen in Blacks (1.9%) and Hispanics (1.6%).\(^13\) Ten percent or more of individuals have one or more of the genes required for psoriasis development. However, only 2-3% of people get the disease. It is thought that the genetic predisposition and external factors must both be involved. External factors that lead to psoriatic flares have been identified, including:\(^5,14,15\)

- Environmental (eg, infection, emotional stress, cold weather, skin injury)
- Medications (eg, beta-blockers, lithium, nonsteroidal anti-inflammatory drugs [NSAIDs], tetracyclines, antimalarials [chloroquine, hydroxychloroquine])
- Lifestyle (eg, tobacco, possibly alcohol)

Abnormal changes take place in epidermal cells with the activation of immune system processes. Predominantly, keratinocytes (epidermal cells producing keratin) initiate the activation of T-cells. It is believed that abnormal T-cell activity contributes to overproduction of epidermal cells, leading to the cutaneous presentation of psoriasis. The inflammatory process leads to the production of various cytokines, such as tumor necrosis factor- (TNF), interferon gamma, and interleukins (IL-12, IL-17A, and IL-23).\(^6,7,16\) Epidermal cells normally turn over every 21 to 28 days; however, turnover occurs every 3 to 4 days in patients with psoriasis.\(^6\)

**Symptoms and Disease Classification**

There are 5 clinical subtypes of cutaneous psoriasis, the most common of which is plaque psoriasis (up to 90% of patients). Classification is generally based on clinical features, which often overlap. Nail involvement is often a marker for psoriatic arthritis. (See Table 1.) Severity may be defined by the percentage of body surface area (BSA) involved. Most patients (80%) have 3 to 10% BSA involvement and are considered to have mild to moderate disease.\(^2,5\) Severe disease involves greater than 10% BSA. However, regardless of BSA, lesions affecting the hands, face, feet or genitals are classified as severe.\(^5\) The tool used most often to assess disease severity in clinical trials is the Psoriasis Area Severity Index (PASI).\(^17\) It combines the degree of severity of lesions (erythema, thickness, and scaling) and the area affected into a single score that ranges from 0 (no disease) to 72 (maximal disease).\(^17\) "PASI 75" is the current benchmark of primary endpoints for most clinical trials; it reflects the percentage of patients who achieve a 75% or more reduction in their PASI score from baseline.

**Treatment Recommendations**

Selection of therapy should be individualized based on patient's age, type of psoriasis, area involved, severity of the disease, previous treatments, cost of treatment, and coexisting conditions.\(^6,10\) Some experts recommend treating to a goal of at least a 50% reduction in the patient’s baseline PASI score (and evaluating treatment every 6 to 8 weeks).\(^6,18\) If an acceptable goal hasn’t been met after 3 months, or improvement isn’t achieved after 6 months, the National Psoriasis Foundation (NPF) recommends changing the dose, adding a new treatment, or switching to a different treatment.\(^2\)
See Table 2 for the mechanism of action, dosing, side effects, and other considerations for selected medications.

**Topical Therapy**

About 80% of patients with mild to moderate psoriasis can be managed well with topical medications.\(^{10,19}\) It is considered first-line treatment for patients with mild disease (up to 5% BSA). In addition, topical therapy is used with systemic therapies in patients with moderate to severe disease (greater than 5% BSA) who require more aggressive treatment. Corticosteroids are the cornerstone of topical therapy. Other agents include emollients, moisturizers, keratolytics, coal tar and anthralin, topical vitamin D analogs (eg, calcipotriene, calcitriol), and a retinoid (eg, tazarotene). Two active ingredients in over the counter (OTC) topicals, salicylic acid and coal tar, are approved by the FDA for the treatment of psoriasis.

### Table 1. Classification of Cutaneous Forms of Psoriasis\(^{1,5,13}\)

<table>
<thead>
<tr>
<th>Type and Frequency Range</th>
<th>Common location(s)</th>
<th>Presentation / Comments</th>
</tr>
</thead>
</table>
| **Plaque** (psoriasis vulgaris) 58-80% | knees, elbows, lower back, scalp (nail involvement is a subtype) | • raised, dry, silvery-white or reddish skin patches which can be itchy and painful  
• nail presentation: pitting, separation of nail bed, nail scaling and translucent discoloration (considered a marker for psoriatic arthritis) |
| **Inverse** (flexural, intertriginous psoriasis) 12-26% | body folds such as: armpits, behind the knee, groin, genitals, buttocks | • smooth, wet, red or white patches  
• no scales due to moist area  
• may have secondary candidiasis |
| **Guttate** (droplet psoriasis) 0.6-20% | trunk, arms, legs | • pink/fine-scale, dot-like lesions  
• often triggered by recent upper respiratory infection (Group A Hemolytic Strep) |
| **Erythrodermic** (exfoliative psoriasis) 0.4-3% | most (or all) of body surface | • rare, severe form with generalized erythema (including intense burning pain itching, fever, chills, malaise)  
• potentially life threatening (hypothermia, heart failure) |
| **Pustular** 1-12% | can occur anywhere, but most often on palms and soles of feet | • pus filled bumps/blisters surrounded by redness; noninfectious  
• may be accompanied by fever and chills |

**Emollients and moisturizers** should be used daily as adjunctive treatment in psoriasis therapy. These products limit the evaporation of water from deeper parts of the skin, relieving itching, redness, and scaling. They also serve as a protective barrier to the outermost skin layers, or the stratum corneum\(^{20,21}\) and enhance the delivery of topical corticosteroids.\(^20\) These products are available in a variety of OTC formulations (eg, lotion, gel, cream, and ointment). Creams and ointments are preferred, since they are more occlusive. They should be applied after showering and washing hands. Ultimately, the formulation should be based on patient preference.\(^20,21\)

**Keratolytic agents**, including salicylic acid, lactic acid, and alpha hydroxyl acids, reduce the “scale load” by helping to normalize the hyperproliferation of keratinocytes. The plaque scales loosen and are lifted off the skin. Keratolytics are available in strengths from 0.5% to 50% in a variety of vehicles – both OTC and by prescription. They are also used as add-on therapy and are most beneficial for thick psoriatic plaques and psoriasis on the scalp.\(^20\) Keratolytics may be used alone or in combination with topical corticosteroids or coal tar.

**Coal tar** is one of the earliest effective psoriatic treatments and continues to be used today. Coal tar slows the rapid turnover of epidermal cells\(^20,21\) and has anti-inflammatory and anti-itch properties.\(^22,23\) Animal data suggested that coal tar is carcinogenic; however, the FDA maintains that there is no evidence that psoriatic treatment strengths (0.5 to 5%)
It has been used alone, and as part of a combination regimen in which patients apply coal tar over the entire body followed by ultraviolet light therapy. Anthralin, also known as dithranol, is similar to coal tar. They have comparable effectiveness (however, both are less effective than topical vitamin D analogs or potent topical corticosteroids) and cause skin discoloration and staining of clothing.

**Topical corticosteroids** are a first-line treatment for mild to moderate psoriasis. They modify the intracellular response of the immune system and decrease vascular permeability, thereby stimulating an immune-mediated anti-inflammatory response. Corticosteroids effectively decrease local cytokine production, reduce skin inflammation, and inhibit hyperproliferation of skin cells. Topical corticosteroids range in potency from Class 1 (super potent) to Class 7 (least potent). It is important for providers to differentiate among potency classes and the side effects associated with each. A useful chart with product classifications is available at https://www.psoriasis.org/aboutpsoriasis/treatments/topicals/steroids/potency-chart. Class 1 topical corticosteroids (eg, fluocinonide 0.1%, clobetasol 0.05%, and halobetasol 0.05%) require a limited duration of treatment. The American Academy of Dermatology recommends limiting application to no more than 2 to 4 consecutive weeks, and not exceeding more than 50 grams of cream or ointment, or 21 capfuls of foam, in a 1-week period. Occlusive dressings should only be used with this class under physician’s supervision. Use of Class 1 topical corticosteroids should be avoided on the face, scalp, armpit, groin, or skin fold areas. Similar considerations may apply to less potent agents, depending on formulation and concentration. The FDA has issued a warning that these medications cause reversible hypothalamic-pituitary-adrenal axis suppression; patients should be monitored closely.

**Topical retinoids** inhibit keratinocyte proliferation, which may reduce the severity of psoriatic plaques. Currently, tazarotene is the only topical retinoid approved for the treatment of psoriasis. Once daily application is similar in effectiveness to twice daily application of topical fluocinonide 0.05%. Compared to tazarotene use alone, combining it with a mid- or high-potency corticosteroid is more effective, producing greater reduction in psoriatic symptom severity and less local irritation. Skin irritation may limit retinoid use; Table 2 lists strategies to minimize this side effect.

**Topical D3 analogs**, such as calcipotriene and calcitriol, are believed to inhibit keratinocyte growth and promote cell differentiation, as well as decrease inflammation of psoriatic lesions by binding to vitamin D receptors on keratinocytes and T lymphocytes. Calcipotriene is the most widely used topical D3 analog. It can be used as monotherapy, or in a combination formulation containing calcipotriene 0.005% and betamethasone dipropionate 0.064%. The combination is more effective and better tolerated than either agent alone. Safety and efficacy data for the combination product show that efficacy was maintained after 1 year of continued use.

---

**Table 2. Selected Medications for Psoriasis**
<table>
<thead>
<tr>
<th>Agent / Indication (Example)</th>
<th>Mechanism</th>
<th>Usual Adult Dosage&lt;sup&gt;A&lt;/sup&gt;</th>
<th>Side Effects&lt;sup&gt;B&lt;/sup&gt;</th>
<th>Comments&lt;sup&gt;B&lt;/sup&gt;</th>
</tr>
</thead>
</table>
| **Topical corticosteroids**<sup>c</sup> | Plaque psoriasis | Class 1 (superpotent): eg, clobetasol propionate 0.05% cream (Temovate<sup>d</sup>)  
Class 2 (potent): eg, fluocinonide 0.05% cream (Lidex<sup>e</sup>, generic)  
Class 3, 4 (upper midpotency, midpotency): eg, triamcinolone 0.5%, 0.1% cream (Kenalog<sup>f</sup>, Triderm<sup>®</sup>, generic) | Antinflammatory; antiproliferative; immunomodulatory; vasoconstrictive  
Class 1 agents: generally applied twice daily for up to 2-4 weeks (max dose, 50 g/week). Class 2-4 agents: generally applied twice daily (no clear treatment duration). Recommendations may vary for specific agents/formulations/concentrations | Local: skin atrophy, striae, telangiectasia, localized burning sensation, folliculitis, acne-like rash (with prolonged use).  
Systemic: HPA axis suppression, hyperglycemia, Cushing syndrome.  
Rapidly reduces inflammation; however, remission may not be complete or lasting. Tachyphylaxis may occur. Once condition improves, ↓ the frequency of applications.  
Local and systemic side effects with chronic use are increased with higher potency agents; systemic absorption is increased by use of occlusive dressings and application to large areas. |
| **Topical vitamin D analogs** | Plaque psoriasis | Calcipotriene: apply ointment once or twice daily; apply cream twice daily.  
Calcitriol: apply twice daily. | Acute: lesional and peri-lesional irritation (especially on face / genitals). Chronic: hypercalcemia (if >100 g/wk), may ↑ sensitivity to UV light (causing skin tumors).  
Calcitriol may be less irritating than calcipotriene. Limiting or avoiding use of phototherapy is recommended. Avoid excessive natural or artificial sunlight exposure. Calcipotriol is another non-proprietary name for calcipotriene. |
| **Topical vitamin D analog with a corticosteroid** | Plaque psoriasis | See topical corticosteroids and topical vitamin D analogs, above. | Ointment: once daily for up to 4 weeks  
Suspension: once daily for up to 8 weeks (max dose, 100 g/week) | Lacks cutaneous side effects & HPA axis suppression; inactivated by UV light, use after phototherapy.  
Efficacy comparable to medium-strength topical steroids. |
| **Topical retinoid (vitamin A derivative)** | Plaque psoriasis | Tazarotene 0.05%, 0.1% gel or cream (Tazorac<sup>®</sup>) | Normalizes keratinocyte proliferation and differentiation; antinflammatory  
Apply at bedtime; start with 0.05% cream or gel; may increase to 0.1% if needed and if tolerated | Common: skin irritation (eg, itching, redness, burning), photosensitiveness. Irritation is less with cream, lower strength, combined with moisturizers and topical steroids, alternate day application, short application contact time (30–60 min).  
Efficacy comparable to medium-strength topical steroids at 12 weeks; however, the duration of response is greater with tazarotene. Tazarotene ↓s the amount of UV light exposure needed for phototherapy. Apply only to affected skin (avoid use on surrounding normal skin); avoid sun exposure; contraindicated in pregnancy (requires pregnancy test). Discontinue if excessive burning, itching, or compromised skin integrity. |

**Oral Immunomodulatory Medications**

| Apremilast (Otezla<sup>®</sup>) | Phosphodiesterase 4 (PDE4) inhibitor specific for cyclic adenosine monophosphate (cAMP) | Starting dose 10 mg on day 1; ↑ to a maintenance dose of 30 mg twice daily by day 6. See PI for titration schedule. | Common: diarrhea, nausea, URI, headache. Less common: depression, insomnia, vomiting, decreased weight.  
Tablet should not be crushed or altered. Titration minimizes diarrhea. Do not coadminister with strong CYP450 inducers (eg, rifampin, phenytoin, carbamazepine); may ↓ apremilast efficacy. |
| Methotrexate | ↓ DNA synthesis and the proliferation of rapidly dividing epithelial cells; also has an immunosuppressive effect on activated T-cells | Weekly single oral dose that is ↑d gradually until an optimal response is achieved; max dose is 30 mg/week. Give with folic acid 1–5 mg/day, (except on the day of methotrexate dosing) to reduce side effects. | Common side effects: fatigue, nausea/vomiting. Boxed warnings include fetal toxicity, bone marrow suppression, skin reactions, GI and liver toxicity, opportunistic infections, pneumonitis, and lymphoma.  
For patients at increased risk of liver toxicity, liver biopsy is recommended at baseline and periodically. Contraindications: pregnancy/ breastfeeding, alcoholism, liver disease, immunodeficiency, bone marrow depression/cytopenias. Drug interactions with folic acid antagonists (eg, sulfonamides), hepatotoxic drugs (eg, acetretin), NSAIDs, cyclosporine. |

---

<sup>A</sup> Usual Adult Dosage: This column lists the typical starting dose and adjustment schedule for each medication as described in the referenced text.

<sup>B</sup> Side Effects and Comments: This column provides a summary of potential side effects and comments related to the use of each medication, as mentioned in the referenced text.
**Table 2. Selected Medications for Psoriasis (continued)**

<table>
<thead>
<tr>
<th>Agent / Indication</th>
<th>Mechanism</th>
<th>Usual Adult Dosage</th>
<th>Side Effects</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **Vitamin A derivatives** Severe psoriasis | Normalizes keratinocyte proliferation and differentiation; anti-inflammatory | Acitretin: 10-50 mg once daily; < 25 mg/day may ↓ side effects.
Isotretinoin: 0.5-1 mg/kg/day in 2 divided doses. Take either drug with meal(s). | Cheilitis (lip inflammation), hair loss, dry mouth, eye and lid dryness, nosebleeds, headache, joint pain, depression (hair loss is less common with isotretinoin). | Not used much due to side effects and warnings. Contraindications: pregnancy (↑ risk of severe birth defects - consult PI for detailed instructions); coadministration of tetracyclines. Acitretin: severe liver or kidney impairment; hyperlipidemia; do not administer with methotrexate. |
| Acitretin (Soriatane®) Isotretinoin (Accutane®, others) - off label use | | | |
| **Biologic Agents** | | | |
| **Adalimumab** (Humira®) Moderate to severe plaque psoriasis and PsA | Fully human anti-TNFα monoclonal antibody | 80 mg subcut at week 0; 40 mg at week 1; then 40 mg every other week. (PsA: 40 mg subcut every other week). | Common: infections, injection site reactions Boxed warnings: serious infections (including TB); malignancies. Other serious side effects: hepatitis B reactivation, new/worsening demyelinating disease, cytopenias, new/worsening heart failure, induction of autoimmunity (eg, lupus-like syndrome). | Biosimilars Amjevita™ and Cytelzo™ have the same indications for plaque psoriasis and PsA. Test for TB and HBV infection before starting treatment; monitor for TB and HBV during treatment. Avoid live vaccines during treatment. |
| **Etanercept** (Enbrel®) Moderate to severe plaque psoriasis (≥ 4 yrs old) and PsA | Fusion protein that binds and inactivates TNFα | 50 mg subcut twice weekly for 3 months; then 50 mg once weekly. | Same as above for adalimumab. | Biosimilar Erelzi™ has the same indications. Same as above regarding TB and HBV tests before and during treatment, and avoiding live vaccines. |
| **Ustekinumab** (Stelara®) Moderate to severe plaque psoriasis (≥ 12 yrs old) and PsA | Fully human anti-IL-12/23 monoclonal antibody | ≤100 kg: 45 mg subcut at weeks 0 and 4; then every 12 weeks. ≤100 kg: 45 mg subcut at same intervals. | Common: infection, headache, fatigue, injection site redness; joint pain and nausea reported in patients with psoriatic arthritis. Serious: serious infections (including TB), malignancies. | Test for TB before starting treatment. Avoid live vaccines during treatment. |
| **Secukinumab** (Cosentyx®) Moderate to severe plaque psoriasis and PsA | Fully human anti-IL17A monoclonal antibody | 150–300 mg subcut weekly for 5 weeks; then 150–300 mg every 4 weeks (usual dose for PsA is 150 mg). | Common: infections (eg, nasopharyngitis, URI, mucocutaneous candidiasis), injection site reactions, diarrhea. Serious: serious infections (including TB), new onset or worsening inflammatory bowel disease. | Test for TB before starting treatment. Avoid live vaccines during treatment. |
| **Ixekizumab** (Taltz®) Moderate to severe plaque psoriasis and PsA | Humanized anti-IL17A monoclonal antibody | 160 mg subcut at week 0; 80 mg at weeks 2, 4, 6, 8, 10, & 12; then 80 mg every 4 weeks (see comments). | Common: infections (eg, URI, oral candidiasis, conjunctivitis, tinea infections), injection site reaction, nausea. Serious: serious infections (including TB), new onset or worsening inflammatory bowel disease. | Dosing schedule is different for PsA (160 mg at week 0, then 80 mg every 4 weeks). Test for TB before starting treatment. Avoid live vaccines during treatment. |
| **Brodalumab** (Sil拾™) Moderate to severe plaque psoriasis | Fully human anti-IL17 monoclonal antibody | 210 mg subcut at weeks 0, 1, and 2; then every 2 weeks. | Common: infections (eg, influenza, candidiasis), joint/muscle pain, headache, fatigue, diarrhea, nausea, injection site reactions. Serious: suicidal ideation/behavior (boxed warning), serious infections (including TB), worsening/new Crohn's disease. | For patients who have failed to respond or have lost response to other systemic therapies. Available only through a REMS program. Test for TB before starting treatment. Avoid live vaccines during treatment. |
| **Gusekumab** (Tremfya®) Moderate to severe plaque psoriasis | Fully human anti-IL23 monoclonal antibody | 100 mg subcut at weeks 0 and 4; then every 8 weeks. | Common: infections (eg, URI, gastroenteritis, tinea, herpes simplex, candidiasis), headache, injection site reactions, joint pain, diarrhea. Serious: serious infections (including TB). | Test for TB before starting treatment. Avoid live vaccines during treatment. |
| **Tildrakizumab-asnm** (Ilumya®) Moderate to severe plaque psoriasis | Humanized anti-IL23 monoclonal antibody | 100 mg subcut at weeks 0 and 4; then every 12 weeks. | Common: URI, injection site reactions, diarrhea. Serious: serious infections (including TB). | Test for TB before starting treatment. Avoid live vaccines during treatment. |

A Some drugs may require dose adjustment for kidney and/or liver impairment; clinicians should consult prescribing information or other sources (eg LexiComp).

B The information in this table is not comprehensive. For more complete information (including agent-specific side effects), consult prescribing information and/or other sources.

C For the examples listed, other concentrations or formulations with different brand names may be available.

Abbreviations: GI, gastrointestinal; HBV, hepatitis B virus; HPA, hypothalmic-pituitary-adrenal; IL, interleukin; IV, intravenous; PI, prescribing information; PsA, psoriatic arthritis; REMS, Risk Evaluation and Mitigation Strategy; TB, tuberculosis; TNF, tumor necrosis factor; URI, upper respiratory infection; UV, ultraviolet
**Phototherapy**
Phototherapy is considered a first-line therapy for moderate to severe psoriasis.\textsuperscript{7,34} It may be considered for patients with lesions in areas that are difficult to treat, such as the palms, soles of the feet, scalp, and intertriginous areas (where 2 skin areas touch or rub together) and for patients resistant to topical therapies.\textsuperscript{2,34} UVB radiation is often recommended in combination with topical agents such as coal tar or Vitamin D analogs.

**Systemic Therapy**
About 20-30\% of people with psoriasis have moderate to severe cases requiring phototherapy and systemic agents.\textsuperscript{35} Often, patients receive topical medication alone when systemic therapy is indicated.\textsuperscript{8} For patients with more than 10\% of BSA affected (or less extensive, but debilitating disease), systemic therapy is recommended. Treatment options include immunosuppressive or immunomodulatory drugs such as methotrexate, cyclosporine, retinoids, apremilast, and biologic agents. Most systemic agents are approved for both cutaneous psoriasis and psoriatic arthritis. In the past, a traditional systemic agent (eg, methotrexate, cyclosporine, oral retinoids) would be tried until toxicity developed or an inadequate response occurred, in which case another medication would be tried. Today, newer treatment classes (eg, apremilast, biologics) are also considered first-line “next step” medications following, or along with, topical treatment. These newer agents are being used with greater frequency. Apremilast, an oral drug, is well tolerated except for gastrointestinal side effects; however, it is less effective than the biologics. It may be a good choice for patients who want to avoid injectable medications. Biologics are highly effective, with subtle differences among them. Choosing one often depends on a patient’s coexisting conditions (eg, TNF inhibitors are more likely to cause or worsen heart failure and demyelinating disease), administration and dosing preferences (eg, every 4 or more weeks versus every week), and insurance/drug benefit considerations. Some pharmacy formularies only include certain biologics due to the high cost of these medications; the increasing availability of biosimilars may help with this issue.

**Methotrexate** has shown effectiveness in treating cutaneous psoriatic lesions as well as psoriatic nail disease. It is believed to suppress the activated T-cells that cause psoriatic flares.\textsuperscript{36} Once-weekly dosing beginning at 7.5 mg per week and increasing to a maximum of 25 mg per week has been used as long-term therapy and is generally well tolerated. In a 16-week controlled trial comparing methotrexate, adalimumab, and placebo, 36\% of patients receiving methotrexate achieved a 75\% improvement in symptom score, compared with 19\% of those taking placebo.\textsuperscript{37} Adalimumab was more effective than methotrexate, with 80\% of patients achieving a 75\% improvement in symptom score.\textsuperscript{37} Folic acid supplementation is recommended during methotrexate therapy to prevent the long term effects of folic acid inhibition caused by the drug.\textsuperscript{10}

**Cyclosporine**, a calcineurin inhibitor, is considered an effective treatment option for patients who are unresponsive to other therapies. It is also effective as bridge therapy when transitioning high need patients with severe or worsening psoriasis from one biologic agent to another.\textsuperscript{38,39} Kidney toxicity and hypertension can occur with long-term use; patients should be monitored closely. Use beyond 1 year is not recommended, and combined use with phototherapy is contraindicated.\textsuperscript{40}

**Apremilast**, an oral selective inhibitor of phosphodiesterase 4 (PDE4), is indicated for the treatment of moderate to severe plaque psoriasis. It is believed to elevate the level of cAMP, which indirectly
modulates the production of inflammatory mediators. In 2 controlled trials, 1 out of 3 apremilast users achieved PASI 75 by week 16, and 1 out of 5 significantly improved according to global physician assessments. This included participants with nail psoriasis and scalp psoriasis, whose symptoms improved significantly compared with participants who received a placebo. Unfortunately, by week 52, efficacy was lost in 33-39% of apremilast users who had previously achieved PASI 75, despite continued treatment. There have been post marketing reports of severe diarrhea, nausea, and vomiting within the first few weeks of apremilast use. Treatment should be initiated by skilled providers with close monitoring for these side effects.

**Biologics**

It is now recognized that psoriasis is the result of immunologic dysregulation involving T-helper cells. Playing the most prominent role are proinflammatory cytokines, which are produced by activated T cells. Biologic therapies target key cytokines, most notably tumor necrosis factor-alpha (TNF), and the interleukins (IL), IL17A, IL-12 and IL-23. While highly effective in the treatment of moderate to severe psoriasis and psoriatic arthritis, biologics have rare but serious side effects patients should be aware of and consider before treatment. These include serious infections, invasive fungal infections, malignancies, tuberculosis, hepatitis B reactivation, heart failure, cytopenias, demyelinating disease, and lupus-like syndrome. See Table 2. Use is contraindicated in patients with active, serious infections and in those who have significantly compromised immune systems. If a serious infection develops (ie, an infection that requires antibiotics), it is important to hold the biologic until the infection has resolved. The formation of antidrug antibodies against biological agents, which may decrease their efficacy, may also be a concern. Antibodies against infliximab, etanercept, adalimumab, ustekinumab, guselkumab, and tildrakizumab have been reported. Antidrug antibodies should be a consideration in patients who experience a diminished treatment response.

**TNF inhibitors** interfere with cytokine-driven inflammatory processes. One of the first effective, target-specific biologics for moderate to severe psoriasis and psoriatic arthritis was etanercept. The TNF inhibitors adalimumab and infliximab are also approved for these conditions. More recently, certolizumab and golimumab were approved for psoriatic arthritis. In a 12-week dose varying study of etanercept (25 mg weekly, 25 mg twice weekly, or 50 mg twice weekly), significantly more patients on the biologic achieved PASI-75 (ranging from 14% to 49%) compared with those on placebo (4%). At 24 weeks, 59% of patients on the highest dose achieved PASI-75. In a 12-week study of adalimumab, 53% of patients taking adalimumab every other week, and 80% being treated every week, achieved PASI 75. Unlike etanercept and adalimumab, which are injected subcutaneously, infliximab is delivered as an infusion. The intravenous route may produce a rapid response; some patients have reported a decrease in symptoms after only 3 infusions.

**Interleukin inhibitors** - Ustekinumab is a human monoclonal antibody that inhibits IL-12 and IL-23 and is approved for the treatment of moderate to severe psoriasis and psoriatic arthritis. Compared with high dose etanercept (50 mg twice weekly for 12 weeks), ustekinumab, at doses of 45 or 90 mg at weeks 0 and 4, was more effective. The percentage of patients achieving PASI-75 in the etanercept group was 57% compared with 67% (45 mg) and 74% (90 mg) in the ustekinumab groups. Secukinumab and ixekizumab are monoclonal antibodies that selectively bind to and neutralize IL-17A. Secukinumab 300 mg or 150 mg (administered once weekly for 5 weeks, then every 4 weeks) was superior to etanercept 50 mg twice weekly and placebo for the treatment of psoriasis. The proportion of patients reaching PASI-75 were 77-82% with 300 mg of secukinumab,
Studies of ixekizumab 80 mg every 2 or 4 weeks have shown that roughly 77-90% of patients achieve PASI 75 within 12 weeks of treatment (compared with 2.7-7% for placebo and 42-53% for etanercept). As a sustained response through 108 weeks has been reported for ixekizumab. Brodalumab is the third IL-17A receptor blocker approved for the treatment of moderate to severe plaque psoriasis in adults who do not respond to other systemic therapies. Brodalumab use resulted in rapid, dose-dependent improvement in moderate to severe plaque psoriasis, with similar PASI response rates as secukinumab or ixekizumab. However, unlike other IL-17A receptor blockers, it has a boxed warning about the increased risk of suicide and suicidal ideation, particularly in patients with a history of depression. It is the only IL-17 blocker that requires a Risk Evaluation and Mitigation Strategy (REMS).

Guselkumab is a first-in-class IL-23, subunit p19 inhibitor that decreases the pro-inflammatory actions of IL-23, resulting in reduced cytokine release. In a controlled study of over 800 patients with moderate to severe disease, significantly more patients achieved PASI 90 with guselkumab (73.3%) than with adalimumab (49.7%) or placebo (2.9%) at 16 weeks. Guselkumab also led to significantly more patients with clear or almost clear skin (85.1%) compared with adalimumab (65.9%) or placebo (6.9%).

Tildrakizumab-asmn is the most recent addition to the treatment armamentarium. It is a high-affinity humanized IL-23p19 inhibitor. Two clinical trials showed that 74% of patients achieved PASI 75 after 28 weeks of treatment (100 mg doses at weeks 0, 4, and every 12 weeks thereafter). In addition, 84% who continued receiving tildrakizumab maintained PASI 75 at week 64 compared with 22% of those in the placebo group.

Summary
Most patients with psoriasis have mild to moderate disease that can be effectively treated with topical therapy. Alternative medications when needed, lifestyle changes, and OTC products can be recommended to help patients. For more severe disease, many treatments are given by self injection; providers should be able to instruct patients on proper administration. Knowing the treatment options for the different types of psoriasis (and degrees of severity) allows healthcare providers to help patients manage their disease, ensuring an adequate response with minimal side effects.
References


Managing Psoriasis • March 2020 • Volume 42, #4


References for Table 2


7. Dovonex® (calcipotriene 0.005% cream) prescribing information. Madison, NJ: LEO Pharma Inc.; June 2017.


16. Lexicomp online. Available to subscribers at:https://online.lexi.com/lico/action/login
28. Taclonex® (calcipotriene and betamethasone dipropionate 0.005%/0.064% ointment) prescribing information. Madison, NJ: LEO Pharma Inc.; June 2017.
29. Taclonex® (calcipotriene and betamethasone dipropionate 0.005%/0.064% topical suspension) prescribing information. Madison, NJ: LEO Pharma Inc.; June 2017.
30. Taltz® (ixekizumab) prescribing information. Indianapolis, IN: Eli Lilly and Company; December 2017.
31. Tazorac® (tazarotene 0.05% and 0.1% cream) prescribing information. Irvine, CA: Allergan; July 2017.
32. Tazorac® (tazarotene 0.05% and 0.1% gel) prescribing information. Irvine, CA: Allergan; July 2017.
33. Temovate® (clobetasol propionate 0.05% cream or ointment) prescribing information. Melville, NY: Fougera Pharmaceuticals Inc.; October 2017.
35. TridermTM (triamcinolone acetonide 0.025%, 0.1% and 0.5% cream) prescribing information. Johnson City, TN: Crown Laboratories, Inc.; September 2017.
37. Vectical® (calcitriol 3 mcg/g ointment) prescribing information. Fort Worth, TX: Galderma Laboratories, L.P.; July 2012.
Managing Psoriasis• March 2020 • Volume 42, #4

Contributing Faculty
Celia MacDonnell, BS Pharmacy, PharmD
Clinical Professor at the College of Pharmacy, University of Rhode Island; Adjunct Associate Professor of Family Medicine at the Alpert Medical School at Brown University

CE-PRN is a publication of PharmCon, Inc. PharmCon, Inc. is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education.

Providers who are accredited by ACPE are recognized by ALL states for fulfilling CE requirements.

Participants completing this activity by May 1, 2021 may receive full credit.
Release Date: June 1, 2021

This lesson furnishes 1.5 (0.15 CEUs) contact hours of credit.
Universal Activity Number for this activity:
Pharmacists: 0798-9999-18-248-H01-P
CE Provider Registered # with CE Broker is 50-3515.

TO DOWNLOAD LESSONS FROM OUR WEBSITE:
• Go to website www.ce-prn.com
• Click on COURSES
• Click on YEAR
• Click on the UAN # “0798-0000-...” for your lesson of interest.

FLORIDA PARTICIPANTS – READ THIS!
Place your Florida license # on every quiz.
Describe psoriasis symptoms and how body surface area and the Psoriasis Area Severity Index (PASI) are used in assessing psoriasis severity.

List commonly used topical treatments. Counsel patients regarding administration, side effects, and precautions.

Discuss the epidemiology and contributing factors for the development of psoriasis.

Compare and contrast systemic treatments used for psoriasis, including effectiveness, side effects, and precautions.

2. Was the program independent & non-commercial?  YES  NO
1) Which of the following regarding psoriasis is a true statement?

A) Psoriasis usually develops after the age of 60 years.
B) In psoriasis, epidermal cells turn over about every 3 to 4 days.
C) Comorbidities that are linked with psoriasis include COPD and asthma.
D) Psoriasis is more common among Hispanics than other ethnic groups.

2) Which of the following is a contributing factor to psoriasis?

A) Genetic predisposition
B) Warm weather, sun exposure
C) Menopause
D) Exercising more than 3 days per week

3) Which of the following medications may cause psoriatic flares?

A) Fluoxetine
B) Penicillin
C) Acetaminophen
D) Propranolol

4) Which of the following is a typical symptom of plaque psoriasis?

A) Pink, fine dot-like lesions
B) Fever and chills
C) Raised silvery-white reddish patches
D) Raised dark brown patches

5) Plaque psoriasis is commonly found in which of the following body locations?

A) Armpits and buttocks
B) Feet and hands
C) Face and scalp
D) Elbows and scalp

6) How is the Psoriasis Area Severity Index (PASI) used to assess the effectiveness of psoriasis treatment?
A) PASI is a symptom score used to rate the severity of side effects to a medication.
B) PASI combines the degree of severity of lesions and the amount of affected area into a single score.
C) PASI is a way to see if 25% of the patients on a medication respond, as subjectively reported by the patient or caregiver.
D) PASI is a new method for measuring the body surface area affected by psoriasis.

7) Which of the following is true of topical treatments for psoriasis?

A) Topical treatments are indicated only in combination with systemic treatments.
B) Emollients and moisturizers, lotions and gels are preferred over ointments because these formulations are more occlusive.
C) The use of salicylic acid may be best for thin plaques or nail psoriasis.
D) Coal tar and anthralin are generally less effective than topical vitamin D analogs and topical corticosteroid therapy.

8) Which of the following side effects may occur with long term use of a class 1 topical corticosteroid such as clobetasol 0.05% cream?

A) Hypothalamic-pituitary-adrenal (HPA) axis suppression
B) New or worsening migraine headaches
C) Hypercalcemia
D) Weight loss

9) What is important to tell patients about tazarotene use?

A) Start with the highest strength cream to insure a rapid response.
B) Tazarotene is safe to use during pregnancy, in contrast to oral vitamin A derivatives.
C) Alternate day application and short application contact time (30-60 minutes) may reduce irritation.
D) Tazarotene is contraindicated in patients using mid- to high-potency corticosteroids.

10) Which of the following is true regarding systemic therapies for psoriasis?

A) All of the biologic agents can be administered as subcutaneous injections.
B) Cyclosporine is recommended for long-term treatment with phototherapy.
C) Methotrexate has been shown to be more effective than adalimumab.
D) Apremilast requires close supervision when initiating treatment due to reports of severe diarrhea and nausea.

11) Which of the following is recommended for all biologics used for the treatment of psoriasis?

A) Get a rapid strep test prior to initiating treatment.
B) Test for hepatitis C infection before initiating treatment.
C) Avoid live vaccines during treatment.
D) Document failure of phototherapy before initiating a biologic.

12) Which of the following biologic agents is only available through an REMS program and carries a black box warning for suicidal ideation/behavior?

A) Secukinumab
B) Brodalumab
C) Guselkumab
D) Adalimumab