

EDUCATIONAL OBJECTIVES

After participating in this activity pharmacists will be able to:

- LIST the pathogenesis and classification of various forms of psoriasis
- DESCRIBE comorbidities associated with psoriasis in children and adults
- DETERMINE the components of individualized treatment plans for pregnant, pediatric, and immunocompromised patients with moderate-to-severe psoriasis based on expert opinion
- USE this information to expand the pharmacist's role in adherence and monitoring to attain therapeutic treatment goals

After participating in this activity pharmacy technicians will be able to:

- LIST the basic pathology and symptoms of psoriasis
- OUTLINE biologic treatments used in psoriasis in special populations
- IDENTIFY when to refer patients to the pharmacists for recommendations or referrals



The University of Connecticut School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Pharmacists and pharmacy technicians are eligible to participate in this application-based activity and will receive up to 0.2 CEU (2 contact hours) for completing the activity, passing the quiz with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the CPE Monitor online system and your participation will be recorded with CPE Monitor within 72 hours of submission.

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Biologics for Psoriasis: Community Pharmacy Interface with Special Populations

ABSTRACT: Psoriasis is a chronic immune-regulated skin disease, often accompanied by several systemic comorbidities. Psoriasis is frequently untreated or undertreated, especially in special populations (pregnant, pediatric, and immunocompromised patients). No clear treatment guidelines exist for special populations because clinical trials usually exclude these patients. Biologics have revolutionized the treatment of psoriasis, with most patients achieving a rapid and complete symptom resolution. Pharmacists and pharmacy technicians can help patients with self-management of psoriasis. Patients need dosing, administration, storage and handling, common adverse effects, and self-management education.

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INTRODUCTION

Psoriasis is a chronic immune-mediated inflammatory skin condition characterized by a wide range of symptoms. The most common form presents as raised red patches covered with silvery scales and dry, cracked, and thickened skin. In the United States, statisticians estimate psoriasis's overall prevalence is 3.1%, affecting more than 6.7 million adults who are 20 years and older.¹ In 2013, economists estimated its financial burden to be as high as \$112 billion annually.²

Treatment options have evolved in the last 150 years. The journal *Lancet* published a paper in which a physician described treating five patients with large doses of arsenic in 1878.³ This practice continued into the 1920s. Today, prescribers can use targeted immune pathway biologics.⁴ Biologics have transformed psoriasis management and most patients can achieve rapid, complete control of

Table 1. Classification of Psoriasis

Type	Affected body part	Morphology
Plaque psoriasis	Scalp, trunk, buttocks, knees, elbows	<ul style="list-style-type: none"> Well-defined sharply demarcated erythematous plaques varying from 1 cm to several centimeters Most common phenotype affecting 80-90% of patients
Pustular psoriasis	Random body sites, palms or soles of feet	<ul style="list-style-type: none"> May be generalized or localized Acute generalized pustular psoriasis is rare, severe, and characterized by pustules, erythematous skin, fever, and systemic toxicity
Guttate psoriasis	Trunk and proximal extremities	<ul style="list-style-type: none"> Small lesions (1 to 10 mm), pink in color, and dew drop shaped, with a fine scale Primarily occurs in younger patients < 30 years May follow streptococcal pharyngitis in younger patients
Nail psoriasis	Fingernails and toenails	<ul style="list-style-type: none"> Pitting, onycholysis (separation of a nail from the nail bed), scaling under the nails, nail bed discoloration A marker for psoriatic arthritis
Erythrodermic psoriasis	Major portions of body surface area	<ul style="list-style-type: none"> Widespread erythema and scaling Can cause hypothermia, chills, dehydration from fluid loss, fever, malaise, lower leg edema, and congestive heart failure Can be life threatening
Inverse psoriasis	Skin folds, genitals, arm pits, abdominal, perineal, breasts	<ul style="list-style-type: none"> Lesions have minimal scale, primarily erythematous in nature Increases risk of secondary fungal infections

symptoms.⁵ Each biologic therapy has a unique mechanism of action, potential benefit, and side effect profile. Selecting an appropriate biologic for each specific subset of the patient population is imperative.

Pharmacists hold several misconceptions about biologics' safety and efficacy, especially in pediatric, pregnant, and immunocompromised patients. Clinicians tend to avoid initiating biologics pursuant to concerns about long-term safety, tolerability, efficacy, and costs. Clinical trials exclude special populations, increasing prescribing hesitation in pregnant, pediatric, and immunocompromised patients. This continuing education (CE) homestudy outlines the ideal choice of biologic therapy for special populations with psoriasis.

Pathophysiology

The Greek word 'psora' means to itch. The Greek physician Galen (133-200 AD) described the skin condition and coined the term psoriasis.⁶ One suggested remedy was application of broth in which a viper had been boiled.

Psoriasis is now recognized as a complex immune-mediated disease characterized by hyperproliferation and abnormal epidermal skin cell differentiation.⁷ In patients with psoriasis, epidermal regeneration occurs every three to four days compared to every 21 to 28 days in people who do not have psoriasis. Keratinocytes, the most predominant epidermal cells, recruit inflammatory dendritic cells to release interleukin (IL)-12 and IL-23. Those interleukins activate T-cells. This results

in a downstream cascade of inflammatory cytokine release; these include IL-17, IL-22, interferon (IFN)-gamma, and tumor necrosis factor- α (TNF- α). IL-17, IL-21, and IL-22 further activate keratinocyte proliferation in the epidermis driving the maintenance phase of psoriatic inflammation. Biologic agents that target TNF- α , IL-23, and IL-17 signaling pathways can manage psoriasis effectively.

Disease Classification

Psoriasis can manifest with a variety of clinical features and severities (see **Table 1**),^{7,8} and patients may present with more than one subtype.

Psoriatic Disease Severity

Psoriasis is classified as mild, moderate, or severe depending on the areas affected and percentage of body surface area (BSA) involved.⁷ If lesions affect the hands, feet, face, scalp, or genitals, psoriasis is considered severe regardless of BSA affected. If these areas are not involved, psoriasis is rated as

1. Mild (<5% of BSA)
2. Moderate (5-10% of BSA)
3. Severe (> 10% of BSA)

Readers need to be familiar with two terms: PASI and PASI scores. The gold standard for measuring psoriatic severity in clinical trials is Psoriatic Area and Severity Index (PASI; see **Table 2**).⁹ PASI measures lesion redness, thickness, and scaliness weighted by the area of involvement. Using the algorithm, clinicians calculate individual scores, which can range from 0-72.

Table 2. Psoriatic Area and Severity Index (PASI)

Lesion (Scores vary from 0-4)	Head (weighted area is 0.1)	Upper Extremities (weighted area is 0.2)	Trunk (weighted area is 0.3)	Lower Extremities (weighted area is 0.4)
Redness	0	0	0	0
Thickness	2	0	1	0
Scaliness	3	0	0	0

□ *The percent of skin area affected is graded as Grade 0-no involvement, Grade 1 (<10%), Grade 2 (10-29%), Grade 3 (30-49%), Grade 4 (50-69%), Grade 5 (70-89%), Grade 6 (90-100%).*

□ *The clinician adds the scores for redness, thickness and scaliness, and then multiplies them by the weighted area and percent of skin area involved to calculate the PASI score. For example, in the above table the PASI score, with grade 3 involvement is $0.1 \times 3 (0+2+3) + 0.3 \times 3 (0+1+0)$ Please see the addendum for additional explanation of PASI calculations!*

PAUSE AND PONDER: If a patient asked you to calculate her PASI score, how would you do it?

Higher PASI scores indicate severe disease.⁹ In patients with severe psoriasis, a 75% improvement in symptoms (denoted by the term PASI 75) is considered clinically meaningful. For example, if a patient's PASI score is reduced from a baseline of 20 to 5 upon therapy it corresponds to a 75% improvement $[(20-5)/(20) \times 100]$ in symptoms (PASI 75)

- PASI 75 indicates 75% improvement or reduction in symptoms, considered good response to therapy; patients can continue with the present regimen
- PASI 50-74, considered partial response to therapy
- PASI <50; considered treatment failure. Therapy needs intensification

TREATMENT IN PREGNANCY

Most people who develop psoriasis develop symptoms between 18-45 years of age.¹⁰ This coincides with women's peak reproductive age. The course of psoriasis in pregnant women is unpredictable. About 55% of pregnant women experience improved symptoms while pregnant and 20% of women experience no change.¹¹ High concentrations of progesterone in pregnancy downregulate the T cell proliferative response associated with psoriasis. Women usually note the most improvement during the late first and second trimesters. In 25% of women, symptoms worsen, requiring intensified treatment.

Traditional Agents

For mild to moderate cases of psoriasis, consensus recommends topical agents—emollients and moisturizers followed by low to moderate potency topical steroids—as first line treatment in pregnant patients.¹² High potency topical steroids can be used only if necessary, and only in the second and third trimesters. High potency topical steroids applied over a large BSA increase the potential for systemic absorption. Topical steroids may increase the risk of stretch marks at the application sites. Anthralin, coal tar, calcipotriene, and topical salicylic acid are not recommended during pregnancy.

Narrow band UVB phototherapy is a potential second line therapy.¹² Select patients with concomitant arthritis and pustular psoriasis may require systemic glucocorticoids in pregnancy. Guidelines do not generally recommend systemic glucocorticoids in the pregnant population because psoriasis will flare severely when they are stopped. Oral methotrexate (MTX) and oral acitretin are contradicted in pregnancy. MTX is a known abortifacient and has mutagenic and teratogenic effects. Acitretin can cause cardiovascular, ocular, auditory, craniofacial, and skeletal abnormalities in the developing embryo. Clinicians should counsel patients with psoriasis considering pregnancy to stop MTX therapy at least three months before and acitretin up to two years before conception.¹²



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Biologics in Pregnancy

In the 25% of pregnant patients with exacerbated psoriasis symptoms, treatment with a biologic agent may be warranted. Currently, the FDA has approved 11 biologic agents for psoriasis in the general population (see [Table 3](#); note that four are TNF inhibitors, and the others address other molecules).

Biologics are monoclonal antibodies (mABs) that target specific inflammatory pathways. Most currently approved mABs are derivatives of immunoglobulin G (IgG) and are actively transported across the placenta during the second and third trimester.¹³ The Fc receptor on the placenta facilitates active transport of complete IgG antibodies across the placenta. The agents' different molecular structures account for the differences in trans-placental transfer and cord blood concentrations.

Adalimumab, infliximab and golimumab are complete IgG

antibodies.¹³ Studies have shown significant concentrations of adalimumab (160%) and infliximab (153%) in the cord blood of newborns born to mothers who receive these medications. Researchers have detected adalimumab and infliximab serum concentrations up to 11 weeks and seven months postpartum, respectively, in neonates exposed to the biologics in the third trimester.

Case studies have shown very low levels of etanercept (4-7%) in the cord blood and below detection to minimal levels for certolizumab.^{14,15} Etanercept, a fusion protein, only contains the IgG₁ Fc portion. It crosses the placenta but less than the complete IgG antibodies, adalimumab and infliximab. Certolizumab pegol, a PEGylated Fc-free mAB, lacks the Fc moiety and does not bind to the Fc receptor in the placenta. Certolizumab does not cross the placenta and is preferred in the pregnant population. Limited data is available for other agents.

Table 3. Monoclonal Antibodies Approved for Psoriasis¹⁶

MAB (Year of approval)	Brand Name	Half Life (in days)	Dosing Schedule (L = Loading dose, M = Maintenance dose)
TNF-α inhibitors			
Etanercept (2004)	Enbrel	3.5	L: 50 mg twice weekly for 12 weeks; M 50 mg every week Pediatric dose <ul style="list-style-type: none"> • ≥138 lbs, 50 mg every week, • <138 lbs, 0.8 mg/kg every week
Infliximab (2006)	Remicade	10	L: 5 mg/kg week 0, 2 and 6; M 5 mg/kg every 8 weeks
Adalimumab (2008)	Humira	14	L: 80 mg week 0, 40 mg week 1; M 40 mg every 2 weeks
Certolizumab pegol (2008)	Cimzia	14	L: Weight ≤ 90 kg (198 lbs), 400 mg week 0, 2, and 4; weight >90 kg, 400 mg week 0; M: Weight ≤90 kg, 200 mg every other week; weight > 90 kg, 400 mg every other week
IL-12, IL-23 inhibitor			
Ustekinumab (2009)	Stelara	21	L: Weight ≤ 100 kg (220 lbs), 45 mg week 0 and 4; weight > 100 kg, 90 mg week 0 and 4; M: Weight ≤ 100 kg, 45 mg every 12 weeks; weight >100 kg, 90 mg every 12 weeks Adolescents: L < 60 kg (132 lbs), 0.75 mg/kg; 60 kg to 100 kg, 45 mg; >100 kg, 90 mg
IL-17 inhibitors			
Secukinumab (2015)	Cosentyx	27	L: 300 mg every week, weeks 1-5; M: 300 mg every 4 weeks
Ixekizumab (2016)	Taltz	13	L: 160 mg week 0, 80 mg every 2 weeks for 12 weeks; M: 80 mg every 4 weeks
IL-17, IL-25 inhibitor			
Brodalumab (2017)	Siliq	11	L: 210 mg at week 0, 1 and 2; M 210 mg every 2 weeks
IL-23 inhibitors			
Guselkumab (2017)	Tremfya	18	L: 100 mg week 0 and 4; M: 100 mg every 8 weeks
Tildrakizumab (2018)	Ilumya	23	L: 100 mg week 0 and 4 M: 100 mg every 12 weeks
Risankizumab (2019)	Skyrizi	28	L: 150 mg (two 75 mg injections) week 0 and 4 M: 150 mg every 12 weeks

A prospective analysis studied pregnancy outcomes in women who received certolizumab, especially in early pregnancy.¹⁷ Of 1137 pregnancies, 538 had known outcomes: 459 live births (85.3%), 47 miscarriages (8.7%), 27 elective abortions (5%), and five stillbirths (0.9%). The rate of congenital malformations, miscarriage, preeclampsia, and gestational diabetes was similar to that reported for the general population. Timing of certolizumab exposure was unrelated to major congenital malformations. The authors concluded that certolizumab has neither a teratogenic effect nor an increased risk of fetal death.

Certolizumab may erroneously elevate activated partial thromboplastin time (aPTT) results.¹⁸ Administration of certolizumab could affect the immune response in newborns. The safety of administering live vaccines in exposed infants is unknown. Pregnant patients receiving certolizumab are encouraged to register in the pregnancy exposure registry. Patients can register in the Mother-To-Baby Pregnancy Studies conducted by the Organization of Teratology Information Specialists (OTIS) at 1-877-311-8972 or visit <http://mothertobaby.org/pregnancy-studies/>.

Treatment in Pediatric Patients

Psoriasis begins in childhood in about one-third of patients.¹⁹ Uncontrolled psoriasis in children can significantly affect quality of life leading to low self-esteem, anxiety, depression, and difficulty with peer relationships. Pediatric psoriasis is associated with several comorbidities: obesity, hypertension, hyperlipidemia, diabetes mellitus, and rheumatoid arthritis. Early detection and subsequent treatment may delay or prevent considerable comorbidities. Pediatric psoriasis is associated with higher levels of T cells producing IL-22 and less IL-17 compared to adult psoriasis.²⁰ Certain factors contribute to under-treatment in children with moderate to severe psoriasis. They include fear of long-term adverse effects, underestimation of disease severity, and few approved medications.

Traditional Agents

In mild to moderate psoriasis, topical corticosteroids are the mainstay of therapy.¹⁹ Short courses (two weeks or fewer) of super high potency topical corticosteroids may be used. Upon improvement, clinicians may

- Discontinue the topical corticosteroid
- Taper it, or
- Transition to a low potency corticosteroid

Medium-to-high potency topical corticosteroids must be avoided in intertriginous areas (areas where two skin areas may touch or rub together). Topical calcineurin inhibitors (tacrolimus and pimecrolimus) may be used in these areas as first line treatment. Combination topical therapy with vitamin D analogues (calcipotriene and calcitriol) and corticosteroids can be used on body and scalp psoriasis. One of the main advantages of vitamin D analogues in children is their corticosteroid-sparing function. Coal tar, tazarotene, and anthralin are used less frequently due to limited data.



In moderate to severe psoriasis, prescribers can consider immunosuppressants (MTX, cyclosporine), phototherapy, and oral retinoids in conjunction with topical agents.¹⁹ Clinicians prescribe MTX most often for moderate to severe pediatric psoriasis. For plaque psoriasis, the starting dose is 0.3 mg/kg given once weekly.²¹ Improvement occurs in four to 10 weeks. MTX should be avoided in children requiring long-term therapy due to cumulative toxicity. Cyclosporine is generally well tolerated and faster acting than other systemic agents. It is a good choice for controlling severe refractory forms of the disease. The dose for pediatric psoriasis is 2-5 mg/kg/day for six weeks.²¹ Due to the potential for cumulative toxicity, prescribers should limit therapy to less than one year.

Biologics in the Pediatric Population

The FDA has not approved the traditional agents, MTX and cyclosporine, for pediatric psoriasis, but they are considered safe for short-term use.²² Under-treatment of children may facilitate the “psoriatic march,” which is a progression from severe untreated inflammation to associated cardiovascular morbidity and mortality in adults.²³ Biologics offer a therapeutic alternative for patients with inadequate response to other treatments. Etanercept is the only biologic approved for pediatric psoriasis in children aged at least four years.²⁴ Ustekinumab is FDA-approved for moderate to severe psoriasis in children who are at least 12.²⁵

Etanercept binds to both soluble and membrane-bound forms of TNF- α . An open label study evaluated etanercept’s long-term safety and efficacy in pediatric patients (ages 4-17) with moderate to severe plaque psoriasis.²⁶ The most common adverse effects were upper respiratory tract infection (37.6%), nasopharyngitis (26%), and headache (21.5%). One patient

reported cellulitis that the researchers considered treatment-related. Patients did not report opportunistic infections or malignancies. Patients maintained PASI 75 and PASI 90 improvement scores through the end of the study at week 264. Children tolerated etanercept well and efficacy continued until the study's end.

Etanercept is dosed at 0.8 mg/kg subcutaneously once weekly.²⁴ Patients weighing 138 lbs or more can receive 50 mg once weekly. Pediatric doses other than 25 mg or 50 mg are made by reconstituting lyophilized etanercept powder from single- or multi-dose vials. Multi-dose vials are the only option for children weighing less than 68 lbs. Mixed multi-dose vials should be used immediately or refrigerated at 2°-8° C for up to 14 days. Etanercept is available as SureClick autoinjectors and Enbrel Mini single dose prefilled cartridge with Autotouch reusable autoinjector. Enbrel prefilled syringe, SureClick autoinjector, Mini cartridge, or dose tray for multi-dose vial may be stored at room temperature (20-25° C) up to 14 days. They should be discarded after 14 days at room temperature.

Ustekinumab targets the IL-12 and IL-23 inflammatory pathways.²⁵ A phase 3 clinical trial conducted in adolescents ages 12-17 randomized patients to placebo and ustekinumab standard dosing (SD-0.75 mg/kg [≤60 kg], 45 mg [>60-≤100kg], 90 mg [>100kg] or half standard dosing (HSD- 0.375 mg/kg [≤60 kg], 22.5 mg [>60-≤100 kg], and 45 mg [>100 kg] or placebo.²⁷ By week 12, more patients receiving SD or HSD achieved PASI 75 and PASI 90 compared to placebo. This was sustained through week 52. Treatment responses and adverse effects in adolescents were comparable to those reported in adults. The most common adverse effects were nasopharyngitis (34.5%), upper respiratory tract infection (12.7%), and pharyngitis (8.2%). Patients did not report opportunistic infections or malignancies. Short-term and long-term adverse effects also did not differ between the placebo and treatment groups.

Ustekinumab's weight-based dosing schedule is convenient.²⁵ Clinicians should monitor patients on concomitant CYP450 substrates with narrow therapeutic index for therapeutic effect (e.g., warfarin) or drug concentration (e.g., cyclosporine).

Adalimumab is approved for children with Crohn's disease (>6 years) and juvenile idiopathic arthritis (>4 years), but not FDA-approved for pediatric psoriasis in the U.S.²² It is approved in the European Union to treat psoriasis in children older than four. A phase 3 clinical trial has shown adalimumab is efficacious, well-tolerated, and safe in children aged four to 18.²⁸

The FDA approved ixekizumab in March 2020 for pediatric plaque psoriasis in children aged six to 17.²⁹ Its pivotal study included 171 patients aged six to 17 with moderate to severe plaque psoriasis. At 12 weeks, 89% of those on ixekizumab achieved a PASI 75, compared with PASI 25 on placebo. The safety profile was consistent with that observed in adult patients, although pediatric patients had higher rates of conjunctivitis, influenza, and urticaria.

PAUSE AND PONDER: How many of your immunocompromised patients also have psoriasis?

TREATMENT IN IMMUNOCOMPROMISED PATIENTS

All systemic agents used to treat psoriasis are immunosuppressive with the exception of aciretin (a second generation retinoid). Current guidelines recommend screening for common infectious diseases (HIV, latent tuberculosis [LTB], hepatitis B virus [HBV], and hepatitis C virus [HCV]) before treatment initiation due to risk of viral reactivation. Treatment in patients with HIV, HCV, HBV, and TB who are already immune-suppressed poses a unique challenge. Most available data on treatment modalities is based on case studies as this population is excluded from clinical trials.

Traditional Agents for Hepatitis

Hepatitis C is considered curable with the advent of direct acting anti-viral agents. We will discuss hepatitis B in detail. Readers should note that this section will be more difficult to comprehend, as hepatitis B serology is complicated. This video is helpful in understanding hepatitis serology:

<https://www.cdc.gov/hepatitis/resources/professionals/training/serology/training.htm>

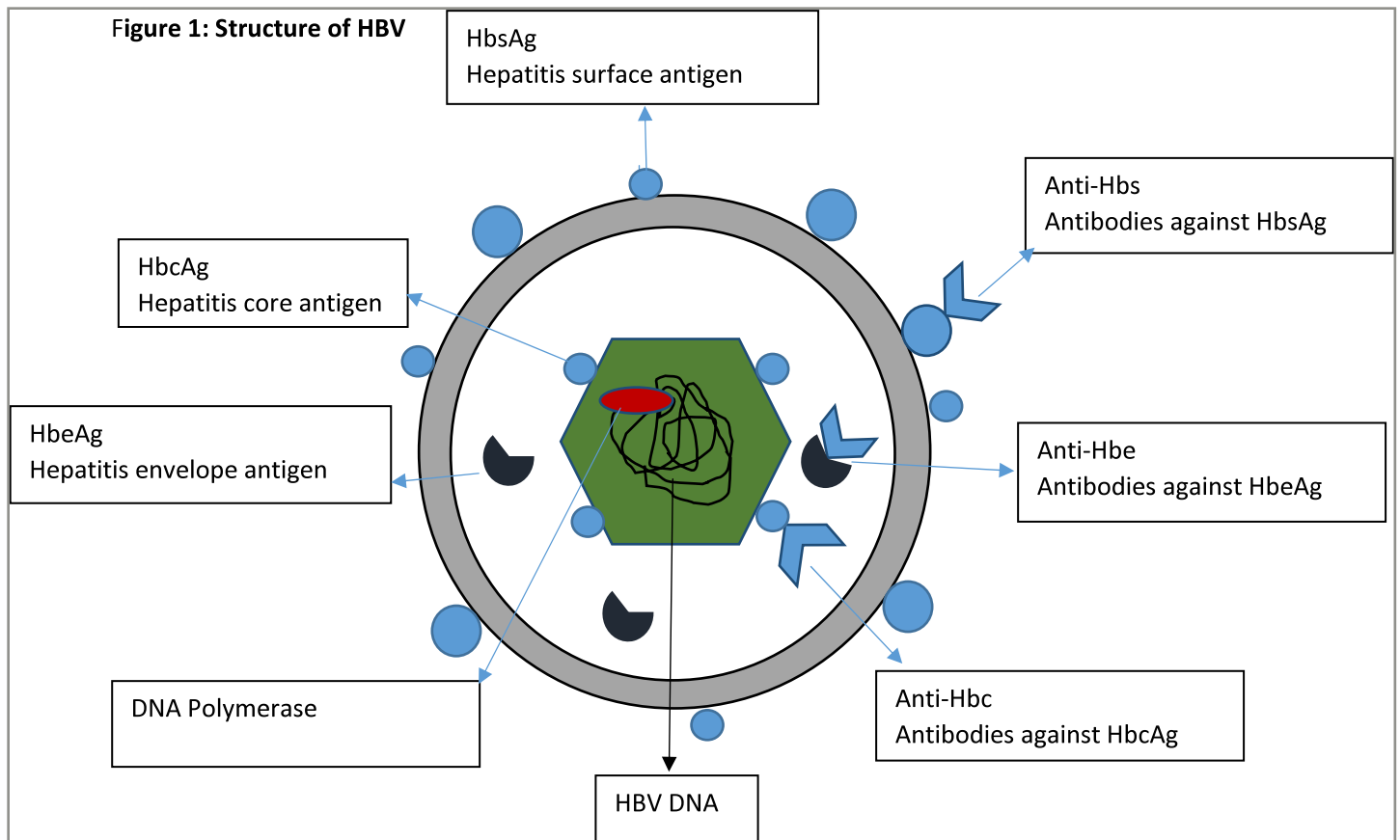
Currently, there are no clear guidelines for the management of patients with concurrent psoriasis and hepatitis B infection. Patients with hepatitis already have compromised hepatic function, so clinicians need to consider drug-induced hepatotoxicity before initiating treatment. MTX and aciretin are associated with liver enzyme elevation. Low-dose MTX therapy has been shown to reactivate hepatitis B (HBV) in rheumatoid arthritis patients resulting in hepatic failure.³⁰ Cyclosporine has also been associated with HBV and HCV reactivation in immunocompromised patients.³¹ Aciretin is the only drug that can be administered during the active stage of HBV. Patients on aciretin need to be co-managed with a hepatologist due to hepatic risks. Aciretin use is limited due to its associated teratogenicity, mucosal dryness, hepatotoxicity, and hypertriglyceridemia.

Hepatitis Serology

Serologic testing of patients can identify patients with active HBV infection, assess the clinical phases of the infection, monitor anti-viral therapy, and reveal the course of chronic HBV infection.³²

CDC guidelines recommend screening all patients considering an immunosuppressive regimen for HBV. Clinicians should screen them for the following markers³³ (See **Figure 1**):

- Surface antigen (HBsAg)
- Core antigen (HBcAg)
- Envelope antigen (HBeAg)
- Antibodies against the virus namely anti-HBs, anti-HBe and anti-HBc both IgM and IgG



An acute HBV infection may last four to six months. Serology shows presence of HbsAg, and high titers of IgM antibodies against core antigen (IgM anti-Hbc), and elevated liver enzymes (AST/ALT).³⁴ During the early phase of the infection, HBeAg is also detectable. Infected individuals will have antibodies against HBsAg and HBeAg in their serum after the resolution of the acute phase of infection (see [Table 4](#)).

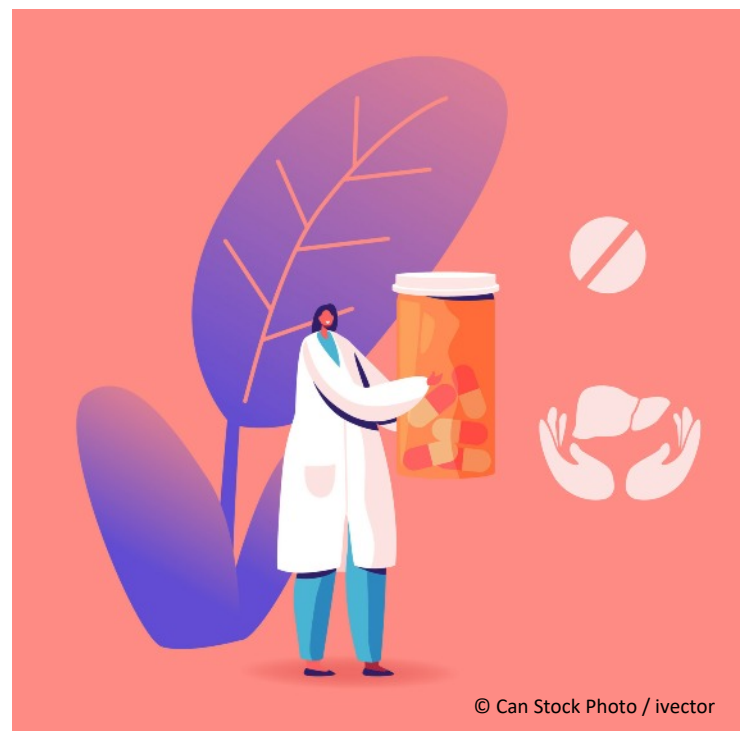
PAUSE AND PONDER: What are the different forms of hepatitis, and how are they treated?

Does [Table 4](#) intimidate you? Why? How can you analyze its contents efficiently?

Chronic HBV infection lasts more than six months. These individuals are HBsAg positive with elevated AST/ALT. Occult HBV is defined as serologically undetectable HBsAg despite circulating HBV DNA.³⁴

In patients with hepatitis who wish to start immunosuppressive therapies for psoriasis, guidelines are clear³¹:

- Active HBV infection: Hold systemic immunosuppressants until infection is controlled on anti-viral therapy
- Inactive carriers: Provide antiviral prophylaxis for inactive carriers for two to four weeks before starting immunosuppressive therapy and continue for six to 12 months after stopping. Monitor patients every month for first three months and then every three months for HBV reactivation
- Chronic HCV: Check liver function in patients with chronic HCV every three to six months while on immunosuppressants
- Anti-viral prophylaxis: The American Gastroenterology Association recommends entecavir or tenofovir because HBV is highly resistant to lamivudine.



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Biologic Agents in Hepatitis

TNF- α works with interferons to clear hepatocytes of HBV and suppress viral replication.³¹ Use of TNF- α inhibitors can increase HBV replication and reactivate chronic hepatitis during and after treatment. During acute phase of an active HBV, treatment with TNF- α inhibitors is not recommended due to risk of increasing viral replication.

This list summarizes TNF- α inhibitors use in patients with hepatitis³¹

- Etanercept was the most frequently used agent, followed by adalimumab and infliximab.
- The majority of the data available for TNF- α in patients with concurrent psoriasis and hepatitis is in inactive, occult carriers or with resolved HBV.
- Occult carriers or patients with resolved hepatitis did not experience a HBV reactivation. None were on anti-viral prophylaxis.
- Among inactive carriers, patients who received anti-viral prophylaxis did not experience HBV reactivation.
- Only one case study of use of TNF- α in an active HBV infection has been reported.

Limited data is available for use of ustekinumab in patients with concurrent psoriasis and HBV infection. Researchers conducted a retrospective study in 18 patients with concurrent psoriasis and HBV infection.³⁷ Upon treatment with ustekinumab, 29% of patients (2/7) who did not receive antiviral prophylaxis developed HBV reactivation. No activation was observed in occult

HBV infected patients. The authors concluded antiviral prophylaxis minimized the risk of HBV reactivation in this population. Another prospective cohort study (n=93) evaluated the risk of viral reactivation (reappearance of HBV DNA) with ustekinumab.³⁸ Among 54 patients classified as inactive HBV carriers, resolved HBV infection and isolated anti-HBc positivity, three patients experienced viral reactivation with ustekinumab. No liver failure was reported. The study outcomes indicated ustekinumab was a safe option and reappearance of HBV DNA requires viral load monitoring.

Insufficient data is available for guselkumab, risankizumab, and tildrakizumab. One case study has reported successful treatment with guselkumab in a patient with HBV infection and refractory palmoplantar psoriasis.³⁹

Researchers have also studied patients with concurrent HBV/HCV with psoriasis (n=63) for the risk of reactivation of HBV/HCV while receiving secukinumab therapy.⁴⁰ In patients not receiving anti-viral therapy, 15.2% (7/46) developed HBV reactivation. HBsAg positive patients were at higher risk of reactivation compared to HBsAg negative/anti-HBc positive patients. In patients receiving anti-viral prophylaxis, none developed viral reactivation. Secukinumab therapy requires close monitoring of viral load in HBsAg positive and HBsAg negative/anti-HBc positive psoriasis patients. All HBsAg positive patients require anti-viral prophylaxis before treatment with secukinumab. Case studies have shown successful management of patients with psoriasis and HBV with secukinumab.^{41,42}

Table 4. Interpretation of Hepatitis Serology and Initiation of TNF- α Inhibitors^{35,36}

(-) HBsAg (-) anti-HBc (-) anti-HBs	Susceptible to infection	<ul style="list-style-type: none"> • Administer HBV vaccination before TNF inhibitor therapy
(-) HBsAg (+) anti-HBc (+) anti-HBs	Immune due to natural infection	<ul style="list-style-type: none"> • Reactivation risk is low. Consider baseline HBV DNA and consulting a hepatologist before TNF inhibitor therapy
(-) HBsAg (-) anti-HBc (+) anti-HBs	Immune due to hepatitis B vaccination	<ul style="list-style-type: none"> • If anti-HBs titer > 10 mIU/mL, TNF inhibitor therapy can be safely administered • If anti-HBs titer < 10 mIU/mL, booster vaccination is recommended before TNF inhibitor therapy
(+) HBsAg (+) anti-HBc (+) IgM anti-HBc (-) anti-HBs	Acute infection	<ul style="list-style-type: none"> • TNF inhibitor therapy should be avoided • Refer to hepatology for treatment of acute HBV infection
(+) HBsAg (+) anti-HBc (-) IgM anti-HBc (-) anti-HBs	Chronic infection	<ul style="list-style-type: none"> • Seek consultation with hepatology to determine if antiviral prophylaxis is necessary • Monitor LFTs, HBsAg, HBeAg, and HBV DNA quantification routinely for reactivation
(-) HBsAg (+) anti-HBc (-) anti-HBs	Occult infection <ol style="list-style-type: none"> 1. Resolved infection 2. False positive anti-HBc 3. Low level chronic infection 4. Resolving acute infection 	<ul style="list-style-type: none"> • Consult hepatology before initiating TNF inhibitor therapy • Monitor LFTs, HBsAg, HBeAg, and HBV DNA quantification routinely for reactivation

In summary, secukinumab may be used in patients with concurrent psoriasis and hepatitis with close monitoring of liver function tests and viral serology. Secukinumab is available as Sensoready pen or prefilled syringe.⁴³ Secukinumab has to be administered within one hour after removal from the refrigerator. Common side effects include upper respiratory tract infections, nasopharyngitis, and mucocutaneous infections. Concurrent administration with CYP450 substrates with narrow therapeutic index (e.g., warfarin) requires additional monitoring for therapeutic effect or drug concentration.

TNF- α inhibitors may be initiated depending on the serology results.

Traditional Agents for HIV patients

The prevalence of psoriasis in the HIV-infected population in the U.S. is 1-3%.⁴⁴ As HIV infection progresses, psoriasis tends to worsen. The current first line therapies are topical therapies, phototherapy, and highly active antiretroviral therapy (HAART). HIV-associated psoriasis often occurs at CD4 counts below 350 cells/mm³. An open label trial of zidovudine therapy in patients with HIV-associated psoriasis lead to improvement in 90% of the 24 patients followed.⁴⁵ Antiretroviral therapy decreases viral load and TNF- α .⁴⁴ TNF- α is associated with HIV replication and is elevated in HIV. Aciretin can be used as the second step in therapy. However, these therapies often control symptoms inadequately due to psoriasis's progressive nature in the HIV population.

A systematic review evaluated systemic immunosuppressive therapies' efficacy and safety in comorbid HIV and patients with psoriasis.⁴⁴ The researchers analyzed eight cases of MTX use. Two patients developed pneumocystis pneumonia; one developed toxic encephalopathy and died five months after discontinuation of MTX from pneumocystis pneumonia. Cyclosporine was used successfully in two patients. Both patients were on antiretroviral therapy and their skin and joint symptoms improved during treatment over one and two years. A task force of the National Psoriasis Foundation Medical Board recommends cautious treatment with MTX and cyclosporine only in severe refractory cases.⁴⁵

Biologics in the HIV Population

Psoriasis can occur before or after HIV infection. The coexistence of both diseases is usually associated with a severe form of psoriasis and low treatment response. TNF- α is involved in both the inflammatory process in psoriasis and in increasing viral load in HIV. Use of biologics that target the TNF- α signaling pathway could theoretically be beneficial to this population.⁴⁴ A retrospective multicenter study in patients with psoriasis and concomitant HIV infection evaluated biologic therapy's safety and effectiveness.⁴⁶ They followed 23 patients for 3.2 years. Patients received etanercept (n=16), MTX (n=6), ustekinumab (n=6), adalimumab (n=4), efalizumab (n=2), cyclosporine (n=1),

and infliximab (n=1). (Efalizumab's manufacturer withdrew it from the U.S. market in 2009.) Viral load improved in most cases and CD4 count was stable and improved throughout the follow-up period. Six patients (26.1%) experienced serious adverse events during follow-up; four were in the AIDS stage of HIV. Of the 17 patients who completed the study, 13 achieved a PASI 75. The authors concluded that in HIV-infected patients, both TNF- α agents (etanercept and adalimumab) and ustekinumab had an acceptable safety profile and high effectiveness.

A systematic review conducted among patients with psoriasis and HIV mirrored these results.⁴⁴ Researchers found that etanercept (n=5), adalimumab (n=1), infliximab (n=6), and ustekinumab (n=3) stabilized or increased CD4 counts and viral count was undetectable or remained stable. These patients were also on concomitant HAART. Treatment with biologic agents in combination with HAART may have beneficial effects on CD4 and viral counts compared to using systemic immunosuppressive agents such as MTX and cyclosporine.

A case report described one HIV-positive individual with plaque psoriasis who responded to gesukumab.⁴⁷ The newer agents secukinumab, ixekizumab, tildrakizumab, golimumab, and certolizumab have accrued little data in HIV and their safety and tolerability is unknown in this population.

In summary, TNF- α inhibitors can be used in the HIV population with close monitoring of CD4 counts and HIV viral loads with regular consultation with an infectious disease specialist.

LATENT TUBERCULOSIS

Tuberculosis (TB) is a serious infectious disease caused by the bacteria *Mycobacterium tuberculosis*. Common symptoms of active lung TB are cough with sputum and blood at times, weight loss, fever, and night sweats. TB is classified as either active or latent disease.⁴⁸ Patients with latent disease are asymptomatic and do not transmit the disease; patients with active disease are contagious. The greatest known risk factor for contracting TB is a HIV infection, with 12% of all new active cases and 25% of all TB-related death occurring in this population.⁴⁸

TNF is a main pro-inflammatory cytokines involved in granuloma formation in response to *Mycobacterium tuberculosis*



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infection.⁴⁸ Patients with LTB have active bacteria enclosed inside the granuloma and are asymptomatic. These patients can progress to active disease when they are immunosuppressed or on immunosuppressive drug regimens. Adequate prophylaxis of LTB prevents up to 70% of patients from developing the active form of the disease.⁴⁹ Thus, screening for TB is recommended before initiating biologics or systemic immunosuppressive agents. Clinicians can use the tuberculin skin test or interferon-gamma release assay as a screening tool for TB. A positive screening is confirmed using a chest radiograph.

The National Psoriasis Foundation consensus statement on screening for LTB in patients with psoriasis and psoriatic arthritis recommends⁴⁹

1. Patients with LTB infection should receive prophylaxis with isoniazid 300 mg for nine months. Immunosuppressive therapy for psoriasis may be initiated one to two months after starting prophylactic isoniazid if necessary.
2. Patients with active TB need referral to an infectious disease specialist. Treatment with the four-drug regimen for TB (isoniazid + rifamycin + pyrazinamide + ethambutol) is recommended.
3. Concurrent therapy with immunosuppressive agents for psoriasis should be avoided in patients with active TB.
4. All patients need TB screening before initiation of therapy with TNF- α inhibitors and at yearly intervals

Traditional Agents in LTB

Topical therapy including steroids, tazarotene, calcipotriene, salicylic acid, and phototherapy do not cause immunosuppression or activate LTB. Clinicians can prescribe these interventions safely in this population.

In patients with psoriasis and rheumatoid arthritis, MTX has been shown to activate LTB.⁵⁰ MTX and isoniazid are toxic to the liver and could have an additive hepatotoxic effect. However, a retrospective chart review conducted in 46 patients found only transient increases in liver function tests (LFTs) in 11% of the patients. None of the patients developed signs or symptoms of TB activation. Cyclosporine is used in psoriasis and in transplant patients.⁴⁹ Reactivation of LTB has been reported in transplant patients. To date, researchers have not associated lower doses used in dermatology with LTB activation.

Biologics in LTB

The different TNF- α inhibitors have varying risks for development of TB.⁴⁹ Infliximab and adalimumab are mAbs and bind more tightly to TNF than etanercept, which is a fusion protein. Adalimumab has a longer half-life (2 weeks) than infliximab (10 days) and etanercept (3.5 days). Patients treated with infliximab and adalimumab have a greater risk of reactivation of LTB than those treated with etanercept.

From January 1998 to September 2002, 335 cases of infliximab-associated TB and 39 cases with etanercept were reported worldwide.⁵¹ Treatment with TNF- α inhibitors has been associated with an increased risk of activating LTB. The incidence of TB in patients treated with TNF- α inhibitors has been shown to increase even after treatment with antivirals and in patients with initially negative LTB results.

In phase 3 clinical trials of ustekinumab (n=3177) for treatment of moderate to severe psoriasis, 167 patients were newly identified with LTB infection.⁵² The majority of patients tolerated isoniazid and continued on ustekinumab treatment as long as they were on isoniazid treatment. One patient who was asymptomatic and not treated prophylactically with isoniazid developed reactivation of LTB infection. In patients with LTB who received isoniazid prophylaxis, no cases of reactivation were reported.

A case of peritoneal tuberculosis has also been described in a ustekinumab-treated patient.⁵³ Studies with larger sample sizes and longer follow-up are required to assess the risks of LTB activation upon treatment with ustekinumab.

In patients (n=2044) treated with secukinumab, pooled safety data from five phase 3 clinical trials showed no cases of TB after one year.⁵⁴ About 81% of patients with a history of pulmonary TB tested positive for LTB infection and received anti-TB medication. None of these patients developed LTB reactivation within one year. TB prophylaxis with isoniazid or rifampin is associated with elevated LFTs and gastrointestinal events. In patients on concomitant secukinumab and anti-TB treatment, rates of liver enzyme abnormalities were low. Secukinumab was well tolerated with anti-TB therapy and none of the patients discontinued therapy.

In a case study with 12 patients with LTB treated with secukinumab, none developed reactivation even without prophylactic TB treatment.⁵⁵ A recent systematic review evaluated whether IL-17 inhibitor therapy increased risk of TB reactivation in patients treated for psoriasis.⁵⁶ It included data from approximately 23 clinical trials. No cases of TB reactivation were reported with secukinumab. Patients on ixekinumab also did not report any active cases of TB from approximately 13 clinical trials. In summary, sufficient data indicates secukinumab therapy appears to be a safe and effective option for patients with LTB and moderate to severe psoriasis.

Barriers to Biologic Use

Most patients with psoriasis are untreated or undertreated, especially those with moderate disease. In a survey conducted by the National Psoriasis Foundation (NPF), 23.6-35.5% of patients diagnosed with moderate psoriasis did not receive any therapy and 29.5% were prescribed just a topical agent.⁵⁷ Overall, 52.3% of patients with psoriasis and 45.5% of patients with psoriatic arthritis were dissatisfied with their treatment. Patients and providers alike are concerned about biologics' long-term safety and



cost. The biologics' average cost is between \$18,000/year and \$28,000/year per patient.⁵⁸ In the NPF survey, 50% of patients skipped treatment because they were uninsured, had difficulty with insurance covering treatment, or were unable to afford high copayments.

Most insurance companies classify biologics as specialty medications.⁵⁸ A large portion of the cost is shifted to the patient by placing the drug in the specialty tier. Tiered cost sharing, increased out of pocket expense, coverage gaps for Medicare patients, step therapy requirements, prior authorization, and reauthorization policies are some barriers facing these patients. Patients with severe psoriasis who need these therapies are more likely to have lower household incomes than those with mild disease. This leads to a vicious cycle of escalating disease severity and under-treatment.

Most biologics are administered subcutaneously. Some patients are afraid of self-injections and hence do not opt for biologic therapy. Such patients can be encouraged to receive doses at the clinic. Auto-injector options are available for adalimumab, etanercept, and secukinumab, and pharmacy staff can explain to the patient that they are easy to use.⁵⁹ Auto injectors are held on the skin and injected by pushing a button. The only option available currently for ustekinumab is the prefilled syringe. Infliximab is administered as an infusion and requires a visit to the infusion center.

TECH TALK: PHARMACY TECHNICIAN AND PSORIASIS MANAGEMENT

Pharmacy staff are routinely asked for recommendations for skin conditions. Pharmacy technicians often field the first questions from patients at point of sale.

- Reinforce that psoriasis is not a contagious condition.
- Making outbound calls for refills and adherence is an important responsibility!
- Always refer questions about latex allergy to the pharmacist for consultation
- Maintain patient profiles and log documented allergies in the dispensing system
- Biologics are very expensive medications.
 - Maintain appropriate storage to maintain product integrity.
 - Upon receiving a delivery order, unpack, retrieve, and store biologics in the refrigerator promptly.
 - Keep filled prescriptions in the refrigerator.
- Record refrigerator temperature logs twice a day and maintain them in a retrievable document.
- Maintain efficient inventory systems so patients on biologics have continuous access to their medications.
- Encourage patients to review their immunization records at least annually
- Refer patients to the pharmacists for appropriate recommendation

IMPLICATIONS FOR PHARMACY

Pharmacists and technicians are accessible health care providers with established interpersonal relationships with their patients. Patients find them approachable. The most important area where they can make a difference is in patient education. Ensure that pregnant, pediatric, and immunocompromised patients with moderate-to-severe psoriasis have individualized treatment plans with the following components:

- Treatment goals and how outcomes will be measured
- Careful documentation of the rationale for each medication used
- Assessment of immunization
- Planned duration of therapy
- Barriers to care and how to address them
- Biologics require extensive patient education.⁶⁰ Patients must be educated on drug dosing, administration, storage, disposal, common adverse effects, management of adverse effects, and considerations for unique situations such as illness or surgery.
- Self-injection education should include choosing an appropriate injection site, cleaning the area, rotating injection sites, and administering injections at a 45- or 90-degree angle according to drug-specific recommendations. Patients should bring biologics to room temperature before injecting. Proper disposal of injection supplies in appropriate sharps containers must be encouraged.
- Patients who are nervous about self-injections should be given the option of easy to use auto-injectors.
- Pharmacists can make routine follow-up phone calls to assess adherence and missed doses and side effects
- Pharmacists can inform patients about copayment assistance programs, drug manufacturer assistance, and foundation funding availability to help patients with high drug costs.⁶⁰
- Pharmacy staff can also explain that initiating treatment with biologics may be expensive initially but will produce economic benefits. Increased productivity, reduced sick days, and less disability can significantly outweigh the direct costs
- Pharmacy staff can also encourage healthy lifestyles and behavioral changes such as quitting smoking, decreasing alcohol consumption, following a healthy diet, and increasing physical activity
- Explain the importance of keeping all lab appointments and clinic visits current and the yearly TB skin test
- The needle shield inside the removable cap of the prefilled syringe contains a derivative of natural rubber latex in some biologics. Latex-sensitive individuals may experience an allergic reaction upon contact.⁶¹ (See [Table 5](#))
- Explain the signs of hepatitis (loss of appetite, fatigue, nausea, jaundice and pruritus) which can occur with some TNF-α agents

- Pharmacy staff needs to be familiar with situations in which patients may need to stop biologic therapy.⁶²
 - High Risk Elective surgery: hold biologic therapy for four to five half-lives for major surgeries. Biologics may be continued for low-risk procedures
 - Administration of live vaccine: hold biologic therapy for two to three half-lives, administer vaccine, resume after two to three half-lives
 - Hold during infections, especially febrile illness requiring antibiotic treatment. Patients can restart treatment after full symptom resolution and completion of antibiotics.

Immunization in Patients Receiving Biologics

Before patients begin therapy with a biologic, pharmacists should review vaccination records and administer appropriate vaccines.⁶³

- Inactive vaccines may be administered at least two weeks before beginning biologics for optimal response
- For patients 19 years of age or older, pneumococcal 13-valent conjugate vaccine followed by pneumococcal vaccine polyvalent at least eight weeks later is recommended
- Recombinant zoster vaccine is recommended for all psoriasis and psoriatic arthritis patients, including those younger than 50
- Live vaccines must be administered at least four weeks before beginning biologics to reduce risk of contracting an infection from the vaccine



Table 5. Biologics that contain Latex⁶¹

Latex	No Latex
Adalimumab pen PFS	Adalimumab CF
Etanercept pen PFS	Brodalumab PFS
Golimumab pen PFS	Certolizumab PFS
Secukinumab pen PFS	Etanercept vial
Ustekinumab PFS	Guselkumab PFS
	Ixekizumab PFS
	Risankizumab PFS
	Tildrakizumab PFS

Patients already on immunosuppressive agents⁶³

- Influenza, pneumococcal, tetanus, hepatitis B, hepatitis A, HPV (3-dose schedule) vaccines can be administered while on therapy
- Live vaccines must be avoided
- Rheumatologic experts recommend a wash out period of two to three half-lives of biologic (at least four weeks) before giving live vaccine and then restarting two to three half-lives after administration of live vaccines (at least one to two weeks).
- The National Board of Psoriasis consensus statement on vaccination in adult patients on systemic therapy for psoriasis or psoriatic arthritis states that recombinant zoster vaccine may be administered safely with concurrent use of biologic, targeted, and conventional synthetic disease modifying antirheumatic drugs.⁶⁴ All patients older than 50 years, and patients younger than 50 years who are on tofacitinib, systemic corticosteroids, or combination systemic therapy can receive the recombinant zoster vaccine. Recombinant zoster vaccine may be considered in patients with psoriasis and psoriatic arthritis younger than 50 years who are on other systemic therapies on a case-by-case basis after individualized risk assessment

CONCLUSION

Selecting the best biologic for patients who are members of special populations is an art and a science. Having psoriasis while pregnant, as a child, or with comorbid immunocompromising conditions or infections (e.g., hepatitis, HIV, or tuberculosis) does not necessarily preclude biologic use.

Certolizumab is the biologic of choice in pregnant women, and all TNF- α inhibitors are considered safe during lactation. The FDA has approved three biologics in children of different ages: Etanercept (children aged 4 to 17); ustekinumab (children aged 12 and older); and ixekizumab (children aged 6 to 17). Patients who have hepatitis can use secukinumab or the TNF- α inhibitors based on serology reports. Those who have HIV can be prescribed TNF- α inhibitors with close monitoring of CD4 counts and HIV viral loads and regular consultation with an infectious disease specialist. Finally, secukinumab is the biologic of choice for patients who have latent tuberculosis.

The key to successful treatment of patients who have psoriasis and are members of special populations is to check the professional literature for evolving guidelines and monitor patients closely. **Figure 2** spells out ways you can maximize your role.

Figure 2. Maximizing the Pharmacy Team's Role in Psoriasis in Special Populations

Best

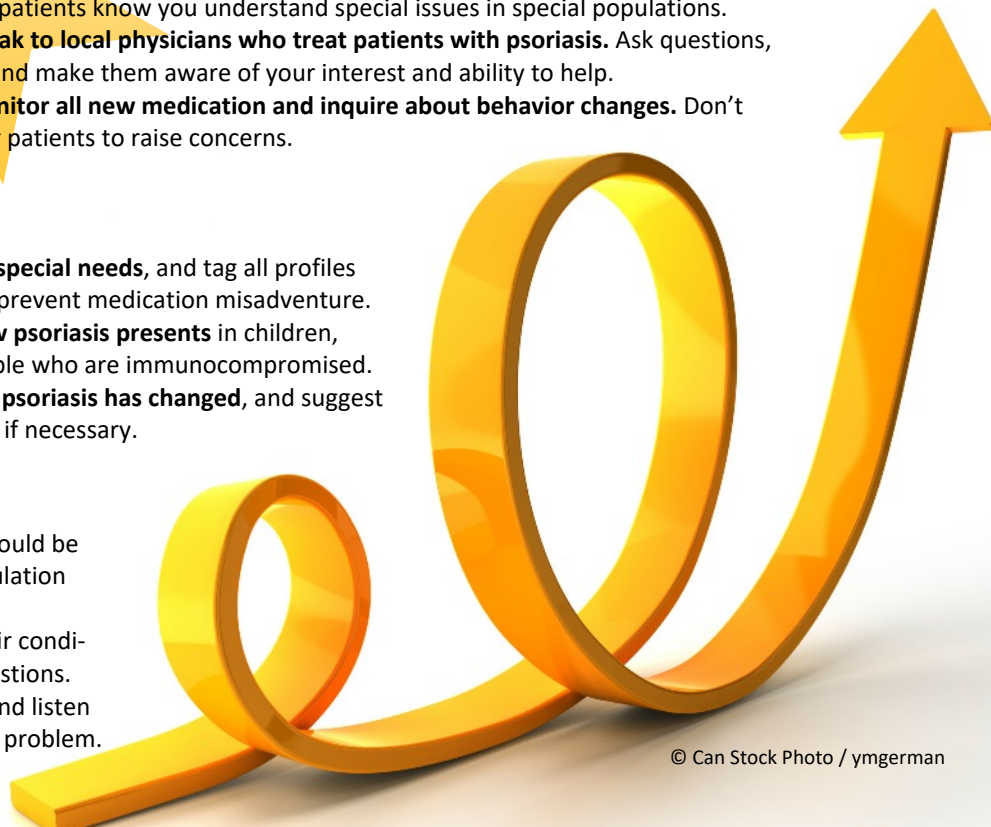
- 1 **Be COMMUNITY CHAMPIONS.** Actively heighten awareness of psoriasis, and let patients know you understand special issues in special populations.
- 2 **Speak to local physicians who treat patients with psoriasis.** Ask questions, listen, and make them aware of your interest and ability to help.
- 3 **Monitor all new medication and inquire about behavior changes.** Don't wait for patients to raise concerns.

Better

- 1 **Consider the patient's special needs,** and tag all profiles with information that may prevent medication misadventure.
- 2 **Know the basics of how psoriasis presents** in children, pregnant women, and people who are immunocompromised.
- 3 **Ask patients how their psoriasis has changed,** and suggest more aggressive treatment if necessary.

Good

- 1 **Know who among your patients** would be considered a member of a special population and has comorbid psoriasis.
- 2 **Talk with these patients** about their conditions, and urge them to always ask questions.
- 3 **Engage patients in conversation,** and listen actively to identify areas that may be a problem.



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How to Calculate a Psoriasis Area and Severity Index (PASI) Score Manually

Numerous learners have told us that they had difficulty calculating a **Psoriasis Area and Severity Index (PASI)** score manually based on the example given in Table 2. Thank you for your feedback. This exercise clarifies the process. Most clinicians now use online calculators, but understanding HOW the score is calculated can help you understand the condition's severity.

1. The four regions are the head (includes scalp and neck), upper extremities (includes arms, hands and palms), trunk (includes armpits and genitals) and lower extremities (includes legs, buttocks, feet and soles) To calculate a PASI, you need to consider

- four AREAS that are column headers shaded blue in the table.
- the LESION GRADE based on redness, thickness, and scaliness in each area
- the INVOLVEMENT GRADE of the AREA affected, in pink text in the table
- the WEIGHTED AREA assigned to the distinct region, which is a constant you will find in the blue shaded area

	Lesion (Scores vary from 0-4)	Head (weighted area is 0.1)	Upper Extremities (weighted area is 0.2)	Trunk (weighted area is 0.3)	Lower Extremities (weighted area is 0.4)
A	Redness				
B	Thickness				
C	Scaliness				
D	Add A+B+C in each column				
E	D x (involvement grade) x (weighted area)				
	TOTAL PASI				

2. First, you **grade the lesions** in the four regions for combined redness, thickness and scaliness on a grade of 0-4.

- Grade 0-no involvement
- Grade 1-slight
- Grade 2-moderate
- Grade 3-severe
- Grade 4-very severe

Enter the numbers in the appropriate column, now highlighted in yellow. Then, add the columns and enter the totals in the row highlighted in green. Note that you are adding the column vertically.

	Lesion (Scores vary from 0-4)	Head (weighted area is 0.1)	Upper Extremities (weighted area is 0.2)	Trunk (weighted area is 0.3)	Lower Extremities (weighted area is 0.4)
A	Redness	0	0	0	0
B	Thickness	2	0	1	0
C	Scaliness	3	0	0	0
D	Add A+B+C in each column	5	0	1	0
E	D x (involvement grade) x (weighted area)				
	TOTAL PASI				

This patient has no redness in any area. He has grade 2 thickness on his head, and grade 1 thickness on his trunk. He has severe scaling, but only on his head, so it is grade 3.

3. For each of the four distinct regions, **find the involvement grade** based on the percentage of the area affected by lesions on a scale of 0-6:

- Grade 0-no involvement
- Grade 1- <10% of skin involved
- Grade 2- 10-29%,
- Grade 3- 30-49%,
- Grade 4- 50-69%,
- Grade 5- 70-89%,
- Grade 6- 90-100%

On the third table, we filled in those numbers in row E in pink text.

	Lesion (Scores vary from 0-4)	Head (weighted area is 0.1)	Upper Extremities (weighted area is 0.2)	Trunk (weighted area is 0.3)	Lower Extremities (weighted area is 0.4)
A	Redness	0	0	0	0
B	Thickness	2	0	1	0
C	Scaliness	3	0	0	0
D	Add A+B+C in each column	5	0	1	0
E	D x (involvement grade) x (weighted area)	D x (3) x (weighted area)	D x (0) x (weighted area)	D x (3) x (weighted area)	D x (0) x (weighted area)
	TOTAL PASI				

Roughly 30% of this patient's head is affected, as is 30% of his trunk. So we inserted 3 in the formula.

5. Next, use the sum of the columns in row D and multiply each by the weighted area for each column.

We replaced the letter D with the number from the green cell in row D in the formula in row E. We inserted the weighted area with the appropriate constant in the blue row. Since this patient has no upper or lower extremity involvement, those numbers will be zero, and we have cleared the column.

	Lesion (Scores vary from 0-4)	Head (weighted area is 0.1)	Upper Extremities (weighted area is 0.2)	Trunk (weighted area is 0.3)	Lower Extremities (weighted area is 0.4)
A	Redness	0	0	0	0
B	Thickness	2	0	1	0
C	Scaliness	3	0	0	0
D	Add A+B+C in each column	5	0	1	0
E	D x (involvement grade) x (weighted area)	$5 \times (3) \times (0.1) = 1.5$		$D \times (3) \times (0.3) = 0.9$	
	TOTAL PASI	1.5 + 0.9 = 2.4			

6. Finally, add the the results from each column—the red numbers— and you have the PASI score

$$1.5 + 0.9 = 2.4$$

We have pasted a blank table below for you to use in the post-test.

	Lesion (Scores vary from 0-4)	Head (weighted area is 0.1)	Upper Extremities (weighted area is 0.2)	Trunk (weighted area is 0.3)	Lower Extremities (weighted area is 0.4)
A	Redness				
B	Thickness				
C	Scaliness				
D	Add A+B+C in each column				
E	D x (involvement grade) x (weighted area)				
	TOTAL PASI				

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