
Psoriasis: Which therapy for which patient



Focus on special populations and chronic infections

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Learning objectives

After completing this learning activity, participants should be able to provide a tailored approach for choosing an appropriate treatment regimen for psoriasis patients based on their individual disease characteristics and comorbidities.

Disclosures

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Despite the availability of several new systemic agents for psoriasis treatment, choosing the right therapy in certain patient populations can be challenging. There are few up-to-date reviews on systemic drugs for moderate to severe psoriasis in pregnant and pediatric patients and in patients with concomitant chronic infections, such as hepatitis, HIV, and latent tuberculosis. These groups are usually excluded from clinical trials, and much of the available evidence is based on anecdotal case reports and case series. As a chronic disease, psoriasis requires long-term treatment, and there are concerns of adverse maternal–fetal outcomes, long-term side effects in children, and the reactivation of latent infections with the use of systemic agents in these patients. The second article in this continuing medical education series provides insights for choosing appropriate systemic agents for treating moderate to severe psoriasis in pregnant and pediatric patients and in the setting of chronic infections, such as hepatitis, HIV, and latent tuberculosis. (*J Am Acad Dermatol* 2019;80:43-53.)

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Abbreviations used:

FDA:	Food and Drug Administration
HBV:	hepatitis B virus
HCV:	hepatitis C virus
LFT:	liver function test
LTBI:	latent tuberculosis infection
PASI:	Psoriasis Area and Severity Index
TNF:	tumor necrosis factor
VACTERL:	vertebral anomalies, anal atresia cardiac defects, tracheoesophageal fistula and/or esophageal atresia, renal and radial anomalies and limb defects

In addition to the comorbidities discussed in the first article in this continuing medical education series, there are certain other clinical scenarios, such as pregnancy, pediatric age group, and concomitant chronic infections that often complicate the choice of systemic agent for psoriasis. The second article in this continuing medical education series provides insights for choosing an appropriate systemic agent for treating moderate to severe psoriasis in pregnant and pediatric patients and in the setting of chronic infections, hepatitis, HIV, and latent tuberculosis.

PREGNANCY

The treatment of psoriasis in pregnant patients can be challenging. Because of the immunomodulatory changes of pregnancy, psoriasis generally tends to improve, but some patients can experience worsening of psoriasis, warranting the need for systemic treatment.¹ Pregnant patients are excluded from clinical trials and much of the available safety data are obtained from case reports.

Traditional agents

Methotrexate is teratogenic, mutagenic, abortifacient, and is contraindicated in pregnancy. Methotrexate is associated with embryopathy leading to central nervous system, craniofacial, and limb and growth abnormalities.² Cyclosporine pregnancy data are mostly obtained from organ transplant patients. Cyclosporine is not a major teratogen, with a prevalence rate for congenital malformations reported to be approximately 3%, similar to that of general population.^{3,4} However, there have been reports of low birth weight and preterm deliveries among infants after in utero exposure to cyclosporine.⁵⁻⁷ Many reports have highlighted the safety of cyclosporine in treating psoriasis in pregnant patients.⁸⁻¹²

The teratogenicity of retinoids is the most important concern in women of reproductive potential. Acitretin causes retinoic acid embryopathy, including cardiovascular, ocular, auditory, central nervous system, craniofacial, and skeletal malformations.¹³

Biologics and other newer agents

There is a lack of well controlled studies assessing biologics during pregnancy. Structural differences between different tumor necrosis factor- α (TNF- α) inhibitors determines their transplacental transfer and cord blood concentrations. Significant elevation of adalimumab (160%) and infliximab (153%) has been noted in the cord blood of newborns, whereas etanercept levels were only 4% to 7% of that in maternal blood.¹⁴⁻¹⁷ Certolizumab is noted to have low levels in cord blood (3.9%) because it has minimal transplacental transfer because of its pegylated structure. Data from >300 certolizumab-exposed pregnancies show no increase of maternal or fetal adverse events.^{18,19} There is concern of a possible association between etanercept and vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula and/or esophageal atresia, renal and radial anomalies, and limb defects (VACTERL) syndrome based on a case report and a review by the US Food and Drug Administration (FDA).^{20,21} However, this report had limitations, such as unclear definitions of VACTERL and poor study design, deeming the results uninterpretable.²² Contrarily, the majority of other studies on etanercept use in pregnancy have been reassuring.²³⁻²⁶ Also worrisome is a case report of fatal disseminated mycobacterial infection following a routine bacillus Calmette-Guérin vaccination in a neonate born to a mother taking infliximab throughout pregnancy, which raised concern of fetal immunosuppression with in utero exposure to infliximab.²⁷ A small study of 8 infants exposed to infliximab in utero concluded that infants mounted an appropriate immune response to routine vaccinations and that there were no concerns for immunosuppression.¹⁵ Overall, the incidence rate of adverse outcomes in several reports observed rates similar to the general US population.²⁸⁻³⁰ The specific data for adalimumab are limited, but several reports of its use in pregnant women with Crohn's disease and rheumatoid arthritis did not show any evidence of maternal or fetal adverse events.^{25,29,31-33} There are no data available for golimumab use in pregnancy. Among the few reports of ustekinumab use in pregnancy, there are 2 reports of delivery of healthy full-term neonates and 1 report of spontaneous abortion.³⁴⁻³⁶ There are no reports of apremilast and IL-17 and IL-23 inhibitor use in pregnant women. The animal data on apremilast, secukinumab, and brodalumab use in pregnancy do not demonstrate any embryo-fetal toxicity. Animal studies on ixekizumab showed an increase in neonatal deaths when it was administered from week 20 to birth.³⁷

Table I summarizes the pregnancy warnings (previous categories) for the approved systemic agents for psoriasis.

Expert opinion

1. Certolizumab is the most preferred agent because of its minimal transplacental transfer. Etanercept is a good alternative because its placental transfer is less than infliximab and adalimumab
2. Ustekinumab and secukinumab were both FDA pregnancy risk category B when pregnancy categories were assigned and are considered safe, but available data are limited. There are minimal data available on ixekizumab, brodalumab, apremilast, and IL-23 inhibitors
3. Methotrexate and acitretin are absolutely contraindicated in pregnancy. Cyclosporine can be used but its use should be limited to the shortest duration at the lowest possible dose

PEDIATRIC POPULATION

Approximately one third of psoriasis cases develop in childhood, and psoriasis accounts for nearly 4% of all dermatoses seen in children <16 years of age.³⁹ Among the multiple systemic treatments available for psoriasis in adults, only a few systemic drugs are approved for use in the pediatric population.

Traditional agents

Van Geel et al⁴⁰ demonstrated methotrexate therapy to be safe with significant improvement in Psoriasis Area and Severity Index score and quality of life in pediatric psoriasis patients. However, it should be used intermittently to prevent cumulative toxicity.⁴¹⁻⁴³ Cyclosporine is considered safe in children based on data from its use for other indications, such as atopic dermatitis.⁴⁴⁻⁴⁶ There are only a few published reports of cyclosporine use in pediatric psoriasis, most of which describe rapid improvement in psoriasis without any major side effects.⁴⁷⁻⁵²

The major concern with the long-term use of retinoids in children are the skeletal side effects, such as premature closure of epiphysis, calcification of tendons, and hyperostotic changes.⁵³ In addition, its mucocutaneous side effects can decrease children's compliance to treatment.^{41,54} However, acitretin has been used successfully for pediatric pustular, erythrodermic, and severe plaque psoriasis without any significant radiologic abnormalities.⁵⁵⁻⁶¹

Biologics and other newer agents

Etanercept is the only biologic approved for use in children >6 years of age.⁶² Adalimumab is approved for the treatment of juvenile idiopathic arthritis in

Table I. US Food and Drug Administration pregnancy category of systemic agents for psoriasis

Pregnancy category	Systemic agents for psoriasis
B*	Etanercept, adalimumab, infliximab, certolizumab, golimumab, ustekinumab, and secukinumab
C†	Cyclosporine and apremilast
Contraindicated	Methotrexate and acitretin

Recent guidelines by the US Food and Drug Administration abolished the previously used pregnancy categories (A, B, C, D, and X). They have been replaced by narrative summaries providing relevant information to aid health care workers in appropriately prescribing and counseling patients.³⁸

*Equivalent to former category B.

†Equivalent to former category C.

patients ≥4 years of age, and it is currently used off-label for pediatric uveitis, psoriasis, and inflammatory bowel disease.⁶³ Adalimumab has demonstrated good safety and efficacy in pediatric psoriasis. A phase III trial compared adalimumab and methotrexate in 114 pediatric patients (4-17 years of age) with severe psoriasis. At week 16, a 75% improvement in the Psoriasis Area and Severity Index score in the adalimumab group was 58%, which was significantly higher than 32% in the methotrexate group.^{64,65} Infliximab is approved for the treatment of Crohn's disease in children ≥6 years of age.⁶⁶ Garber et al⁶⁷ reported high clearance rates in pediatric psoriasis with TNF-α blockers (67% with etanercept and adalimumab) and ustekinumab (33%). Data on certolizumab and golimumab use in the pediatric population are limited.

A phase III study (CADMUS) of ustekinumab randomized 110 psoriasis patients who were 12 to 17 years of age to receive placebo or ustekinumab at standard dosing (0.75 mg/kg [≤60 kg], 45 mg [>60-≤100 kg], and 90 mg [>100 kg]) or half standard dosing (0.375 mg/kg [≤60 kg], 22.5 mg [>60-≤100 kg], and 45 mg [>100 kg]). Overall, the standard dose of ustekinumab produced a clinical response in the pediatric population similar to that observed in the adult population and was accompanied by a favorable safety profile.⁶⁸ The safety and efficacy of apremilast and IL-17 and IL-23 inhibitors has not been established in the pediatric population as yet, and the related literature is scarce.

Expert opinion

1. Data on TNF-α blockers suggest that these are safe and effective in managing pediatric psoriasis, and etanercept is approved by the US FDA for the treatment of pediatric psoriasis in patients ≥6 years of age
2. Ustekinumab has a convenient dosing schedule for children, making it a preferred agent in

pediatric psoriasis. It is approved for use in adolescents

3. Data on apremilast and IL-17 and IL-23 inhibitors in the pediatric population are limited
4. None of the traditional agents (methotrexate, cyclosporine, and acitretin) are approved by the US FDA for the treatment of pediatric psoriasis, but they are considered safe for intermittent and short-term use

CHRONIC INFECTIONS

Most systemic agents for psoriasis are immunosuppressive, which poses a unique treatment challenge in patients with psoriasis with chronic infections because they are already immunosuppressed. In this section, we discuss treatment strategies for patients with psoriasis who have concomitant hepatitis B virus (HBV) and hepatitis C virus (HCV), HIV, and latent tuberculosis.

Hepatitis

Patients who are eligible for systemic therapy must be screened for the following markers: antibody to hepatitis B core (anti-Hbc Ag), hepatitis B surface antigen (HbsAg), and antibody to HCV (anti-HCV). Based on serology, patients can be categorized into the following groups: 1) HbsAg indicates that person is infectious; 2) anti-Hbc Ag appears with acute infection and persists for life, and immunoglobulin M anti-Hbc indicates acute infection; 3) anti-HbsAg antibody indicates either recovery or immunity because of vaccination; and 4) anti-HCV indicates presumptive or current HCV infection and warrants additional HCV RNA testing.

Traditional agents

Methotrexate is hepatotoxic and has been associated with HBV reactivation.⁶⁹⁻⁷¹ A case series reported hepatic fibrosis and cirrhosis in 24% of patients after 5 years of treatment with methotrexate.⁷²⁻⁷⁴ The role of cyclosporine in patients with hepatitis is controversial. There are multiple case reports of HBV and HCV reactivation with cyclosporine in patients who are immunocompromised.^{75,76} Cyclosporine is also reportedly associated with the recurrence and progression of HCV leading to severe fibrosis and cirrhosis.⁷⁷ Cyclosporine increased the risk of HBV reactivation in patients who were HbsAg-negative/HbcAb-positive transplant patients.⁷⁸ Conversely, cyclosporine has demonstrated inhibition of both HBV and HCV in vitro and discontinuation of cyclosporine has been associated with reactivation of the viral

infection.⁷⁹⁻⁸² All systemic therapies for psoriasis except acitretin are immunosuppressive, but acitretin is potentially hepatotoxic.⁷⁴ Nonetheless, Roenigk Jr et al⁸³ reported no significant change in liver histology after 2 years of acitretin use in patients with psoriasis.

Biologics and other newer agents

TNF- α plays an important role in the clearance of hepatitis virus from infected hepatocytes; therefore, TNF- α inhibitors may lead to hepatitis reactivation or disease worsening.⁸⁴ There are several reports of hepatitis reactivation in patients who are receiving TNF- α inhibitors.⁸⁵⁻⁸⁷ Di Nuzzo et al⁸⁸ identified 26 publications describing a total of 61 HCV-positive patients who had received anti-TNF- α agents. Most patients did not have any significant change in liver function and HCV viral load. Another study in 15 patients with HCV and psoriatic arthritis showed no significant change in liver enzymes and viral load after anti-TNF- α therapy.⁸⁹ There are no reports of golimumab and certolizumab use with HCV infection.

An analysis of 257 HbsAg-positive or anti-Hbc-positive patients receiving anti-TNF- α therapy showed HBV reactivation in 39% of HbsAg-positive patients compared with 5% of anti-Hbc-positive patients. HBV reactivation was more frequent in patients without antiviral prophylaxis compared with patients with antiviral prophylaxis (62% vs 23%; $P = .003$). Patients with anti-Hbc positivity pose a lower risk of viral reactivation compared with patients with HbsAg positivity. If possible, biologics should be avoided in HbsAg-positive patients, but if deemed necessary, patients should receive antiviral prophylaxis before treatment initiation.⁸⁵

In a review of HBV and HCV reactivation in patients with psoriasis who were taking biologics, virus reactivation was noted in 2 of 175 patients who were positive for anti-Hbc antibody, 3 of 97 patients with HCV infection, and 8 of 40 patients with positive HbsAg. The authors concluded that biologics pose minimal risk for viral reactivation in patients with anti-HCV or anti-Hbc antibodies, but they are of considerable risk in HbsAg-positive patients.⁹⁰ There are multiple reports of successful etanercept use in patients with psoriasis with coexisting HCV infection.^{89,91-98} Zein⁹⁹ used etanercept as an adjuvant to interferon and ribavirin for the treatment of HCV infection. The etanercept-treated group noted a higher percentage of patients with HCV-RNA absence and liver fibrosis regression compared with the placebo group. The infliximab package insert warns about rare severe hepatic reactions,

some fatal or necessitating liver transplantation. It also warns about HBV reactivation and recommends monitoring of HBV carriers during and several months after therapy.¹⁰⁰ Frider et al¹⁰¹ reported a case of drug-induced liver injury caused by adalimumab. Data on certolizumab and golimumab use in hepatitis are limited.

The safety profile of ustekinumab in patients with hepatitis is controversial. Chiu et al¹⁰² assessed the safety of ustekinumab in patients with psoriasis with concurrent HCV and HBV infection. Viral reactivation and hepatocellular cancer were reported in 1 of 4 patients with HCV and in 2 of 7 HbsAg-positive patients who had not received antiviral prophylaxis; reactivation was not noted in 3 HbsAg-negative but anti-Hbc-positive patients. A few other cases of HBV reactivation have been reported with ustekinumab.¹⁰³⁻¹⁰⁵ Contrarily, Abuchar et al¹⁰⁶ reported the successful use of ustekinumab for psoriasis without any impact on liver function or viral load in a patient with coexisting HCV. Secukinumab use in hepatitis has been reported in 5 patients with HBV, 3 patients with HCV, and 1 patient with HBV-HCV coinfection. No significant elevation in liver enzymes or virus reactivation was noted in any of these patients.^{90,107,108} Data on apremilast use in hepatitis infection are limited. Reddy et al¹⁰⁹ reported a case of concomitant HCV, HIV, and psoriasis treated with apremilast. They did not note any worsening of liver function or viral reactivation.¹⁰⁹ There are no available data on IL-23 inhibitor use in patients with hepatitis.

Expert opinion

Patients should not be treated with immunosuppressive therapies during the acute stage. However, biologic treatment can be initiated in patients with chronic or resolved hepatitis under close monitoring and collaboration with a gastroenterologist.

Anti-HCV-positive

1. TNF- α inhibitors can be used in patients with chronic HCV but with close monitoring of liver function and viral titers, and in conjunction with antiviral therapy
2. The safety profile of ustekinumab is controversial
3. IL-17 inhibitors and apremilast appear to have a favorable safety profile, but the available data are limited. Data are limited on IL-23 inhibitor use in hepatitis
4. Methotrexate is absolutely contraindicated. Acitretin requires monitoring of liver function tests (LFTs). Cyclosporine is controversial, but if used requires monitoring of LFTs and viral titers, and antiviral therapy is prudent

HBV: HbsAg-positive

1. Using TNF- α inhibitors and ustekinumab can lead to viral reactivation, but IL-17 inhibitors appear safe if used after antiviral prophylaxis and with close monitoring of LFTs and viral titers
2. There are no data on apremilast and IL-23 inhibitors
3. Methotrexate and cyclosporine are contraindicated
4. If acitretin is used, monitoring of LFTs is necessary

HBV: Anti-Hbc-positive

1. Lesser risk of HBV reactivation than HbsAg-positive patients; therefore, TNF- α inhibitors, ustekinumab, and IL-17 inhibitors can be used with close monitoring of LFTs and viral titers. There are no data on apremilast and IL-23 inhibitors
2. Methotrexate and cyclosporine are contraindicated
3. If acitretin is used, monitoring of LFTs is necessary

HIV

The prevalence of psoriasis among HIV-positive patients in the United States is reported to be 1% to 3%, which is similar to rates reported in the general population.¹¹⁰

Traditional agents

Methotrexate is associated with a high risk of opportunistic infections in patients with HIV. In a case series, 1 patient developed toxic encephalopathy that improved after methotrexate was discontinued.¹¹¹ In another study, 4 HIV patients were treated with antiretroviral treatment and received prophylaxis for opportunistic infections before starting methotrexate for psoriasis; 2 of 4 patients developed *Pneumocystis carinii* pneumonia.^{112,113}

Data supporting the use of cyclosporine in patients with HIV are limited. There are 2 case reports of successful treatment of psoriasis with cyclosporine in patients with HIV without the development of opportunistic infections or worsening immunosuppression.^{114,115} Acitretin is recommended as second-line therapy for moderate to severe psoriasis in patients with HIV because it is a nonimmunosuppressive agent.¹¹⁶ Buccheri et al¹¹⁷ treated 11 patients with HIV-associated psoriasis with acitretin monotherapy. Significant clearance was achieved in 36% of patients after 20 weeks of treatment without any deterioration in immune function.¹¹⁷ Of special note, though not approved for psoriasis,

Table II. Factors to consider when selecting systemic psoriasis treatment

Class of drugs	Drug/special population	Pregnancy	Pediatric	Anti-HCVAb+	HbsAg+	Anti-Hbc+	HIV	Latent TB
TNF- α inhibitors	Etanercept	+	++	++*	—	+/-*	+	—
	Adalimumab	+	++	+	—	+/-*	+	—
	Infliximab	+	+	+	—	+/-*	+	—
	Certolizumab	++	+	+	—	+/-*	+	—
	Golimumab	+	++	+	—	+/-*	+	—
IL-12/23 inhibitor	Ustekinumab	+	++	—	—	?/+*	+	—
IL-17 inhibitors								
Anti-IL-17A	Secukinumab	?/+	?/+	?/+*	?/+*	?/+*	?/+*	+
Anti-IL-17A	Ixekizumab	?/+	?/+	?/+*	?/+*	?/+*	?/+*	+
Anti-IL-17 receptor	Brodalumab	?/+	?/+	?/+*	?/+*	?/+*	?/+*	+
IL-23 inhibitors	Guselkumab	?	?/+	?	?	?	?	?
	Tildrakizumab	?	?/+	?	?	?	?	?
	Risankizumab	?	?/+	?	?	?	?	?
	Mirikizumab	?	?/+	?	?	?	?	?
Oral novel	Apremilast	?	?/+	?/+*	?	?	+	+
Oral traditional	Methotrexate	x	+	x	x	x	x	x
	Cyclosporine	+	+	+/-*	x	x	x	x
	Acitretin	x	+	+	+	+	+	+

Note: Two plus symbols (++) indicates preferred agents; one plus symbol (+) indicates that the agent can be used; one plus symbol and one minus symbol (+/-) indicate that the drug can be used but is controversial; one minus symbol and one plus symbol (-/+) indicates that the drug is not preferred but can be used; one question mark and one plus symbol (?/+) indicates that there are not enough data but that the drug is likely safe to use; one question mark (?) indicates that there are not enough data; one minus symbol (—) indicates that use of that drug is controversial because there are not enough data; and x indicates that a drug is contraindicated.

Anti-Hbc, Antibody to hepatitis B core; anti-HCV, antibody to hepatitis C virus; HbsAg, hepatitis B surface antigen; TB, tuberculosis.

*Additional monitoring required.

hydroxyurea has been recommended in patients with psoriasis and HIV infection because of its antiretroviral properties and historic use for psoriasis.¹¹⁸

Biologics and other newer agents

There are a few reports of successful etanercept use in patients with HIV with psoriasis, with only 1 report of polymicrobial infection; CD4 and viral counts either improved or remained stable after treatment.¹¹⁹⁻¹²³ Infliximab has also been used successfully in patients with HIV and psoriasis. Cepeda et al¹²⁴ reported 8 patients with HIV with various rheumatologic diseases that were treated with etanercept or infliximab. During therapy, CD4 counts remained stable and no opportunistic infections were reported.¹²⁴⁻¹²⁶ There is 1 case report of successful treatment of HIV-associated psoriasis with adalimumab with significant improvement in his CD4 count and viral load.¹²⁷ There are no reports on the use of certolizumab and golimumab in HIV-positive patients. Ustekinumab has also been used successfully in patients with HIV on antiretroviral treatment with improvement in CD4 and viral counts.^{128,129} Apremilast use has been reported in a patient with concomitant HIV and HCV without any

adverse events.¹⁰⁹ There are no data on the use of IL-17 and IL-23 inhibitors in HIV-associated psoriasis.

Expert opinion

1. TNF- α inhibitors, ustekinumab, and apremilast can be used to treat psoriasis in HIV, but these patients should be managed in collaboration with infectious disease specialists for close monitoring of CD4 count and viral load
2. There are no data on IL-17 and IL-23 inhibitor use in patients with HIV, but they are less commonly complicated by opportunistic infections than TNF- α inhibitors
3. Acitretin can be used in patients with HIV, but methotrexate and cyclosporine should be avoided because of the risk of opportunistic infections

LATENT TUBERCULOSIS

Approximately 4.2% of the US population is affected by latent tuberculosis infection (LTBI).^{130,131} All patients should be screened for LTBI with either a tuberculin skin test or interferon gamma release assay (IGRA) before starting any immunosuppressive systemic therapy.¹³² A positive screening test requires further medical evaluation and a chest radiograph.

Normal chest radiography suggests LTBI, and these patients should receive isoniazid prophylaxis for 1 to 2 months before biologic initiation can also be considered acceptable.^{132,133}

Traditional agents

There is a well-recognized association between methotrexate-induced immunosuppression and LTBI reactivation. Several cases of pulmonary and extrapulmonary tuberculosis have been reported in patients with rheumatoid arthritis and psoriasis on methotrexate therapy.¹³⁴⁻¹³⁶

Higher doses of cyclosporine have been associated with LTBI reactivation in solid organ transplant patients, but no cases have been reported in patients with psoriasis, likely because of relatively lower doses used in the dermatologic setting.¹³⁷⁻¹³⁹ There are no reports of LTBI reactivation with acitretin.

Biologics and other newer agents

TNF- α is essential for granuloma formation and plays an important role in host defense against intracellular pathogens like mycobacteria. Multiple cases of tuberculosis infection have been described with all TNF- α blockers.^{140,141} The FDA adverse event reporting system reported tuberculosis infection in 144 of 100,000 patients receiving infliximab and in 35 of 100,000 patients receiving etanercept. Among the TNF- α blockers, infliximab is the most frequently associated agent with LTBI reactivation, likely because of the greater and prolonged TNF blockade.¹⁴² Certolizumab and golimumab have also led to LTBI reactivation, specifically in patients who did not receive isoniazid prophylaxis.^{143,144} Phase III trials of ustekinumab identified 167 patients with LTBI before treatment initiation; only 1 patient who had not received INH prophylaxis experienced LTBI reactivation. Another case of LTBI reactivation has been reported with ustekinumab even though the patient received isoniazid prophylaxis.¹⁴⁵ So far, no cases of LTBI reactivation have been reported with apremilast or IL-17 and IL-23 blockers.

Expert opinion

1. It is safe to use IL-17 inhibitors and apremilast in patients with LTBI
2. TNF- α inhibitors and ustekinumab can be used only after tuberculosis prophylaxis has been initiated for at least a month
3. Additional safety data are needed for IL-23 inhibitors
4. Methotrexate and cyclosporine can be used in patients with LTBI after tuberculosis prophylaxis
5. Acitretin is safe to use in this setting

In conclusion, the decision to use systemic agents to treat psoriasis in pregnant and pediatric populations requires careful analysis of the risks and benefits to maternal–fetal health and long-term safety in children. In addition, most systemic agents used in psoriasis are immunosuppressive and require appropriate screening, monitoring, and prophylaxis when used in patients with chronic infections, such as hepatitis, HIV, and LTBI. A summary of our expert opinion is shown in Table II. Up-to-date literature on the use of systemic agents in these settings is scarce, and more long-term studies and safety data are warranted.

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Answers to CME examination

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