FROM THE ACADEMY

Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients

Alan Menter, MD (Co-Chair),[a] Kelly M. Cordoro, MD,[b] Dawn M. R. Davis, MD,[c] Daniela Kroshinsky, MD, MPH,[d] Amy S. Paller, MD,[e] April W. Armstrong, MD, MPH,[f] Cody Connor, MD,[g] Boni E. Elewski, MD,[g] Joel M. Gelfand, MD, MSCE,[h] Kenneth B. Gordon, MD,[i] Alice B. Gottlieb, MD, PhD,[j] Daniel H. Kaplan, MD, PhD,[k] Arthur Kavanaugh, MD,[l] Matthew Kiselica, BA/BS,[m] Dario Kivelevitch, MD,[a] Neil J. Korman, MD, PhD,[n] Mark Lebwohl, MD,[o] Craig L. Leonardi, MD,[p] Jason Lichten, MD,[m] Henry W. Lim, MD,[q] Nehal N. Mehta, MD, MSCE,[r] Sylvia L. Parra, MD,[s] Arun L. Pathy, MD,[t] Elizabeth A. Farley Prater, MD,[u] Reena N. Rupani, MD,[o] Michael Siegel, PhD,[v] Benjamin Stoff, MD, MA,[w] Bruce E. Strober, MD, PhD,[x,y] Emily B. Wong, MD,[z] Jashin J. Wu, MD,[aa] Vidhya Hariharan, PhD,[bb] and Craig A. Elmets, MD (Co-Chair)[g]

Dallas, Texas; San Francisco, California; Rochester, Minnesota; Boston, Massachusetts; Chicago, Illinois; Los Angeles, California; Birmingham, Alabama; Philadelphia, Pennsylvania; Milwaukee, Wisconsin; New York, New York; Pittsburgh, Pennsylvania; San Diego, California; Cleveland, Ohio; St Louis, Missouri; Detroit, Michigan; Bethesda, Maryland; Sumter, South Carolina; Centennial, Colorado; Oklahoma City, Oklahoma; Indianapolis, Indiana; Atlanta, Georgia; Cromwell and New Haven, Connecticut; San Antonio, Texas; Irvine, California; and Rosemont, Illinois

Psoriasis is a chronic, multisystem, inflammatory disease that affects approximately 1% of children, with onset most common during adolescence. This guideline addresses important clinical questions that arise in psoriasis management and provides evidence-based recommendations. Attention will be given to pediatric patients with psoriasis, recognizing the unique physiology, pharmacokinetics, and patient-parent-provider interactions of patients younger than 18 years old. The topics reviewed here mirror those discussed in the adult guideline sections, excluding those topics that are irrelevant to, or lack sufficient information for, pediatric patients. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2019.08.049.)

Key words: clinical guidelines for psoriasis; comorbidities; dermatology; guidelines; pediatric; pediatric psoriasis; psoriasis; psoriasis guidelines; skin disease.

From the Baylor University Medical Center, Dallas[a]; University of California, San Francisco School of Medicine, Department of Dermatology, San Francisco[b]; Mayo Clinic, Rochester[c]; Massachusetts General Hospital, Boston[d]; Northwestern University Feinberg School of Medicine, Chicago[e]; University of Southern California, Los Angeles[f]; University of Alabama, Birmingham[g]; University of Pennsylvania Perelman School of Medicine, Philadelphia[h]; Medical College of Wisconsin, Milwaukee[i]; Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York[j]; University of Pittsburgh[k]; University of San Diego[l]; National Psoriasis Foundation[m]; University Hospitals Cleveland Medical Center[n]; Icahn School of Medicine at Mount Sinai, New York[o]; Central Dermatology, St Louis[p]; Department of Dermatology, Henry Ford Medical Center, Detroit[q]; National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda[r]; Dermatology and Skin Surgery, Sumter[s]; Colorado Permanente Medical Group, Centennial[t]; University of Oklahoma Health Sciences Center, Oklahoma City[u]; Pediatric Dermatology Research Alliance, Indianapolis[v]; Emory University School of Medicine, Atlanta[w]; Central Connecticut Dermatology, Cromwell[x]; Yale University, New Haven[y]; San Antonio Uniformed Services Health Education Consortium, Joint-Base San Antonio[z]; Dermatology Research and Education Foundation, Irvine[aa]; and American Academy of Dermatology, Rosemont.[bb]

Funding sources: None.

Conflicts of interest: Listed in text.

Accepted for publication August 14, 2019.

Reprints not available from the authors.

Correspondence to: Vidhya Hariharan, PhD, American Academy of Dermatology, 9500 W Bryn Mawr Ave, Rosemont, IL 60018. E-mail: vhariharan@aad.org.

Published online October 23, 2019.

0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2019.08.049

CONFLICT OF INTEREST STATEMENT

The American Academy of Dermatology (AAD) strives to produce clinical guidelines that reflect the best available evidence supplemented with the judgment of expert clinicians. Significant efforts are taken to minimize the potential for conflicts of interest to influence guideline content. The management of conflict of interest for this guideline complies with the Council of Medical Specialty Societies' Code of Interactions with Companies. Funding of guideline production by medical or pharmaceutical entities is prohibited, full disclosure is obtained and evaluated for all guideline contributors throughout the guideline development process, and recusal is used to manage identified relationships. The AAD conflict of interest policy summary may be viewed at www.aad.org.

The authors' disclosed relationships with industry during guideline development appear at the end of this guideline. Authors (listed alphabetically) with relevant conflicts with respect to this guideline are noted with an asterisk*. In accordance with AAD policy, a minimum 51% of workgroup members did not have any relevant conflicts of interest.

Participation in 1 or more of the following activities constitutes a relevant conflict:

- Service as a member of a speaker bureau, consultant, or advisory board member for pharmaceutical companies on the psoriasis disease state or psoriasis drugs in development or approved by the US Food and Drug Administration.
- Sponsored research funding or investigator-initiated studies with partial/full funding from pharmaceutical companies on the psoriasis disease state or psoriasis drugs in development or approved by the US Food and Drug Administration.

If a potential conflict was noted, the work-group member recused himself or herself from discussion and drafting of recommendations pertinent to the topic area of interest. Complete group consensus was obtained for draft recommendations. Areas in which complete consensus was not achieved are shown transparently in the guideline.

DISCLAIMER

Adherence to these guidelines will not ensure successful treatment in every situation. Furthermore, these guidelines should not be interpreted as setting a standard of care, nor should they be deemed either inclusive of all proper methods of care or exclusive of other methods of care reasonably directed toward obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician, the patient, and the caregiver in light of circumstances presented by the individual patient and the known variability and biological behavior of the disease. Furthermore, the treatment dosages used in clinical trials may not be effective in certain cases, and some patients may require shorter intervals between doses and/or higher treatment doses of a particular treatment methodology. This guideline reflects the best available data at the time the guideline was prepared. The results of future studies may require revisions to the recommendations in this guideline to reflect new data.

SCOPE

This guideline addresses the management of psoriasis and its extracutaneous manifestations in children and adolescents, with attention to topical and systemic treatment options, phototherapy, and comorbidities, including psychosocial wellness and quality of life (QOL). The importance of a robust physician and patient/caregiver relationship is emphasized to facilitate and promote patient participation in choices in a shared decision-making model.

METHOD

For detailed methodology, see Appendix 1.

DEFINITIONS

For full definition statement, see Appendix 1.

PSORIASIS IN PEDIATRIC PATIENTS

Psoriasis is a chronic, multisystem, inflammatory disease that affects approximately 1% of children, with onset most common during adolescence. One third of psoriasis cases begin in the pediatric years. Although skin involvement is often the impetus for patients to seek medical care, recognition of the condition as a potentially multisystem disorder is imperative to optimize disease management. Psoriasis often follows a relapsing course and can negatively affect QOL. Psoriasis in children may be associated with a variety of comorbid conditions, of which psoriatic arthritis (PSA) has the largest evidence base.

This section of the guidelines will review the approach to the pediatric patient with psoriasis, taking into consideration the unique characteristics of younger patients relative to adults, such as physiology, pharmacokinetics, and family structure (Table I). Comorbidities and other individualized factors must be considered when selecting the appropriate management strategy for any patient with psoriasis.[1,2] Some of the more common comorbidities in children are discussed below. The goal of

Abbreviations used:

AAD:	American Academy of Dermatology
AAP:	American Academy of Pediatrics
aHR:	adjusted hazard ratio
AOR:	adjusted odds ratio
BMI:	body mass index
BSA:	body surface area
CDLQI:	Children's Dermatology Life Quality Index
CI:	confidence interval
FDA:	US Food and Drug Administration
GI:	gastrointestinal
HPA:	hypothalamic-pituitary-adrenal
ICD:	International Classification of Diseases
IL:	interleukin
LDL:	low-density lipoprotein
NAFLD:	nonalcoholic fatty liver disease
NB:	narrowband
OR:	odds ratio
PASI:	Psoriasis Area and Severity Index
PASI 75:	75% improvement in Psoriasis Area and Severity Index
PPD:	purified protein derivative
PSA:	psoriatic arthritis
PUVA:	psoralen ultraviolet light A
QOL:	quality of life
TCI:	topical calcineurin inhibitor
TNF:	tumor necrosis factor
UV:	ultraviolet
UVA:	ultraviolet light A
UVB:	ultraviolet light B

this section is to educate physicians, patients, and their caregivers about the potential impact of psoriasis on multiple domains of health, its impact on the patient and family, and the scope of treatments available to pediatric patients.

SEVERITY MEASURES

In adult patients, the severity of psoriasis is generally defined by the total body surface area (BSA) involved, with less than 3% BSA considered mild, 3% to 10% BSA considered moderate, and greater than 10% BSA considered severe disease. This method can also be used for children and is the most common method for determining disease severity in clinical practice.[3] A standard way to measure BSA in children is the "rule of 9s," with adjustment of regional relative proportions based on age. (Computer BSA models are available for children but not widely used). Importantly, BSA should not be the sole predictor of disease severity. Psoriasis can have a significant negative impact on QOL, including physical, emotional, social, and psychological functioning, and these features should be strongly considered along with clinical and patient-reported assessments. For example, a child with psoriasis limited to the face or the entire scalp does not have severe disease based on BSA definitions, but if this involvement causes shame, social withdrawal, or bullying, it satisfies criteria for severe disease based on impact beyond the skin.[4]

A formal method of determining the impact on QOL as a proxy for severity may be considered, such as the Children's Dermatology Life Quality Index (CDLQI). The CDLQI is a 10-question survey, a derivative of the Dermatology Life Quality Index commonly measured in adults. It aims to assess QOL for patients ages 4 through 16 years, addressing QOL variables such as itch, sleep, hygiene,

Table I. Clinical questions

1. What are the available screening tools used to effectively measure psoriasis severity and response to therapy in children with psoriasis?
2. What are the available screening and/or therapeutic interventions used to manage the following comorbidities in children with psoriasis?
   a. Psoriatic arthritis
   b. Cardiovascular disease
   c. Metabolic syndrome
      i. Obesity
      ii. Dyslipidemia
      iii. Hypertension
      iv. Insulin resistance
   d. Mental health
   e. Inflammatory bowel disease
3. What are the efficacy, effectiveness, and adverse events of the following treatments used as monotherapy and/or combination therapy with other management options for psoriasis in pediatric and adolescent patients?
   a. Topical treatments
      i. Topical corticosteroids
      ii. Topical calcineurin inhibitors
      iii. Topical Vitamin D analogues
      iv. Combination topical therapy
      v. Topical tazarotene
      vi. Anthralin
      vii. Topical coal tar
   b. Phototherapy and photochemotherapy treatments
      i. Narrowband ultraviolet light B
      ii. Psoralen ultraviolet light A
   c. Nonbiologic systemic treatments
      i. Methotrexate
      ii. Cyclosporine
      iii. Systemic retinoids
      iv. Systemic fumaric acid esters
   d. Biologic therapy
      i. Etanercept
      ii. Adalimumab
      iii. Infliximab
      iv. Ustekinumab

Table II. Recommendations for pediatric psoriasis and disease severity measures

Recommendation No.	Recommendation	Strength of recommendation
1.1	Body surface area measurement of involved skin is recommended as a useful measure of psoriasis severity in children.	C
1.2	Disease location on the body and impact on physical, social, and psychological quality of life and/or activities of daily living are recommended as measures of psoriasis severity and should be taken into consideration when determining psoriasis severity in children.	C

Table III. Level of evidence for pediatric psoriasis and disease severity measures

Recommendation	Recommendation No.	Level of evidence	Studies
Body surface area	1.1	III	7
Quality of life measures	1.2	II-III	5,6,8,9

impact on relationships and activities, and treatment efficacy. It is available in written and cartoon form. Its use for patients with pediatric psoriasis has been validated in 8 studies, summarized by Salek et al in 2013.[5] Patients find the questionnaire easy to use, and the cartoon questionnaire is faster to complete and is preferred by patients and parents regardless of age, although the cartoon version is designed for patients ages 4 through 11 years.[5,6]

Although the CDLQI addresses pruritus, this symptom is poorly addressed in general and is underrecognized in pediatric psoriasis, in contrast to atopic dermatitis. Pruritus is frequently reported by patients with pediatric psoriasis, and this symptom should be elicited and treated in practice.

The Psoriasis Area and Severity Index (PASI) is a more specific means of quantifying the extent and severity of psoriasis because it takes into account BSA and the intensity of redness, scaling, and plaque thickness, ultimately producing a score from 0 (no disease) to 72 (maximal disease severity). The PASI is frequently used in research for monitoring response to treatments, but it is rarely used by dermatologists in general practice. There is limited literature available to measure the effectiveness or practicality of PASI scoring in children.

The strength of recommendations and levels of evidence for pediatric psoriasis and disease severity measures are summarized in Tables II and III.[5-9]

TRIGGERS AND COMORBID CONDITIONS

Psoriasis may be triggered or exacerbated by infections; physiologic, emotional, and environmental stressors; and cutaneous trauma—the latter referred to as the *Koebner phenomenon*. Pediatric psoriasis, in particular, can be associated with emotional stress,[10] increased body mass index (BMI),[11,12] second-hand cigarette smoke,[10] pharyngeal and perianal group A β-hemolytic *Streptococcus* infection,[13-15] Kawasaki disease,[16-18] withdrawal of systemic corticosteroids, and, paradoxically, tumor necrosis factor (TNF) α inhibitor medications.[19-21] Other triggering factors noted in adults with psoriasis, including certain medications (beta-blockers, lithium, antimalarials, nonsteroidal anti-inflammatory medications, and tetracyclines), are rarely inciting agents in children.[22] These potential triggering factors should be elicited during the clinical history and physical examination and addressed objectively when possible (ie, culture-directed antibiotics in patients with positive results on streptococcal pharyngeal, anal, or vulvar culture).

Psoriasis is a complex, potentially multisystem disease featuring extracutaneous manifestations in a subset of patients. As discussed in a previously published guideline,[23] adult patients with psoriasis have numerous potential comorbidities that may affect their health and QOL, such as arthritis, heart disease, dyslipidemia, obesity, metabolic syndrome, and depression, among others. It is becoming increasingly clear that pediatric patients with psoriasis may also have these comorbidities. Asthma has also been reported recently as a possible emerging comorbidity.[24,25] Awareness and early recognition of extracutaneous associations allow for earlier intervention, which may optimize patient health and QOL.

Psoriatic arthritis

The prevalence of inflammatory arthritis is lower in children than adults affected by psoriasis, with an estimated prevalence of 0.7% for all children with psoriasis, increasing to 1.2% of patients with psoriasis by age 18 years.[26] It is estimated that PSA accounts for approximately 6% to 8% of all pediatric cases of inflammatory arthritis.[26]

Table IV. Strength of recommendations for pediatric psoriasis and psoriatic arthritis

Recommendation No.	Recommendation	Strength of recommendation
2.1	Pediatric patients with psoriasis should be educated about the risk of PSA and its clinical manifestations.	C
2.2	Pediatric patients with psoriasis should be routinely screened for PSA via a thorough history and physical examination.	C
2.3	Pediatric patients with psoriasis who show signs and symptoms of inflammatory arthritis should be referred to a rheumatologist with pediatric expertise, if available, for further evaluation and management.	C
2.4	Pediatric psoriasis patients with PSA should be routinely screened for uveitis by history and physical examination.	C
2.5	Pediatric patients with psoriasis who show signs and symptoms of uveitis should be referred to an ophthalmology specialist for further evaluation and management.	C

PSA, Psoriatic arthritis.

Table V. Level of evidence for pediatric psoriasis and psoriatic arthritis

Recommendation	Recommendation No.	Level of evidence	Studies
Psoriatic arthritis education	2.1	II-III	25,27,30-32
Psoriatic arthritis screening	2.2	III	27
Referral to a specialist due to signs of PSA	2.3	III	Expert opinion
Uveitis screening for pediatric psoriasis	2.4	III	27
Specialist referral for signs of uveitis	2.5	III	Expert opinion

PSA, Psoriatic arthritis.

Although the prevalence of PSA in the pediatric population globally is uncertain, it is 0.15% in German children.[25] In 80% of children with PSA, joint inflammation develops before skin disease onset, usually 2 to 3 years in advance of skin involvement.[27] Although PSA can occur in children of any age, the 2 most common age ranges for joint involvement are 2 to 3 years old and 10 to 12 years old.[27]

Pediatric patients with PSA have typical symptoms associated with inflammatory arthritis, including joint pain, joint swelling, and stiffness at rest or upon awakening. Younger children with PSA, particularly girls, tend to present with oligoarticular disease and/or dactylitis. Older children, particularly boys, tend to present with enthesitis and axial joint involvement.[27-29] Patients with psoriasis are also at a slightly increased risk for rheumatoid arthritis development, presumably due to similar immune cascade mechanisms. As such, providers may need to distinguish between psoriatic and rheumatoid arthritis in patients with psoriasis with musculoskeletal concerns from physical examination, laboratory evaluation, and imaging.[30]

Uveitis may occur in pediatric patients with PSA, and the prevalence varies widely (1.5%-25%). Uveitis has been identified only in patients with concomitant arthritis and not in those with skin-limited psoriasis. Thus, routine screening for uveitis for pediatric patients with psoriasis with skin-limited disease is not warranted, assuming PSA has been excluded. Screening by history and ophthalmologic examination is essential if patients develop eye pain, redness, visual loss, or photophobia.[27]

The strength of recommendations and levels of evidence for pediatric psoriasis and psoriatic arthritis are summarized in Tables IV and V.[25,27,30-32]

Obesity and metabolic syndrome

Metabolic syndrome is the term used to describe the collective cardiovascular risk factors of (1) obesity, (2) hypertension, (3) hypertriglyceridemia, (4) hypercholesterolemia, and (5) insulin-resistant diabetes. These conditions are frequently coexistent in affected patients and have a significant role in overall wellness, morbidity, and mortality. Thought to be due to insulin resistance and adipose tissue dysfunction, metabolic syndrome is a common finding in the general population, and its incidence increases with age. The diagnosis of metabolic syndrome is rendered when patients have at least 3 of the 5 conditions listed above. The incidence of

Table VI. Recommendations for pediatric psoriasis and obesity

Recommendation No.	Recommendation	Strength of recommendation
3.1	Pediatric patients with psoriasis should be routinely assessed for obesity status either by their primary care provider or dermatologist.	B
3.2	Pediatric psoriasis patients with obesity should be routinely assessed for the comorbidities of obesity (independent of psoriasis) by their primary care provider or dermatologist.	B

Table VII. Level of evidence for pediatric psoriasis and obesity

Recommendation	Recommendation No.	Level of evidence	Studies
Screen for obesity	3.1	II-III	11,12,25,27,30-35,37,38
Screen for obesity and metabolic syndrome	3.2	II-III	11,12,25,27,30-35,37,38

metabolic syndrome is increased among pediatric patients with psoriasis relative to unaffected children. A study comparing 20 patients with pediatric psoriasis ages 9 to 17 years with an age- and sex-matched cohort of patients seen for acne, nevi, and warts found that 30% of the patients with pediatric psoriasis met criteria for metabolic syndrome compared with 5% of the unaffected control patients.[33]

Adipose tissue is metabolically active, secreting proinflammatory cytokines that alter metabolism at the end organ level, including interleukin (IL) 1, IL-6, TNF-α, and the anti-inflammatory cytokine adiponectin. In obesity, expression of these proinflammatory cytokines is increased, whereas adiponectin expression is decreased.[34] Both obesity and psoriasis cause systemic inflammation via the upregulation of types 1 and 17 T helper cells; thus, each condition perpetually exacerbates the other.[11] Similar to adults, patients with pediatric psoriasis have a higher prevalence of obesity relative to unaffected children, and some studies have found the rate to be approximately double that of unaffected control individuals (8.4% vs 4.9%[30] and 7.1% vs 3.6%).[25] The obesity in patients with psoriasis tends to be central obesity (increased waist circumference percentile relative to weight and height ratio percentile) and usually develops around 8 years of age. The association between central obesity and psoriasis was strongest for pediatric patients in the United States compared to patients from other countries,[11] especially those of African American and Hispanic descent. A multicenter, cross-sectional study of 409 pediatric patients found the odds ratio (OR) of obesity and psoriasis to be greater for pediatric patients than previously reported ORs of obesity and psoriasis in some adult studies.[11]

The temporal association between obesity and psoriasis suggests that the onset of psoriasis occurs in the presence of obesity. Boccardi and colleagues[35] compared 96 children ages 0 through 15 years with new-onset psoriasis in their pediatric dermatology clinic in Italy with 100 pediatric patients with another skin disease. In this cohort, there was an association between new-onset psoriasis and pre-existing overweight (OR, 2.55; 95% confidence interval [CI], 1.31-4.96) or underweight status (OR, 1.52; 95% CI, 0.60-3.89) relative to patients without psoriasis. The association was particularly strong for male patients (OR, 4.63; 95% CI, 1.40-15.28) and children younger than age 10 years (OR, 3.19; 95% CI, 1.40-7.28). These data support obesity as a risk factor for psoriasis development.[35] Similarly, another study[12] reviewed the relationship over time of the BMI percentiles of 27 overweight or obese patients with pediatric psoriasis 2 years before, during, and 2 years after skin disease onset. Twenty-five of the 27 (92.6%) patients were overweight or obese before psoriasis onset, and they retained their adiposity through at least the 2 years of follow-up. Children with a family history of obesity (almost 50%) developed skin disease earlier in life, and BSA involvement increased as BMI increased.[12] Although the direction of the relationship/temporal association between obesity and psoriasis goes both ways, these studies position psoriasis as a comorbidity of excess adiposity, in contrast to the development of obesity from being more sedentary once

Table VIII. Recommendations for pediatric psoriasis and cardiovascular disease

Recommendation No.	Recommendation	Strength of recommendation
4.1	Pediatric patients with psoriasis and their families should be educated about the increased risk of cardiovascular disease.	C
4.2	Pediatric patients with psoriasis should be screened for cardiovascular risk factors when history and physical examination findings show a potential risk.	B
4.3	Pediatric patients with psoriasis who have been identified as having cardiovascular risk factors such as obesity, dyslipidemia, diabetes, hypertension, or metabolic syndrome should be referred to appropriate specialists for further evaluation and management.	C

Table IX. Level of evidence for pediatric psoriasis and cardiovascular disease

Recommendation	Recommendation No.	Level of evidence	Studies
Cardiovascular disease education	4.1	II-III	25,27,30,32,39,40
Cardiovascular disease screening for at-risk patients	4.2	III	Expert opinion
Specialist referral for patients with cardiovascular disease comorbidity	4.3	III	Expert opinion

psoriasis develops or from its psychological impact. Pediatric patients with psoriasis should be followed closely for the development of obesity, and those already obese should be provided with referrals and resources for weight management as available.

Adult patients with psoriasis and obesity have an increased risk of nonalcoholic fatty liver disease (NAFLD). Current data are insufficient to know if a similar association exists in the pediatric psoriasis population; however, because obesity and metabolic syndrome can be independently associated with NAFLD, it is recommended that all pediatric patients, including those with psoriasis, who are overweight or obese be screened for NAFLD via alanine aminotransferase level monitoring every 2 to 3 years beginning at age 9 years.[36]

The strength of recommendations and levels of evidence for psoriasis and obesity are summarized in Tables VI and VII.[11,12,25,27,30-35,37,38]

Cardiovascular disease

Adult data show a link between psoriasis and cardiovascular disease. Although there are insufficient data to clarify the link between psoriasis and development of heart disease (or risk of its development) in children, there are associations between children with pediatric psoriasis and cardiovascular risk factors such as obesity, dyslipidemia, and other components of metabolic syndrome. In the absence of obesity, the data pertaining to cardiovascular risk are weak. Patients with pediatric psoriasis should have American Academy of Pediatrics (AAP)—recommended age-related cardiovascular screening regardless of the presence of signs or symptoms.[36]

Koebnick et al[39] reviewed the medical records of 710,949 children ages 2 through 19 years, 2119 of whom had psoriasis based on International Classification of Diseases (ICD), ninth revision, code. The OR of psoriasis increased with body weight ($P < .001$). After adjustment for BMI, adolescents with psoriasis had elevated total cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride, and alanine aminotransferase levels (compared with matched patients without psoriasis). A review of inpatient medical records of pediatric patients ages 0 through 17 years by Kwa et al[40] found an association with 5 cardiovascular risk factors: obesity (adjusted OR [AOR], 3.15; 95% CI, 2.46-4.05), hypertension (AOR, 2.63; 95% CI, 1.93-3.59), diabetes (AOR, 2.90; 95% CI, 1.90-4.42), arrhythmia (AOR, 1.39; 95% CI, 1.02-1.88), and valvular heart disease (AOR, 1.90; 95% CI, 1.07-3.37). These findings were more prominent in African American and Hispanic children ages 0 through 9 years. Psoriasis was not associated with heart conduction disorder, composite lipid abnormality, cerebrovascular accident, or chest pain. The clinical implications of this study remain unclear.

An epidemiologic review[30] of a German health insurance database of 33 981 children ages 0 through 18 years found the ischemic heart disease prevalence rate (based on ICD-10 code) for patients with psoriasis versus unaffected control individuals to be

Table X. Recommendations for pediatric psoriasis and dyslipidemia

Recommendation No.	Recommendation	Strength of recommendation
5.1	Pediatric patients with psoriasis should be educated about their increased risk of dyslipidemia.	C
5.2	Pediatric patients with psoriasis should be screened for dyslipidemia between ages 9 and 11 years and 17 and 21 years, as recommended by the AAP for all children.	B
5.3	Pediatric psoriasis patients with increased risk for dyslipidemia may be screened more frequently at the provider's discretion.	C
5.4	Pediatric psoriasis patients with dyslipidemia should be referred to their primary care provider or an endocrinologist for further assessment and management.	C

AAP, American Academy of Pediatrics.

Table XI. Level of evidence for pediatric psoriasis and dyslipidemia

Recommendation	Recommendation No.	Level of evidence	Studies
Education on dyslipidemia	5.1	II-III	11,25,27,30-33,37,40,43
Dyslipidemia screening according to AAP guidelines	5.2	III	27
Screening frequency for at-risk patients	5.3	III	27
Specialist referral for dyslipidemia diagnosis	5.4	III	Expert opinion

AAP, American Academy of Pediatrics.

1.52%, with hyperlipidemia also increased at 2.15%. A similar study[25] of health insurance claims based on ICD-10 diagnoses of 1313 patients with pediatric psoriasis compared with age-matched control individuals found that patients with psoriasis had increased prevalence rates of "ischemic heart disease" and "hyperlipidemia" diagnoses relative to the cohort without psoriasis, at 1.27% and 1.79%, respectively. The clinical significance of these findings remains unclear.

The proposed mechanism for the increased risk and prevalence of cardiovascular disease in patients with psoriasis is the chronic inflammatory state caused by psoriasis. This, in theory, could result in insulin resistance, endothelial cell damage, and an atherogenic predisposition that, if present in childhood, may explain the increased risk of cardiovascular disease identified in adults with psoriasis.[41] This has been called the *psoriatic march*, similar to the atopic march of atopic dermatitis.[41] This theoretical pathway may be amplified in obese patients with psoriasis because adipose tissue also produces systemic inflammation via similar pathways.[27,42,43]

The strength of recommendations and levels of evidence for pediatric psoriasis and cardiovascular disease are summarized in Tables VIII and IX.[25,27,30,32,39,40]

Dyslipidemia

Hypercholesterolemia and hypertriglyceridemia directly affect the risk of atherosclerosis and cardiovascular disease and may contribute to the psoriatic march from chronic psoriasis-related inflammation to cardiovascular and cerebrovascular events. The estimated prevalence of dyslipidemia in patients with pediatric psoriasis based on available data is approximately twice that of children without psoriasis.[40] Two database reviews by Augustin et al[25,30] found the dyslipidemia prevalence ratios to be 1.79% and 2.15% in children with psoriasis. A multicenter study in France of 2201 patients with psoriasis found that childhood onset of the disease did not correlate to severity of dyslipidemia in adulthood.[31] Patients with pediatric psoriasis with obesity are more likely to have dyslipidemia relative to patients with pediatric psoriasis who are of normal weight.[11] Goldminz et al[33] compared 20 patients with pediatric psoriasis to unaffected matched control individuals and found that dyslipidemia was not increased in the psoriasis group when weight and waist circumference were equal in both groups. Tom and colleagues[43] studied the lipid profiles of 44 patients with pediatric psoriasis ages 8 through 17 years and compared them with age-matched control individuals. After adjusting for sex, fasting glucose levels, and BMI, abnormal atherogenic components (including elevated

Table XII. Recommendations for pediatric psoriasis and hypertension

Recommendation No.	Recommendation	Strength of recommendation
6.1	In accordance with the AAP screening guidelines, pediatric patients with psoriasis ages 3 years and older should be screened annually for hypertension by their primary care provider.	B

AAP, American Academy of Pediatrics.

Table XIII. Level of evidence for pediatric psoriasis and hypertension

Recommendation	Recommendation No.	Level of evidence	Study
Screen for hypertension according to AAP guidelines	6.1	III	[27]

AAP, American Academy of Pediatrics.

apolipoprotein B levels, reduced high-density lipoprotein particle size and number, and decreased cholesterol efflux capacity) were noted in the patients with psoriasis.

In summary, the data available to date do not suggest a need to alter the screening recommendations for dyslipidemia in patients with pediatric psoriasis relative to other children. The standard lipid screening guidelines of the AAP may be used: universal lipid screening between ages 9 through 11 years and again at ages 17 through 21 years. Patients at increased risk for dyslipidemia should be screened more frequently at the provider's discretion. Screening includes total cholesterol, high-density lipoprotein cholesterol, LDL cholesterol, and triglyceride levels. Serum LDL levels are lower in adolescence, which should be taken into consideration during laboratory test interpretation.[27]

The strength of recommendations and levels of evidence for pediatric psoriasis and dislipidemia are summarized in Tables X and XI.[11,25,27,30-33,37,40,43]

Hypertension

Unlike the adult classification, *pediatric hypertension* (as defined by the American Heart Association) refers to the normative distribution of blood pressure values in children by age, sex, and height. For patients ages 0 through 13 years, *hypertension* is defined as systolic and/or diastolic blood pressure measurements consistently greater than the 95th percentile based on age, sex, and height. For patients ages 14 through 17 years, the American Heart Association hypertension criteria for adults apply.[44] Although these strict definitions of hypertension exist, their use in clinical practice (and research activities/subsequent publications) is not guaranteed; thus, it is difficult to determine the precise risk of hypertension in children with psoriasis based on the available data. A small study comparing patients with pediatric psoriasis to age-matched control children showed no significant differences in systolic or diastolic blood pressure between groups.[33]

A study by Kwa et al[40] found that hypertension was increased in patients with pediatric psoriasis relative to unaffected age- and race/ethnicity-matched control children (AOR, 2.63; 95% CI, 1.93-3.59; $P < .0001$), with the greatest risk for patients of African American and Hispanic descent. Although both male and female patients were at increased risk, the association of hypertension and psoriasis was strongest for patients ages 0 through 9 years and decreased with adolescence. The risk of hypertension was found in pediatric patients regardless of family income level or insurance carrier status. Similarly, a survey by Augustin et al[25] of 1313 patients with psoriasis ages 0 through 18 years found a prevalence rate ratio of 2.09 (95% CI, 1.18-3.69) for arterial hypertension compared with unaffected control individuals. An analysis of insurance claims data by Augustin and colleagues[30] of patients with psoriasis ages 0 through 20 years found the prevalence ratio of arterial hypertension to be 1.65 in patients with psoriasis, compared with 0.83 in unaffected control individuals (95% CI, 1.47-2.67). In contrast, a multicenter, international, cross-sectional study of 409 patients with pediatric psoriasis ages 5 through 17 years by Paller and colleagues[11] did not find an increased risk of hypertension in the psoriasis group relative the control group (52.2% vs 52.5%).

Overall, the data available thus far, primarily from large claims databases, suggests an association between psoriasis and high blood pressure in children. As noted, studies designed to look specifically at this association by using appropriate definitions are lacking, and therefore there is a lack of solid evidence to make definitive statements about the true nature of the observed association between hypertension and pediatric psoriasis independent of obesity. However, because an independent relationship between psoriasis and hypertension exists

Table XIV. Recommendations for pediatric psoriasis and insulin resistance

Recommendation No.	Recommendation	Strength of recommendation
7.1	Pediatric patients with psoriasis should be educated about the potential association between psoriasis, insulin resistance, and diabetes mellitus.	C
7.2	Pediatric patients with psoriasis who are obese should be screened for insulin resistance and diabetes by their dermatologist or primary care provider every 3 years at the onset of puberty or age 10 years, whichever is sooner.	C
7.3	Pediatric patients with psoriasis who are overweight and have increased risk for insulin resistance may be screened similarly to obese patients at the provider's discretion.	C
7.4	Pediatric psoriasis patients with insulin resistance or diabetes mellitus should be referred to their primary care provider or an endocrinologist for further assessment and management.	C

in adults, it is reasonable and recommended that all pediatric patients ages 3 years and older should receive annual blood pressure screening. This is in accordance with AAP guidelines. Note that the normal value ranges for blood pressure vary by age, sex, and height. Use of a properly sized blood pressure cuff plus measurement on more than 1 occasion should be used to ensure accuracy.[27]

The strength of recommendations and levels of evidence for pediatric psoriasis and hypertension are summarized in Tables XII and XIII.[27]

Insulin resistance

Diabetes is a metabolic disorder characterized by hyperglycemia induced by defects in insulin production or action. Chronic hyperglycemia is associated with long-term organ damage from the improper processing and storage of circulating glucose. Insulin resistance affects overall health both directly and indirectly and contributes as well to cardiovascular disease via the proposed psoriatic march from chronic inflammation to cardiovascular and cerebrovascular events in adulthood.[41] The data available to date on the prevalence of insulin resistance in patients with pediatric psoriasis are limited and have been extrapolated from 3 studies. The prevalence of insulin resistance in pediatric patients with psoriasis is thought to be approximately twice that of unaffected children.[40] Two database studies by Augustin and colleagues[25,30] found the prevalence ratios to be 1.97 and 2.01.

Patients with pediatric psoriasis with obesity are more likely to have insulin resistance relative to patients with pediatric psoriasis of normal weight.[11] Goldminz et al[33] compared 20 patients with pediatric psoriasis to unaffected matched control children and found that fasting blood glucose was elevated in the psoriasis group when weight and waist circumference were equal in both groups; in contrast, no differences were found in other components of metabolic syndrome. Tom and colleagues[43] analyzied metabolic profiles of 44 patients with pediatric psoriasis ages 8 through 17 years relative to controls and noted that patients with psoriasis had a higher homeostasis model assessment of insulin resistance value, with BMI being the best predictor of impaired homeostasis.

Although most discussion regarding diabetes and psoriasis involves type 2 diabetes mellitus, type 1 diabetes mellitus may also be linked to psoriasis. Type 1 diabetes is the most common childhood endocrine disorder and occurs via the autoimmune destruction of pancreatic islet cells. Psoriasis is associated with the upregulation of IL-17 production by T helper cells. IL-17 is an inflammatory mediator of islet cell destruction, which may explain the relationship between type 1 diabetes and psoriasis. Di Costanzo and colleagues[45] studied 191 Italian pediatric patients with type 1 diabetes and found their incidence of psoriasis to be higher than the incidence regionally (4.7% vs 2.1%). No specific relationship to obesity was noted (mean BMI, 20.5 kg/m^2).

Screening for both forms of diabetes in children can be accomplished by measuring fasting serum glucose. Screening for diabetes in patients with pediatric psoriasis is the same as screening in the general pediatric population, in accordance with the American Diabetes Association pediatric screening guidelines. Fasting serum glucose measurement is essential every 3 years in all obese pediatric patients at the onset of puberty or age 10 years, whichever is sooner. Patients with pediatric psoriasis who are overweight but not obese should also be screened if other risk factors for diabetes are present (strong

Table XV. Level of evidence for pediatric psoriasis and insulin resistance

Recommendation	Recommendation No.	Level of evidence	Studies
Education on the relation of insulin resistance and diabetes with pediatric psoriasis	7.1	II-III	11,25,30-33,40,43,45
Screening for insulin resistance	7.2	III	27
Frequency of insulin resistance screening for at-risk patients	7.3	III	Expert opinion
Specialist referral for a positive screening result	7.4	III	Expert opinion

Table XVI. Recommendations for psoriasis and mental health

Recommendation No.	Recommendation	Strength of recommendation
8.1	Pediatric patients with psoriasis should be screened routinely for mental health diseases including depression and anxiety, regardless of age. This may be achieved through careful assessment of interactions during the visit in the presence of parents, as well as via a private conversation with the patient. Although a specific mental health inventory screening may be used, it is not required for routine mental health assessment in the context of a dermatology office visit.	C
8.2	Pediatric patients with psoriasis should be asked about substance abuse.	C
8.3	Pediatric patients with psoriasis found to have mental health or substance abuse concerns should be referred to an appropriate health care professional for further assessment and management.	C

Table XVII. Level of evidence for psoriasis and mental health

Recommendation	Recommendation No.	Level of evidence	Studies
Screen for mental health comorbidities	8.1	II-III	8,27,32,46-50
Screen for substance abuse	8.2	III	Expert opinion
Referral to a specialist for patients with positive screening results for mental health or substance abuse	8.3	III	Expert opinion

family history, history of gestational diabetes, hypertension, dyslipidemia, ethnic predisposition).

The strength of recommendations and levels of evidence for pediatric psoriasis and insulin resistance are summarized in Tables XIV and XV.[11,25,27,30-33,40,43,45]

Mental health

Having visible skin disease is highly stressful for children. Psoriasis has as much of an impact on patient QOL as diabetes, epilepsy, and atopic dermatitis.[8] An interview study of 15 patients with pediatric psoriasis showed that 65% experienced stigmatization in the forms of bullying, name calling, and shaming.[46] Patients express concern about the continual shedding of skin and the malodor of the rash. These factors negatively affect recreational activity for 15% to 30% of children with psoriasis.[47] This stigmatization may result in behavioral changes, depression, anxiety, and risk-taking behavior. In addition, the close link between psoriasis and obesity creates an additional dimension to the complexity of this relationship, whereby the presence of psoriasis and obesity may be mutually reinforcing and, thus, may escalate social isolation, withdrawal, anxiety, and depression.

Todberg and colleagues[48] studied 4410 patients with pediatric psoriasis and 41 285 unaffected age-matched control children from Denmark. After eliminating pre-existing mental illness and risk

Table XVIII. Recommendations for pediatric psoriasis and inflammatory bowel disease

Recommendation No.	Recommendation	Strength of recommendation
9.1	Pediatric patients with psoriasis who show signs and symptoms of inflammatory bowel disease should be considered for consultation with a gastroenterologist with pediatric expertise, if available, for further evaluation and management.	C

Table XIX. Level of evidence for pediatric psoriasis and inflammatory bowel disease

Recommendation	Recommendation No.	Level of evidence	Studies
Screen for inflammatory bowel disease in at-risk patients and refer patients with positive screening results to a specialist	9.1	II-III	25,27,30

behavior, the adjusted hazard ratio (aHR) of development of depression after psoriasis onset was 1.94 (95% CI, 1.27-2.96). Such patients also had an increased risk of alcohol abuse (aHR, 1.42; 95% CI, 1.14-1.76), drug abuse (aHR, 1.51; 95% CI, 1.04-2.19), eating disorders (aHR, 2.03; 95% CI, 1.20-3.43), the use of benzodiazepines (aHR, 3.57; 95% CI, 2.13-5.97), and antipsychotic medications (aHR, 1.35; 95% CI, 1.10-1.68). Although the prevalence of anxiety was not statistically significant compared with controls, the researchers hypothesized that the use of psychiatric medications and higher frequency of eating disorders serve as surrogate indicators of anxiety. In a study of 48 patients with pediatric psoriasis versus control children ages 8 through 18 years, Bilgic et al[49] found no association between psoriasis and anxiety. However, depression was more prevalent in the 8- to 12-year-old patients (*t* test, 2.57; $P < .05$) and in their parents (*t* test, -3.62; $P < .001$), as evidenced by the Child Depression Inventory and the Pediatric Quality of Life Inventory Child and Parent scoring. The presence of depression did not correlate with PASI score or the duration of psoriasis. Neither adolescent patients with psoriasis ages 13 through 18 years nor their parents showed an increased depression risk.

A retrospective chart review of a health insurance database by Kimball and colleagues[50] of 7404 patients with pediatric psoriasis and 37 020 unaffected age-matched control children found an increased risk of both depression (3.01% vs 2.42%, $P = .036$) and anxiety (1.81% vs 1.35%, $P = .048$). The prevalence of these mental health disorders collectively was greater than the cumulative risk of all other psoriatic comorbidities for the same patient population (2%). The use of psychotropic medication was 47% higher in the group with psoriasis, with prescriptions dispensed for antidepressants and anxiolytics being greater than the incidence of depression or anxiety (3.4% and 4.1% use, respectively, vs 3.0% and 1.8% incidence, respectively). The increased use of antidepressants and anxiolytics by the patients with pediatric psoriasis relative to the documented incidence of depression and anxiety for such patients suggests that there could be stigma associated with the diagnosis of a mental health disease or that the mental health signs and symptoms are considered part of the psoriatic disease and not a separate medical concern.

Although the adult literature shows a consistent, strong correlation between psoriasis and alcohol intake, and this may also exist among adolescents with psoriasis, to date there are insufficient data to correlate pediatric psoriasis with the use of alcohol. Similarly, although smoking is prevalent among adult patients with psoriasis and is thought to exacerbate disease, there are insufficient data regarding the correlation between smoking and pediatric psoriasis.[27] Nonetheless, given the strong association in adults and the prevalence of substance use and mental health disorders among adolescents in general, patients with pediatric psoriasis should follow the general AAP mental health screening guidelines for substance use and abuse, with annual screening beginning at age 11 years.[36]

The strength of recommendations and levels of evidence for pediatric psoriasis and mental health are summarized in Tables XVI and XVII.[8,27,32,46-50]

Inflammatory bowel disease

Crohn's disease and ulcerative colitis are the 2 most common forms of inflammatory bowel disease, with inflammation potentially involving the full

Table XX. Recommendations for pediatric psoriasis and topical steroid therapy

Recommendation No.	Recommendation	Strength of recommendation
10.1	Topical corticosteroids are recommended for the treatment of pediatric psoriasis as an off-label therapy.	B
10.2	The use of ultra-high-potency topical corticosteroids as monotherapy is effective for short-term treatment of localized psoriasis in pediatric patients.	C

Table XXI. Level of evidence for pediatric psoriasis and topical steroid therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Topical corticosteroids for pediatric psoriasis	10.1	II	52-54
Short-term ultra-high-potency topical corticosteroids for pediatric psoriasis	10.2	II	53,54

gastrointestinal (GI) tract (from mouth to anus) versus the colon and rectum, respectively. Although the exact etiology is unknown, a maladaptive immune response in patients with genetic susceptibility is suspected.[51] The rate of inflammatory bowel disease in children with psoriasis has been assessed via claims database studies and is thought to be 3 to 4 times higher than in children without psoriasis.[25,27,30] Augustin et al[25] studied the records of 1313 children ages 0 through 18 years in a German health claims database and found that the prevalence of inflammatory bowel disease in patients with psoriasis relative to unaffected control individuals was 0.15% versus 0.05% for ulcerative colitis and 0% versus 0.07% for Crohn's disease. A separate study of a German database by Augustin and colleagues[30] found the prevalence rate of inflammatory bowel disease in patients ages 0 through 20 years relative to unaffected control individuals to be 0.51% versus 0.14% for Crohn's disease (prevalence rate, 3.69; 95% CI 2.15-6.35) and 0.12% versus 0.10% for ulcerative colitis (PR, 1.13; 95% CI 0.38-3.31). Screening for inflammatory bowel disease is recommended if patients have gastrointestinal symptoms, poor growth, or unintentional weight loss.[27]

The strength of recommendations and levels of evidence for pediatric psoriasis and inflammatory bowel disease are summarized in Tables XVIII and XIX.[25,27,30]

TOPICAL TREATMENTS

Topical corticosteroids

Topical steroid use for psoriasis in children is technically an off-label treatment (due to lack of clinical trials in this population) but is frequently practiced and widely considered for localized disease. Topical corticosteroids are available in a wide variety of delivery vehicles and are used in all phases of the disease, from gaining control during flares to maintenance. There are many clinical approaches to treatment with topical corticosteroids, and selection of a therapeutic routine (potency, delivery vehicle, frequency of application) should take into account sites of involvement, type and thickness of psoriasis, age of the patient, total BSA of application, anticipated occlusion, and disease acuity, among other patient-, disease-, and drug-related factors. Given the multiple variables that should be considered when determining the preferred regimen, a criterion standard or 1-size-fits-all approach does not exist. A popular routine is dual topical therapy with a high- or ultra-high-potency topical steroid and topical vitamin D analogue. Given the exorbitant cost of commercially available combination products, individual products are often prescribed for simultaneous (eg, mixing calcipotriene/calcipotriol with a compatible steroid 1:1 on the finger) or serial use. Although this simultaneous or serial use improves adherence by making it simpler for the patient, studies addressing the efficacy of compounded versus separate, simultaneous treatments are lacking.

These are variably applied, most often either each once daily or mixed in the hand and applied together twice daily for the first 2 weeks. Thereafter, topical application is reduced to weekends for topical corticosteroids and weekdays for topical calcipotriene. Although a systematic review concluded that topical vitamin D monotherapy is a first-line therapy for pediatric psoriasis (with the addition of mild to moderate topical corticosteroids for the trunk and extremities and topical calcineurin inhibitors (TCIs) for the face and folds for refractory disease),[52] this is not the typical approach of providers experienced in the treatment of pediatric psoriasis (expert opinion). Rather, this reflects the lack of objective controlled

Table XXII. Recommendations for pediatric psoriasis and topical calcineurin inhibitors

Recommendation No.	Recommendation	Strength of recommendation
11.1	Tacrolimus 0.1% ointment is recommended for off-label use as monotherapy for pediatric psoriasis of the face and genital region.	C

Table XXIII. Level of evidence for pediatric psoriasis and topical calcineurin inhibitors

Recommendation	Recommendation No.	Level of evidence	Studies
Tacrolimus 0.1% for off-label use	11.1	II-III	52,55-57

data regarding topical corticosteroid use for pediatric psoriasis treatment. It is advisable to avoid the use of ultra-high-potency topical corticosteroids in the face, fold, and genitalia of infants and children.

A study by Frangos and Kimball[53] denoted the effectiveness of short-term (2 weeks) use of clobetasol foam for psoriasis in children. There was no limit on BSA of application. In patients younger than 12 years of age, hypothalamic-pituitary-adrenal (HPA) axis suppression was found but was reversible. No HPA suppression was noted in patients ages 12 through 18 years. Herz and colleagues[54] studied the efficacy of halobetasol monotherapy in 11 pediatric patients with psoriasis for 14 days. Ten of the 11 (90.9%) patients reported marked improvement, and 8 (72%) patients reported complete clearance at study end. The study recommended limiting use to 1 week, switching to a moderate- or mild-potency steroid thereafter and avoiding use on the face, body folds, and genitalia.

The adverse effect profile for topical corticosteroids in children is analogous to that in adults, particularly relating to burning and stinging at the application site.[52] Younger patients ages 0 through 6 years, and especially infants given their high BSA-to-volume ratio compared with older children and adults, are vulnerable to HPA suppression. High-potency or ultra-high-potency topical corticosteroids should be used with caution, and patients should be followed closely by a dermatologist to ensure proper use and to monitor for overuse and adverse effects. Careful instruction on the amount to apply and safe sites for use should be reiterated, and a limited quantity should be supplied. Providers and caregivers should be aware of the potential for rebound flare if high-potency corticosteroids are abruptly discontinued without transition to an appropriate alternative treatment.[53,54]

The strength of recommendations and levels of evidence for pediatric psoriasis and topical steroid therapy are summarized in Tables XX and XXI.[52-54]

Topical calcineurin inhibitors

Most data related to the pediatric use of TCIs have been derived from studies in atopic dermatitis. The systematic review of pediatric psoriasis treatment by de Jager et al[52] recommends TCIs as the preferred first-line therapy for psoriasis of the face, genitalia, and body folds and includes pimecrolimus, tacrolimus, and cyclosporine. A single-center, open-label study of 11 children (ages 6-15 years) with facial or inverse psoriasis reported clearance or excellent improvement within 30 days in the 8 patients who continued the trial for at least 30 days. Seven of the 8 patients had subsequent flares but responded well to repeat treatment.[55] In a case series of 4 patients treated with 0.1% tacrolimus for facial psoriasis, 1 of whom was a child, complete clearance was achieved within 72 hours.[56] Similarly, a retrospective chart review of 12 children with facial psoriasis who used tacrolimus 0.1% reported clearance within 2 weeks.[57] Amichai[58] reported clearance of penile psoriasis in a 10-year-old boy after 3 weeks of topical pimecrolimus use. Mansouri and colleagues[59] noted clearance of periocular and anogenital psoriasis in a 10-year-old girl with topical pimecrolimus use after 20 days.

Burning, stinging, pruritus, and irritation have been reported as adverse effects of TCI use in children.[55,57] There are no pediatric psoriasis studies that clarify best practices related to use of TCI with or after topical steroid treatment. In 2006, the US Food and Drug Administration (FDA) issued a boxed warning related to the theoretical risk of lymphoma from the chronic intermittent use of TCIs. The possibility of risk was not based on reports with TCIs but rather on the development of lymphoma in a small number of patients with transplants who were given systemically administered tacrolimus and cyclosporine (although detectable levels after topical application of tacrolimus are low to absent) and from challenges with high concentrations in animals. Siegfried et al[60] analyzed 21 long-term (12 weeks or greater) clinical trials of TCI use in 5825 pediatric

Table XXIV. Recommendations for pediatric psoriasis and topical vitamin D analogue therapy

Recommendation No.	Recommendation	Strength of recommendation
12.1	Calcipotriene/calcipotriol is recommended as a treatment option for childhood plaque psoriasis.	B
12.2	Because of the theoretical risk of increased calcium absorption and systemic effects of hypercalcemia, occlusion of calcipotriene/calcipotriol applied to large body surface areas is not recommended.	B
12.3	Monitoring of vitamin D metabolites may be considered during calcipotriene/calcipotriol therapy when applied to a large body surface area.	B

Table XXV. Level of evidence for pediatric psoriasis and topical vitamin D analogue therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Calcipotriene/calcipotriol for pediatric psoriasis	12.1	II	52,64
Calcipotriene/calcipotriol application limited to small areas of the body	12.2	III	Expert opinion
Monitor vitamin D metabolites with calcipotriene/calcipotriol use	12.3	I-II	65,67

patients with atopic dermatitis. Adverse effects of TCI use were similar to those of topical vehicle, with no cases of lymphoma reported. To date, there is no evidence suggesting a causal relationship between topical tacrolimus or pimecrolimus and either lymphoma or nonmelanoma skin cancer in pediatric patients with atopic dermatitis, its labeled indication.[61,62] For further data regarding the boxed warning, please see the topical treatments section (for adults) in this guideline set.

The strength of recommendations and levels of evidence for pediatric psoriasis and TCIs are summarized in Tables XXII and XXIII.[52,55-57]

Topical vitamin D analogues

Vitamin D_3 analogs calcipotriene, calcipotriol, and calcitriol inhibit keratinocyte proliferation and DNA synthesis and promote keratinocyte differentiation. They frequently are used in combination with topical corticosteroids. An important advantage of the vitamin D analogues, especially for pediatric use, is their corticosteroid-sparing function.[63] Treatment with vitamin D analogues is safe, effective, and relatively well tolerated in children of all ages. Several small case series and clinical trials of low to good quality have been performed in children.

Fifty-eight patients with pediatric psoriasis ages 3 through 14 years were treated with twice daily calcipotriol for 8 weeks in a trial by Darley and colleagues.[64] Sixty-five percent of patients experienced complete clearance or excellent outcomes. Calcipotriol also reduced redness and scale, with good tolerance, in an 8-week study of 77 patients with pediatric psoriasis with mild to moderate disease, ages 2 through 14 years.[65] The systematic review of childhood psoriasis by de Jager et al[52] concluded that vitamin D analogues as monotherapy are the first-line treatment for pediatric plaque psoriasis, although in practice they are frequently used in combination with a topical steroid to gain initial control (expert opinion).

Vitamin D analogue preparations can cause local irritation and are often avoided on the face, genitals, and intertriginous skin.[66,67] Irritation is often improved or ameliorated with the concomitant application of an emollient. Caution must be taken regarding quantities used, given the theoretical risk of hypercalcemia and hypovitaminosis D from systemic absorption, although no specific data or recommendations exist on maximum use in children. This is especially true when used on widespread psoriasis of infants and very small children, as well as under occlusion of large surface areas.

Vitamin D analogues, alone or in a combination formulation with betamethasone dipropionate, are available in cream, ointment, suspension, and foam vehicles. In practice, these agents may be used in combination with other topical therapies to enhance efficacy and limit possible adverse effects. In adults, the maximum recommended dosages to prevent hypercalcemia are 50 g/wk/m^2 for calcipotriol and 100 g/wk/m^2 for calcipotriene. Similarly, a limit of 80 g/wk for adolescents has been recommended in the label for the combination scalp formulation.

Table XXVI. Recommendations for pediatric psoriasis and topical combination therapy

Recommendation No.	Recommendation	Strength of recommendation
13.1	The combination of calcipotriol/betamethasone dipropionate ointment applied once daily for up to 4 weeks at a time is recommended as a safe and effective treatment for children ages 12 years and older with mild to moderate plaque psoriasis.	B
13.2	The combination of calcipotriol/betamethasone dipropionate suspension applied once daily for up to 8 weeks at a time is recommended as a safe and effective treatment for children ages 12 years and older with mild to moderate plaque psoriasis of the scalp.	B
13.3	The use of emollients (at the same time or different time of day) with topical calcipotriene may be considered to reduce irritation and enhance the efficacy of calcipotriene.	C
13.4	Rotational therapy with topical vitamin D analogues, topical calcineurin inhibitors, emollients, tar-based therapies, and topical corticosteroids may be considered in children as steroid-sparing regimens that may reduce potential adverse effects from overreliance on topical steroid therapy.	C

Table XXVII. Level of evidence for pediatric psoriasis and topical combination therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Calcipotriol/betamethasone ointment combination therapy	13.1	I-II	68,69,72-75
Calcipotriol/betamethasone suspension combination therapy	13.2	II	68,69
Emollient use in combination with calcipotriol/betamethasone	13.3	III	66
Rotational therapy to avoid using steroid-based therapy	13.4	II	70

Otherwise, there are no guidelines for pediatric patients. At any age, vitamin D analogues should be used with caution in patients with disorders of calcium metabolism or renal disease.

The strength of recommendations and levels of evidence for pediatric psoriasis and topical vitamin D analogue therapy are summarized in Tables XXIV and XXV.[52,64,65,67]

Combination topical therapy

Combination topical therapies for psoriasis are convenient to use and potentially increase compliance. Combination products containing calcipotriol and betamethasone dipropionate (ointment and suspension) are FDA approved for use in children ages 12 years and older for use on the body and scalp, respectively. Given the exorbitant cost of commercially available combination products, individual products are often prescribed for simultaneous (eg, mixing calcipotriene/calcipotriol with a compatible steroid 1:1 on the finger) or serial use. Although this simultaneous or serial use improves adherence by making it simpler for the patient, studies addressing the efficacy of compounded versus separate, simultaneous treatment are lacking.

A phase 2 open-label trial[68] was performed that included 31 patients with pediatric psoriasis ages 12 through 17 years treated with combination calcipotriene and betamethasone dipropionate suspension once daily for 8 weeks for scalp psoriasis. Patients had at least 20% of the scalp area involved. Eighteen of the patients (58%) reported clearance of disease based on Patient's Global Assessment scoring. The medication was well tolerated. Sixty-five percent of patients experienced pruritus with the medication at trial initiation, but this decreased to 10 % at trial end. One patient experienced transient mild HPA suppression at week 4, which resolved 4 weeks after discontinuation. No patients experienced hypercalcemia. Combination calcipotriol and betamethasone dipropionate improved skin disease, pain, itch, and quality of life, with no serious adverse events, for 73 pediatric patients with plaque psoriasis ages 3 through 18 years after an average of 35 weeks of use.[69]

Table XXVIII. Recommendations for pediatric psoriasis and topical tazarotene therapy

Recommendation No.	Recommendation	Strength of recommendation
14.1	The off-label use of topical tazarotene may be recommended as monotherapy or in combination with topical corticosteroids for the treatment of localized pediatric skin or nail psoriasis.	C

Table XXIX. Level of evidence for pediatric psoriasis and topical tazarotene therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Off-label use of topical tazarotene for monotherapy or combination therapy	14.1	III	Expert opinion

Transitioning from combination therapy to topical vitamin D monotherapy upon disease improvement may be beneficial to decrease topical steroid use. Pretreating involved skin with 6% to 10% salicylic acid for 1 week may enhance the efficacy of subsequent calcipotriene monotherapy,[70] but this adds an extra step for patients before initiating anti-inflammatory therapy. However, care must be taken when salicylic acid is used with calcipotriene because the acid pH of salicylic acid will inactivate calcipotriene when the 2 are given simultaneously. The use of emollients concomitantly, or separately, with calcipotriol is also thought to enhance its efficacy as monotherapy while decreasing adverse effects of stinging, burning, and itching.[66,71]

Combination calcipotriene and betamethasone may result in adverse effects (such as striae and HPA axis suppression) due largely to the steroid component. Thus, it is important to follow the maximum weekly dosage guidelines. However, this combination may also be synergistic, with greater efficacy together than either of the individual components alone. Rotational therapy with topical vitamin D analogues, TCIs, emollients, tar-based therapies, and topical corticosteroids should be considered in children as steroid-sparing regimens to reduce potential adverse effects from overreliance on topical steroid therapy.

The strength of recommendations and levels of evidence for pediatric psoriasis and topical combination therapy are summarized in Tables XXVI and XXVII.[66,68-70,72-74]

Topical tazarotene

Tazarotene is a third-generation retinoid that is FDA approved for the treatment of stable plaque psoriasis of less than 20% BSA in adults. Controlled studies of tazarotene have not been performed in the pediatric or adolescent populations.

The literature on tazarotene treatment for pediatric psoriasis is limited to a case report by Diluvio and colleagues[75] of a 6-year-old girl with isolated nail psoriasis. Daily application of tazarotene 0.05% gel to the nails for 8 weeks afforded improvement of the nail disease, but local irritation occurred.

Adverse effects are common and include burning, pruritus, and erythema; they are often concentration related and thus, tazarotene is often used in combination with topical corticosteroids to minimize the irritation and increase efficacy. Tazarotene may be considered for use on localized, hyperkeratotic lesions. Tazarotene is teratogenic and should be avoided in pregnant female patients or used with strong caution and only after counseling in adolescents of childbearing potential.

The strength of recommendations and levels of evidence for pediatric psoriasis and topical tazarotene therapy are summarized in Tables XXVIII and XXIX.

Anthralin

Anthralin (dithranol) is a natural quinone that impairs skin growth by inhibiting mitosis and DNA synthesis. Its use in psoriasis has been studied primarily in adult patients, but some pediatric studies exist. de Jager and colleagues[76] performed a retrospective chart review of 60 patients with psoriasis ages 3 through 18 years who received short contact anthralin treatment on involved skin (with concentration increasing from 0.01% to 4% and time increasing from 15 to 45 minutes). Although only 3.7% of patients rated their clinical response as excellent, 69.5% of patients had a good response, and only 4.9% of patients rated their treatment response as disappointing. Patients had an average remission time of 5.5 months at the 12-month follow-up. Irritation was common in all patients in the study, with 63% rating the irritation as severe. The researchers concluded that anthralin is an effective therapy for psoriasis in children and should be considered before initiation of ultraviolet (UV) therapy or systemic therapy.

Table XXX. Recommendations for pediatric psoriasis and anthralin therapy

Recommendation No.	Recommendation	Strength of recommendation
15.1	Long-term use (12 weeks or longer) of topical anthralin is recommended for the treatment of mild to moderate psoriasis. Short-contact anthralin protocols are recommended to limit adverse effects.	B

Table XXXI. Level of evidence for pediatric psoriasis and anthralin therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Topical anthralin use in pediatric psoriasis	15.1	II	69,76,77,79

A separate retrospective review[77] of 58 children with psoriasis who applied 0.1% to 2% dithranol (anthralin) cream daily for 30 minutes reported that 81% of patients experienced complete resolution of skin erythema within 2 months of treatment initiation. The median duration of effect was 4 months. The medication was well tolerated, with only 1 patient discontinuing the treatment because of irritation. Oostveen et al[78] performed a prospective observational study of anthralin use in 34 pediatric patients with psoriasis ages 3 through 17 years who failed to improve with topical corticosteroids and calcipotriene. Mean duration of treatment was 11 weeks. Patients saw an average CDLQI improvement of 5.1 points and a mean PASI reduction of 69%. The medication was well tolerated by all patients, with no adverse events reported.

Anthralin has many adverse effects, including burning, stinging, pruritus, and perilesional erythema. Staining often results upon application and removal, affecting the skin, clothing, and tub/shower. As such, anthralin application is usually limited by poor tolerability and cosmetic concerns and is rarely used on the face and intertriginous areas. Because there are more cosmetically elegant treatments, anthralin is typically an alternative treatment for localized areas of psoriasis.

The strength of recommendations and levels of evidence for pediatric psoriasis and anthralin therapy are summarized in Tables XXX and XXXI.[69,76,77,79]

Topical coal tar

Topical coal tar is used in the treatment of psoriasis, atopic dermatitis, and seborrheic dermatitis as an antiproliferative and anti-inflammatory agent. Its exact mechanism of action is unclear, although it has been identified as an aryl hydrocarbon receptor agonist. Coal tar is available in both over-the-counter and prescription-strength formulations. Its modalities of use are numerous, including shampoo (for scalp involvement), bath (soaking affected areas), and combined with topical corticosteroids as combination treatment. Although it can be used as monotherapy, tar is commonly used in combination with phototherapy (Goeckerman treatment) to treat psoriasis.[80,81] There is no current literature studying coal tar in pediatric psoriasis as monotherapy.

A retrospective review[80] of 54 children ages 1 through 16 years with plaque or guttate psoriasis treated with a combination of coal tar and phototherapy in a day care treatment center for an average of 12 days showed that lesions cleared in 64% of patients. Of these patients 83% had persistent clearance at the 4-month follow-up mark and only 43% maintained persistent clearance at the 12-month follow-up mark. A 21-year retrospective review by Kortuem et al[81] of 65 pediatric patients ages 3 months to 18 years with recalcitrant psoriasis who had combination tar and phototherapy found significant improvement in all patients treated, with 85% experiencing a prolonged remission (average, 2.6 years).

Known adverse effects of coal tar application include folliculitis, irritation, contact dermatitis, and photosensitivity/phototoxicity. Application and removal may also stain the skin, clothing, and tub/shower. The use of coal tar and phototherapy in combination, although effective for treating psoriasis, has a theoretical increased risk of carcinogenicity with prolonged use. Studies have shown that urinary excretion of coal tar metabolites and chromosomal aberrations of lymphocytes occur in children with psoriasis treated with combination coal tar and phototherapy.[82,83] If coal tar/phototherapy combination therapy is an effective treatment for a particular patient with pediatric psoriasis, this risk may be decreased by alternating this treatment method with other modalities and should be considered on an individual basis.

The strength of recommendations and levels of evidence for pediatric psoriasis and topical coal tar are summarized in Tables XXXII and XXXIII.[80-85]

Table XXXII. Recommendations for pediatric psoriasis and topical coal tar

Recommendation No.	Recommendation	Strength of recommendation
16.1	Coal tar preparations can be used as a monotherapy or combined with other topical therapies for the treatment of pediatric psoriasis.	C
16.2	The use of coal tar preparations in conjunction with phototherapy is effective for the treatment of psoriasis in children but may be limited by the theoretical long-term risk of carcinogenesis.	B

Table XXXIII. Level of evidence for pediatric psoriasis and topical coal tar

Recommendation	Recommendation No.	Level of evidence	Studies
Coal tar preparations for the treatment of pediatric psoriasis	16.1	II-III	81,83
Coal tar preparations in combination with phototherapy for pediatric psoriasis	16.2	II-III	80-85

PHOTOTHERAPY AND PHOTOCHEMOTHERAPY TREATMENTS

Historically, phototherapy using a combination of UV light and anthralin (Ingram regimen) or coal tar (Goeckerman therapy) has served as the mainstay of psoriasis therapy. The first reported use was by Dr Goeckerman in 1925, who successfully treated patients with psoriasis with broadband UVB light in combination with crude coal tar (now referred to as *Goeckerman therapy* in his honor).[86] Please refer to the topical coal tar section of this guideline for the studies available on Goeckerman therapy for pediatric psoriasis.

Since the days of Ingram and Goeckerman, significant advances in the delivery technology of therapeutic wavelengths of light have relegated the use of these traditional combination phototherapy options to treatment-resistant cases in specialty psoriasis centers. NB-UVB phototherapy (wavelength of 311-313 nm) is a safe and effective treatment for pediatric plaque and guttate disease.[87] Excimer laser and UVA light with various forms of psoralen (topical, and in some cases oral psoralen plus UVA [PUVA] photochemotherapy) may be used in children with psoriasis and may be efficacious and well tolerated, but these options have limited supporting evidence. There are insufficient data to report the preferred type, safety, or efficacy of phototherapy for pediatric patients with pustular psoriasis.

A retrospective study by Ersoy-Evans et al[88] analyzed the efficacy of NB-UVB phototherapy for 68 pediatric patients with psoriasis ages 5 to 17 years. The cohort contained patients with plaque and guttate psoriasis, and 92% of patients had significant improvement, with minimal adverse effects recorded. A similar retrospective review of the efficacy of NB-UVB for pediatric patients with psoriasis and atopic dermatitis showed disease clearance in 50% of patients with psoriasis with no adverse effects from the treatment noted.[89] Twenty patients with pediatric psoriasis were given twice weekly NB-UVB for refractory guttate or plaque psoriasis in a prospective study by Jain and colleagues.[90] Patients were 6 to 14 years old, and all had Fitzpatrick type IV skin. At 12 weeks of therapy, 60% of patients had at least a 90% skin clearance. Two patients discontinued treatment because of intolerable erythema. The severity of disease did not correlate to the number of treatments needed to clear the skin, nor the dosage required to see improvement.

Some studies in adult psoriasis showed improved efficacy of UV light treatment when patients pretreat the skin with an emollient. Jain et al[91] pretreated 18 pediatric patients with psoriasis with mineral oil over one half of the body before treating the entire skin surface with NB-UVB. Patients had greater than 20% BSA involvement and were treated twice weekly. Patients were assessed at weeks 3, 6, 9, and 12. Mineral oil pretreatment improved BSA involved, erythema, and scale relative to the untreated side of the body. The dosage at which skin clearance was noted was lower for the pretreated skin relative to the control areas. No patients experienced adverse effects from the regimen. The researchers concluded that pretreatment of psoriasis with an emollient may improve the efficacy of the UV treatment, decrease the dosage needed for disease improvement, and decrease the number of treatments required to successfully treat patients with pediatric psoriasis. The ideal initial frequency of treatment per studies and reports is 3 days per week; by expert consensus, this often can be decreased to 2 days a week upon

Table XXXIV. Recommendations for pediatric psoriasis and phototherapy/photochemotherapy

Recommendation No.	Recommendation	Strength of recommendation
17.1	NB-UVB is recommended as a treatment option for moderate to severe pediatric plaque and guttate psoriasis.	B
17.2	The use of excimer laser or PUVA therapy in children with psoriasis may be efficacious and well tolerated but has limited supporting evidence.	C

NB-UVB, Narrowband ultraviolet light B; *PUVA*, psoralen plus ultraviolet light A.

Table XXXV. Level of evidence for pediatric psoriasis and phototherapy/photochemotherapy

Recommendation	Recommendation No.	Level of evidence	Studies
NB-UVB therapy in pediatric psoriasis	17.1	II-III	88-100
PUVA therapy in pediatric psoriasis	17.2	III	92

NB-UVB, Narrowband ultraviolet light B; *PUVA*, psoralen plus ultraviolet light A.

disease improvement. Twice-weekly therapy reduces time constraints and cost, lowers the risk of adverse effects, and improves adherence. Once the skin clears, patients can continue maintenance therapy at increasingly longer intervals.

Adverse effects of phototherapy in children are similar to those of adults. These include erythema, burning, blistering, hyperpigmentation, pruritus, and viral reactivation for UVB and PUVA, as well as an additional risk of cutaneous carcinogenesis with long-term use of PUVA. Precautions must be taken to ensure adequate eye protection during treatment, especially for younger children who may need a parent to accompany them in the booth. Psoralen use is avoided in children younger than 12 years old. Phototherapy is contraindicated in patients with generalized erythroderma or cutaneous cancer syndromes; it should be used with caution in patients with photodermatoses by taking into account the action spectrum of the specific photodermatoses. UV light treatment in pediatric patients with numerous atypical nevi should proceed with caution and close follow-up after careful discussion of the risks and benefits of phototherapy compared with other systemic therapies.

A UV equipment machine can be an imposing structure for a child (and sometimes the caregiver). Younger children or children with anxiety may be unable to participate appropriately in therapy or may require special preparation, education, and assistance before, during, and after the treatment session to remain motivated and comfortable with the treatment.

Office-based phototherapy may be time consuming, expensive, and inconvenient for many patients. In addition, there is a well-recognized delay in onset of efficacy for the majority of patients, often more than 4 weeks, which can be frustrating and can lead to nonadherence or premature discontinuation of therapy. In-home UV light equipment, with appropriate parent and patient education, is a viable alternative for those who are geographically isolated or unable to consistently receive in-office phototherapy. Given these various practical and logistical constraints, some providers recommend natural sunlight in moderation in lieu of prescription home or in-office phototherapy.

The strength of recommendations and levels of evidence for pediatric psoriasis and phototherapy-photochemotherapy are summarized in Tables XXXIV and XXXV.[88-100]

NONBIOLOGIC SYSTEMIC TREATMENTS

The decision to treat a pediatric patient with systemic therapy is based on baseline severity of disease, subtype of psoriasis, speed of disease progression, lack of response to more conservative therapies such as topical agents and phototherapy (when appropriate), impaired physical or psychological functioning or QOL due to disease extent, and the presence of comorbidities such as PSA. There are several nonbiologic medications used to treat moderate to severe psoriasis in children. In general, the goal with all systemic therapies used in children is to control or clear the disease, maintain stability for several months, and then taper to the lowest effective dose and, ultimately, transition off systemic therapies if possible. If systemic therapy is required, long-term maintenance at the lowest effective dose with the least toxic therapy is the preferred approach.

Methotrexate

Methotrexate is the most common systemic medication used for moderate to severe pediatric psoriasis

Table XXXVI. Suggested monitoring for nonbiologic systemic medications for pediatric psoriasis*

Medication†	Baseline	Follow-up	Miscellaneous	References
Methotrexate Dose range: 0.2-0.7 mg/kg/wk Maximum: 25 mg/wk (see text for details)	CBC with diff, platelets Renal function‡ Liver function If at risk: hepatitis A, B, C, HIV PPD or other TB tests for latent TB screening‡	CBC with diff, platelets (5-7 days after initiating therapy) Renal function‡ LFTs (monthly for the first 3 months, then every 3 to 6 months) Annual TB test if at risk‡	Liver enzymes rise after dose; check labs 4-6 days after the last dose Liver biopsy often avoided/not indicated in pediatric patients but should be individualized to clinical context Avoid in children with liver risk factors Chest radiograph for symptoms	101,133,134
Acitretin Dose range: 0.1-1 mg/kg/d (see text for details)	CBC Fasting lipids Liver function Pregnancy test (if appropriate)	Liver function and fasting lipids after 1 month of treatment and with dose increases, then every 1-3 months Monthly pregnancy test (if appropriate)	Bone imaging based on symptoms and duration of treatment (see text)	101,133,134
Cyclosporine Dose range: 2-5 mg/kg/d (see text for details)	Blood pressure CBC Renal function Liver function Fasting lipids Serum magnesium and potassium uric acid HIV if at risk	Blood pressure once a week for the first month and at follow-up visits as needed. CBC, serum creatinine, BUN, uric acid, potassium, lipids, and magnesium every 2 weeks for the first month and then at least monthly thereafter	Whole-blood cyclosporine trough level if inadequate clinical response or concomitant use of potentially interacting drugs	101,133,134

BUN, Blood urea nitrogen; *CBC*, complete blood count; diff, differential; *LFT*, liver function test; *PPD*, protein derivative test; *TB*, tuberculosis.

*Some monitoring suggestions are not evidence-based recommendations and are expert consensus. These recommendations may vary based on patient age and specific protocols. Practicing physicians should individualize monitoring protocols according to the clinical context. For all pediatric patients receiving long-term systemic therapy, growth parameters should also be monitored.

†Dosing is based on actual weight.

‡At the discretion of the physician based on the clinical situation/individual risk factors.

Table XXXVII. Recommendations for pediatric psoriasis and methotrexate therapy

Recommendation No.	Recommendation	Strength of recommendation
18.1	Methotrexate is recommended as an effective systemic therapy for moderate to severe plaque psoriasis and other psoriasis subtypes in children.	B
18.2	Methotrexate is recommended as an effective systemic therapy for pustular psoriasis in children.	B
18.3	Methotrexate weight-based dosing is recommended in younger children, ranging from 0.2 to 0.7 mg/kg/wk (maximum, 25 mg/kg/wk).	B
18.4	Folic acid supplementation daily or 6 times weekly during treatment with methotrexate is recommended.	B
18.5	Routine clinical and laboratory monitoring is recommended before and during treatment with methotrexate.	B

Table XXXVIII. Level of evidence for pediatric psoriasis and methotrexate therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Methotrexate for pediatric psoriasis	18.1	II-III	103-107
Methotrexate for pediatric pustular psoriasis	18.2	III	Expert opinion
Methotrexate dosage	18.3	III	101,102,104-106
Folic acid supplementation during methotrexate use	18.4	II	101
Laboratory monitoring	18.5	III	Expert opinion

worldwide.[101] It is often selected because it is inexpensive, has long-term efficacy and safety data, and has been used extensively by dermatologists. Methotrexate is dosed weekly, making it somewhat less burdensome than other options, and it can be administered orally or injected subcutaneously. Although it is not necessarily a fast-acting medication, its slow onset of action gives way to eventual efficacy in every subtype of psoriasis. Methotrexate is also used for PSA, making it particularly useful for children with concomitant psoriasis and PSA. Methotrexate may be used as monotherapy or in combination with a biologic agent to either increase efficacy and/or theoretically prevent the formation of anti-drug antibodies.

Several studies since the publication of the previous AAD psoriasis guidelines in 2009 have highlighted the efficacy, safety, and beneficial effect on QOL of methotrexate for pediatric psoriasis. Kaur and colleagues[102] retrospectively reviewed the administration of methotrexate in 24 pediatric patients with severe refractory psoriasis. Seventeen had plaque disease, 3 were erythrodermic, 3 had pustular disease, and 1 had primarily palmoplantar involvement. The dosage of methotrexate ranged from 7.5 to 20 mg per week. Twenty-two patients noted major improvement of their skin disease, defined as greater than 75% improvement in PASI score (PASI 75). Patients responded to therapy in an average of 5 weeks, with remission times ranging from 1.5 months to 3 years. Nine patients experienced mild GI adverse effects of nausea, vomiting, and poor appetite, but this did not preclude the continuation of therapy. A case series by Collin et al[103] of 13 patients with pediatric psoriasis ages 3 through 15 years treated with methotrexate at 0.03 to 0.24 mg/kg once weekly for refractory plaque psoriasis found that 11 patients responded to the medication (defined as skin clearance), although 4 patients needed multiple treatment cycles to maintain skin clearance. Two of the 13 patients discontinued therapy despite skin clearance because of elevated liver function test results, although no adverse events occurred.

The impact of methotrexate therapy on patient QOL was directly assessed in a prospective, longitudinal, observational study of 25 children prescribed 0.14 to 0.63 mg/kg of methotrexate once weekly for plaque disease. At the 24-week follow-up, the mean CDLQI score of the cohort decreased from 9.0 to 3.8, and the Physicians Global Assessment mean score also improved, decreasing from 3.0 to 1.2, showing significant positive impact for the patients.[104] This study suggests the time to reach peak efficacy for

Table XXXIX. Recommendations for pediatric psoriasis and cyclosporine therapy

Recommendation No.	Recommendation	Strength of recommendation
19.1	Cyclosporine is recommended as an effective systemic therapy for moderate to severe plaque psoriasis in children.	B
19.2	Cyclosporine is recommended as an effective systemic therapy for moderate to severe pustular psoriasis in children.	B
19.3	Cyclosporine is recommended for short-term crisis management of severe or unstable plaque, erythrodermic, or pustular psoriasis until the patient can be transitioned to a medication appropriate for long-term use.	C
19.4	Routine blood pressure clinical and laboratory monitoring is recommended during therapy with cyclosporine.	A
19.5	Modified cyclosporine (for microemulsion in capsules or solution) is recommended for use and is not interchangeable with unmodified forms of cyclosporine.	C

Table XL. Level of evidence for pediatric psoriasis and cyclosporine therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Cyclosporine for pediatric psoriasis	19.1	II-III	108,109,112-117
Cyclosporine for pustular pediatric psoriasis	19.2	III	110
Cyclosporine for short-term crisis therapy	19.3	III	Expert opinion
Laboratory monitoring during treatment	19.4	III	118
Modified cyclosporine use in pediatric psoriasis	19.5	III	Expert opinion

methotrexate is much longer than for biologic therapy, such that patients showing partial benefit within 3 to 4 months of treatment initiation should continue methotrexate therapy for an additional 3 to 4 months before determining if methotrexate is adequately controlling the disease.

The benefit of methotrexate relative to other systemic therapies for 289 pediatric patients with psoriasis was examined by Ergun and colleagues[105] via a multicenter cohort study. Patients ranged in age from 9 to 14 years and were treated with methotrexate, acitretin, or cyclosporine. Methotrexate was well tolerated, with 90.8% of patients reporting no adverse events. Eight percent of patients experienced nausea, and 1 patient discontinued treatment because of elevated liver function test results (without adverse sequelae). All 3 medications were efficacious, with 34.1% of methotrexate users showing improvement greater than or equal to PASI 75 during treatment. No medication was concluded to be superior to another.

Dosing of methotrexate in young children (<13 years) is weight based and often started at 0.2 to 0.3 mg/kg/week (range, 0.2 to 0.7 mg/kg/week to a maximum of 25 mg/week) with increasing titration of 1.25 to 5 mg/week until an effective or maximum dose is attained. Pediatric patients ages 13 years and older of average weight can be dosed similarly to adults, with a maximum dose of 25 mg/week. Subcutaneous administration is preferred over oral because of fewer GI adverse effects, better bioavailability, and higher efficacy at lower doses, but administration can be psychologically traumatic in younger children. Methotrexate can be administered as scored 2.5-mg tablets that can be split and crushed. There are several concentrations of methotrexate solution for subcutaneous injection. This formulation can also be given orally (for example, mixed with juice) and is less expensive (other than fixed-dose pens) and often more readily available than the standard oral solution, which is supplied in a concentration of 2.5 mg/mL. Most children who respond to treatment will show improvement 5 to 12 weeks after treatment initiation, but it may take an additional 3 to 4 months to reach peak treatment efficacy.[106] There is no consensus on treatment duration, although a slow taper after 2 to 3 months of sustained clearance is a reasonable approach. Methotrexate use requires folic acid supplementation, usually 1 mg daily (or 6 days a week, sparing the day of methotrexate administration). Folic acid dosing of daily to 6 days a week decreases

Table XLI. Recommendations for pediatric psoriasis and systemic retinoid therapy

Recommendation No.	Recommendation	Strength of recommendation
20.1	Acitretin is recommended as an effective, nonimmunosuppressive systemic therapy for children with extensive guttate or moderate to severe (ideally thin plaque) psoriasis vulgaris at a dosage of 0.1 to 1 mg/kg/d.	B
20.2	Acitretin is recommended as an effective systemic therapy for pustular psoriasis in children.	B
20.3	Acitretin combined with NB-UVB therapy may be synergistic for plaque and pustular psoriasis in childhood and allows for a reduction in dosing of both agents.	C
20.4	Acitretin may be combined with other systemic therapies such as methotrexate or cyclosporine, or biologics, depending on the individual clinical situation.	C
20.5	Routine clinical and laboratory monitoring is recommended during therapy with acitretin.	C

NB-UVB, Narrowband ultraviolet light B.

Table XLII. Level of evidence for pediatric psoriasis and systemic retinoid therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Acitretin for guttate or moderate to severe psoriasis	20.1	II	52,120,121
Acitretin for pustular psoriasis	20.2	II-III	120,122,123,129
Acitretin plus NB-UVB combination therapy	20.3	III	Expert opinion
Acitretin and other systemic or biologic combination	20.4	III	Expert opinion
Laboratory monitoring while receiving acitretin	20.5	III	Expert opinion

NB-UVB, Narrowband ultraviolet light B.

both the GI intolerance and hepatic adverse effects of methotrexate compared with weekly folic acid dosing.[101]

Elevations in hepatic transaminases are common, especially transient increases within 3 to 4 days after dosing. Because of this, monitoring laboratory tests should be performed at least 4 to 6 days after dosing. More serious adverse effects of methotrexate are rare in children and include bone marrow suppression, hepatotoxicity, and pulmonary toxicity. To date, there has not been a signal for lymphoproliferative disorders arising in a patient with pediatric psoriasis using methotrexate as monotherapy.

Bone marrow suppression generally occurs early in treatment (first 4-6 weeks) and is reversible with cessation of methotrexate. Based on the risk of acute idiosyncratic bone marrow failure, an initial test dose of 1.25 to 5 mg of methotrexate may be considered, followed by a complete blood count 5 or 6 days later to check for bone marrow toxicity. Bone marrow toxicity may be increased by medications that interfere with the folic acid metabolic pathway (such as trimethoprim-sulfamethoxazole) and nonsteroidal anti-inflammatory drugs, which may decrease the renal clearance of methotrexate. Immunosuppression is a risk of treatment with methotrexate, although serious infections appear rare and may be less frequent compared with psoriasis treatment with some biologic agents (eg, mycobacterial infection with TNF inhibitors).

Hepatic fibrosis is an adverse effect of long-term methotrexate use in adults but has not, to our knowledge, been reported in a child using methotrexate for psoriasis. Liver biopsies are very rarely recommended or required for children, especially those with cumulative doses below 1.5 g and without laboratory test result abnormalities. Some providers have advocated for noninvasive monitoring for hepatic fibrosis, but these tests appear unreliable and unproven in children with psoriasis.

In general, recommended monitoring for methotrexate includes complete blood count, hepatic transaminases, and creatinine, although there is no consensus regarding a particular monitoring protocol. Serum creatine levels are not 100% accurate and should be checked at the provider's discretion depending on patient need. Monitoring laboratory tests should be performed at least 4 days after dosing to avoid making dosage adjustments based on transient elevations of hepatic transaminases (Table XXXVI). Proper timing of the laboratory evaluation is imperative to accurately interpret the data. Monitoring for latent infections such as tuberculosis, hepatitis, or HIV should be considered before therapy based on individual circumstances and local epidemiology. Methotrexate should be

Table XLIII. Recommendations for pediatric psoriasis and fumaric acid ester therapy

Recommendation No.	Recommendation	Strength of recommendation
21.1	Fumaric acid esters may be considered as a potentially effective alternative therapy for pediatric patients with moderate to severe psoriasis who are candidates for systemic therapy.	C
21.2	Clinical and laboratory monitoring is recommended during treatment with fumaric acid esters.	C

Table XLIV. Level of evidence for pediatric psoriasis and fumaric acid ester therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Fumaric acid ester therapy for pediatric psoriasis	21.1	II-III	101,106,130-132
Laboratory monitoring while receiving fumaric acid esters	21.2	III	Expert opinion

avoided in the settings of pregnancy or liver dysfunction and used with caution, if at all, in children with poorly controlled diabetes or obesity. Dose adjustments should be made for renal dysfunction, but it is not an absolute contraindication. Adolescents should be counseled about the risk of alcohol ingestion and becoming pregnant while taking methotrexate, which is a pregnancy category X drug.

The strength of recommendations and levels of evidence for pediatric psoriasis and methotrexate therapy are summarized in Tables XXXVII and XXXVIII.[101-107]

Cyclosporine

Cyclosporine inhibits immunocompetent T lymphocytes and suppresses the production of IL-2 and interferon gamma, blocking the inflammatory signaling pathway that perpetuates psoriasis. Cyclosporine is generally well tolerated in children. It is an excellent choice for the rapid control of severe, unstable plaque, pustular, or erythrodermic psoriasis in children. Several studies support its efficacy and tolerance in the pediatric population.

Bulbul Baskan and colleagues[108] treated 22 pediatric patients with psoriasis refractory to other therapies with cyclosporine A, including patients with pustular and erythrodermic disease. Seventeen (77%) patients had an excellent response, with skin clearance achieved in a mean duration of 4 weeks. Patients tolerated the medication well with a mean treatment duration of 5.7 ± 3.3 months. A retrospective chart review by Dogra et al[109] found similar results in 10 pediatric patients with refractory psoriasis, including erythrodermic and pustular variants. Seven (70%) patients had improvement greater than PASI 75 in a median time of 4 weeks. The remaining 3 patients all had erythrodermic disease and did not show improvement greater than PASI 75. Two patients developed abdominal pain and elevated creatinine levels, but no adverse events occurred. The researchers concluded that cyclosporine is an effective medication for crisis management in psoriasis treatment with appropriate clinical and laboratory monitoring.

The administration of cyclosporine for pustular psoriasis has been successful in very young children. Kilic and colleagues[110] report using cyclosporine at 1 mg/kg/d in a 10-month-old boy with generalized pustular psoriasis. His skin disease was well controlled within 4 weeks of therapy, allowing discontinuation after 6 months of medication. The patient was clear of disease at the 2-year follow-up. They similarly treated a 17-month-old boy with cyclosporine at 1 mg/kg/d, with disease clearance after 2 weeks of treatment. Both patients tolerated the medication without adverse effects.

Cyclosporine is typically dosed at 2 to 5 mg/kg/d in children of all ages and is available as a modified microemulsion (Neoral; Novartis Pharmaceuticals Corporation, East Hanover, NJ) in 25-, 50-, and 100-mg capsules and 100-mg/mL oral solution. The modified version is preferred, and the formulations are not interchangeable with unmodified cyclosporine (Sandimmune, Novartis). Oral absorption may be less in children than in adults, and clearance may be faster; therefore, children may require higher doses by weight than adults. The total daily dose should be administered in 2 divided doses. It is preferable to initiate cyclosporine at the higher range of the daily dose spectrum and reduce to the lowest

Table XLV. Supplementary information about baseline and ongoing monitoring for TB in patients receiving biologics*

Monitoring for TB
Baseline monitoring:
• Pretreatment test for latent TB (PPD, T-Spot [Oxford Immunotec, Inc, Marlborough, MA], or QuantiFERON Gold [Qiagen, Germantown, MD])[147]
Ongoing monitoring:
• Yearly testing for latent TB (PPD, T-Spot, or QuantiFERON Gold) should be done in patients at high risk (eg, patients receiving anti-TNF agents; patients who are in contact with individuals with active TB because of travel or a family relationship; and patients with selected underlying medical conditions). For patients who are not at high risk, screening should be done at the discretion of the dermatologist. This screening is particularly important for patients who are taking TNF-α inhibitors. Furthermore, the result of the QuantiFERON Gold test can remain positive after treatment of latent TB. Caution should be exercised when using the QuantiFERON Gold test.[148,149]
○ An annual chest radiograph may be considered at the discretion of the treating dermatologist (expert opinion; complete WG consensus was not achieved).

PPD, Purified protein derivative; *TB*, tuberculosis; *TNF*, tumor necrosis factor.
*Supplemental information is expert consensus and not part of evidence-based recommendations.

effective dose once the disease is controlled (expert opinion).

Trough levels of cyclosporine are not used to dictate dosing adjustments for short-term psoriasis treatment, although they may be beneficial for determining adherence. Instead, adjustments are made based on clinical response, serum creatinine levels, and blood pressure. Improvement may be observed within in 1 to 2 weeks, although the full effect is most often seen between 4 and 8 weeks after initiation. Once psoriasis has been stable for a month or 2, gradual tapering should begin, often with transition to another agent if necessary, given the potential toxicity of long-term use.

Renal toxicity is the most concerning adverse effect of long-term cyclosporine use because of the vasoconstriction of the renal afferent arterioles.[111] Given the risk of hypertension, it is thus advisable to evaluate blood pressure every week for the first month and then during follow-up visits as needed. Cyclosporine is immunosuppressive, although serious infections in the setting of monotherapy for psoriasis are rare. Long-term use of cyclosporine is associated with an increased risk of nonmelanoma skin cancers and is not recommended in children with a history of PUVA treatment or those receiving concurrent phototherapy.

Additional risks associated with high-dose cyclosporine used in organ transplantation, such as GI upset, hypertrichosis, headache, paresthesias, arthralgias, and gingival hyperplasia, are less common in children having treatment for psoriasis. Of particular concern in children is the increased risk of lymphoproliferative malignancies observed in the population with transplants; however, the risk appears minimal in children receiving short-term, low-dose treatment in the absence of concomitant use of multiple immunosuppressive medications (clinical observation).

Before and during treatment with cyclosporine, evaluation of complete blood count, serum electrolytes (including magnesium), creatinine, urea, cholesterol, triglycerides, and blood pressure is recommended. Administration of live-virus vaccines is contraindicated during cyclosporine treatment and should be discussed with the child's primary care provider. Cyclosporine should be avoided in pediatric patients with severe or active infections, those with inherited immunosuppressive disorders, and those whose immunizations are not up to date. Cyclosporine should not be used in children with acute or chronic kidney disease or high blood pressure. It is pregnancy category C.

The strength of recommendations and levels of evidence for pediatric psoriasis and cyclosporine therapy are summarized in Tables XXXIX and XL.[108-110,112-118]

Systemic retinoids

The systemic retinoids are vitamin A–based compounds that improve psoriasis by reducing inflammation, regulating keratinocyte maturation, and slowing keratinocyte turnover. This causes decreased plaque thickness and scale. In addition, retinoids may inhibit neutrophil chemotaxis, which may explain their efficacy in pustular psoriasis. They serve as a nonimmunosuppressive treatment option for patients with pediatric psoriasis, which may be desirable in specific situations, such as treatment of patients with organ transplants or very young children. Acitretin has greater efficacy in papulosquamous diseases than does isotretinoin and is the preferred agent for psoriasis. Acitretin is particularly effective for widespread guttate psoriasis, pustular psoriasis, and palmoplantar disease, reportedly successful in patients as young as 6 weeks of age.[119] Isotretinoin may be substituted for acitretin,

Table XLVI. Summary of biologic agents*

Drug	Mechanism of action	Dosing schedule†	References
Etanercept	Soluble fusion protein of TNF-α receptor and Fc portion of human IgG	0.8 mg/kg weekly subcutaneous If $\geq$ 63 kg, 50 mg	133,143
Adalimumab	Fully humanized monoclonal IgG antibody targeting TNF-α	24 mg per m^2 subcutaneous or 0.8 mg/kg (maximum, 40 mg) weekly for the first 2 weeks then every 2 weeks	139,143
Infliximab	Chimeric monoclonal IgG antibody targeting TNF-α	Intravenous infusions 5 mg/kg at weeks 0, 2, and 6 and then every 8 weeks after	133,143
Ustekinumab	Fully human monoclonal antibody targeting the p40 subunit of IL-12 and IL-23	If $<$ 60 kg: 0.75 mg/kg/dose If 60 to $\leq$100 kg: 45 mg If $>$ 100 kg: 90 mg Subcutaneous, weeks 0 and 4, and then every 12 weeks	133,143

IL, Interleukin; *TNF*, tumor necrosis factor.
*See text for monitoring.
†Dosing based on actual weight.

particularly for female adolescents given their increased risk, but it requires patient and provider enrollment in and compliance with the iPLEDGE monitoring program.

Popadic and Nikolic[120] treated 17 patients with generalized or pustular psoriasis ages 1 month to 13 years with acitretin. Most patients maintained topical therapy with emollients and corticosteroids. Fourteen (82%) patients experienced skin clearance with acitretin as systemic monotherapy, and 3 patients experienced clearance after the addition of cyclosporine. There was 1 patient in the trial for whom prior methotrexate and cyclosporine monotherapy had failed. All patients were followed by orthopedists for bony abnormalities, which did not occur, and no additional adverse events were noted. A retrospective chart review of 15 patients with pediatric psoriasis with generalized or palmoplantar involvement treated with acitretin as monotherapy showed that 14 of the 15 patients (93%) experienced skin clearance without adverse effects.[121]

Concomitant treatment of acitretin with NB-UVB is synergistic in patients old enough to cooperate with therapy and often allows for a reduction in acitretin dosing. Most of the supporting literature regarding dual therapy is adapted from etretinate (which is no longer available), showing efficacy for pediatric patients with severe generalized and pustular psoriasis.[122,123] A case report by Kopp and colleagues[124] notes the successful treatment of refractory generalized pustular psoriasis in a 3-year-old boy who was dependent on acitretin and oral high-dose corticosteroids until the addition of NB-UVB to his treatment regimen afforded discontinuation of both systemic steroids and decreased dosing of acitretin.

Acitretin is usually dosed at 0.1 to 1 mg/kg/d for all patients of pediatric ages and is supplied in 10-, 17.5-, and 25-mg capsules. Improvement of plaque disease is generally seen after 2 to 3 months of therapy, whereas pustular psoriasis may respond in as early as 3 weeks. The most common clinical adverse effects of systemic retinoids are mucocutaneous. Dryness of the skin and mucous membranes is common because of the retinoid effects on sebaceous glands. Hyperlipidemia may be encountered and is typically transient and dose dependent; acitretin should be used with caution in children with baseline hyperlipidemia.

Teratogenicity is a major concern in female patients of childbearing potential because acitretin may remain stored in the body for up to 3 years when reverse-esterified to etretinate in the presence of alcohol. This effect may be produced by the accidental ingestion of alcohol via cough syrup and cooking recipes. Thus, its use in female patients of approaching childbearing potential is discouraged. Because isotretinoin clears the body within 1 month of discontinuation, it is a rational substitute for acitretin in female adolescents who require an oral retinoid for treatment of psoriasis.[125]

The most concerning long-term effects of systemic retinoid use in young children are bony changes. Although administration of high doses of vitamin A and synthetic retinoids has been associated with premature epiphyseal closure, hyperostosis resembling diffuse idiopathic skeletal hyperostosis, calcification of anterior spinal ligaments, formation of periosteal bone, and decreased bone mineral density,[126] these complications have been reported primarily in the context of chronic use of high doses, such as those doses previously used for disorders of

Table XLVII. Recommendations for pediatric psoriasis and biologic therapy

Recommendation No.	Recommendation	Strength of recommendation
22.1	Etanercept is recommended as an effective therapy for moderate to severe psoriasis in children 6 years of age and older.	A
22.2	Etanercept dosing is typically once weekly and is dosed subcutaneously at 0.8 mg/kg with a maximum of 50 mg weekly.	A
22.3	Adalimumab is recommended for off-label use as an effective therapy in children and adolescents with moderate to severe psoriasis.	B
22.4	The dose of adalimumab is 0.8 mg/kg (maximum, 40 mg) at weeks 0 and 1 and then is given every other week. Adalimumab administered at a dose of 0.8 mg/kg is more efficacious than at a dose of 0.4 mg/kg.	B
22.5	Infliximab can be recommended as monotherapy or in combination with methotrexate for use in pediatric patients with severe plaque or pustular psoriasis that is unresponsive to other systemic medications, rapidly progressive, unstable, and/or life threatening.	C
22.6	The starting dose of infliximab is an infusion of 5 mg/kg administered on weeks 0, 2, and 6 and then every 8 weeks.	C
22.7	Ustekinumab is recommended as an effective therapy for adolescents 12 years and older with moderate to severe plaque psoriasis.	A
22.8	Ustekinumab can be used as an effective therapy for pediatric patients younger than 12 years old with moderate to severe plaque psoriasis	C
22.9	Ustekinumab is given at weeks 0, 4, and 16 and then every 12 weeks with weight-based dosing as follows: 0.75 mg/kg if $<$60 kg, 45 mg if 60 to $\leq$100 kg, and 90 mg if $>$ 100 kg.	B
22.10	Biologics may be safely combined with topical corticosteroids, with or without a vitamin D analogue, to augment effectiveness for the treatment of moderate to severe plaque psoriasis.	C
22.11	The major risk for biologics in children is injection site reaction, but patients should be monitored for their increased risk of infection.	B

cornification. There seems to be much less risk for bone toxicity when long-term doses are kept low (1 mg/kg/d or less).[127] There is no consensus regarding a bone monitoring protocol for patients receiving oral retinoids. The product information for acitretin suggests radiography periodically while receiving long-term therapy or in the presence of symptoms of hyperostosis including aches, pain in bones, joint, muscle, back, trouble moving, or loss of sensation in hands or feet.[128]

Monitoring during treatment with systemic retinoids includes baseline and periodic serum lipids and liver function testing. Specific regimens should be tailored to each clinical situation. Female patients of childbearing potential must be counseled on pregnancy prevention, and contraceptive methods and regular pregnancy monitoring should be considered. Isotretinoin can be considered in female patients of childbearing potential when they have achieved stability with acitretin and wish to continue retinoid treatment. When using isotretinoin, the iPLEDGE program mandates monthly pregnancy monitoring.

Screening for alterations in mood and signs or symptoms of depression and other psychiatric symptoms during retinoid use, including feelings of aggression or thoughts of self-harm, is prudent. Concomitant administration of vitamin A in excess of 5,000 IU daily should be avoided.

The strength of recommendations and levels of evidence for pediatric psoriasis and systemic retinoid therapy are summarized in Tables XLI and XLII.[52,120-123,129]

Systemic fumaric acid esters

Fumaric acid esters are small molecules with a broad range of immunomodulatory effects whose mechanism of action is unclear. These agents are used commonly outside the United States as first-line systemic therapy for psoriasis. In Germany, they are the most frequently used systemic treatment for psoriasis and appear generally safe and moderately effective. Fumaric acid esters are not currently approved for use in the United States for treating psoriasis. There are limited studies of their use in

Table XLVIII. Level of evidence for pediatric psoriasis and biologic therapy

Recommendation	Recommendation No.	Level of evidence	Studies
Etanercept for pediatric patients (≥6 year. of age)	22.1	I-III	135-138,141,144,145
Etanercept dose • 0.8 mg/kg per week • 0.4 mg/kg 2×/week • Maximum dose: 50 mg/week	22.2	I, III	135,136,146
Adalimumab off-label use for pediatric psoriasis	22.3	I, III	139,141
Adalimumab dose • 0.8 mg/kg at weeks 0 and 1, then every other week • Maximum dose: 40 mg	22.4	I	139
Infliximab monotherapy or combination with methotrexate for pediatric pustular psoriasis	22.5	III	Expert opinion
Infliximab dose • 5 mg/kg at weeks 0, 2, and 6, then every 8 weeks	22.6	III	Expert opinion
Ustekinumab for pediatric psoriasis (≥12 years of age)	22.7	I, III	140,141
Ustekinumab for pediatric psoriasis (<12 years of age)	22.8	III	141
Ustekinumab dose based on weight • 0.75 mg/kg (<60 kg) • 45 mg (60 to ≤100 kg) • 90 mg (>100 kg)	22.9	I	140
Combination therapy of biologic and topical agents	22.10	III	Expert opinion
Injection site reaction and monitoring	22.11	II	101

pediatric patients with psoriasis, but such studies do note efficacy.[106,130,131]

A multicenter retrospective chart review of 390 patients with pediatric psoriasis treated with at least 1 systemic medication for a minimum of 3 months included a cohort of 19 patients treated with fumaric acid esters.[101] Thirteen (68%) of the patients developed adverse events, which led to treatment discontinuation, including abdominal pain, diarrhea, flushing, and headache. Two patients (10%) discontinued therapy because of serious adverse events (pericarditis and bone marrow suppression). The rates of adverse events and serious adverse events were very high for fumaric acid esters relative to other systemic therapies despite shorter treatment durations. The medication is dispensed as 120- and 240-mg delayed-release capsules pills. Doses range from 1 to 6 pills/d.

The strength of recommendations and levels of evidence for pediatric psoriasis and fumaric acid ester therapy are summarized in Tables XLIII and XLIV.[101,106,130-132]

Other systemic agents

Presently, there are insufficient data to make recommendations regarding the use of apremilast, azathioprine, hydroxyurea, leflunomide, mycophenolate mofetil, sulfasalazine, oral calcineurin inhibitors, or 6-thioguanine for the treatment of pediatric patients with psoriasis. These agents may be selected based on individual clinical factors in selected cases but will not be discussed here.

Monitoring suggestions for nonbiologic systemic medications for pediatric psoriasis are summarized in Table XXXVI.[101,133,134]

BIOLOGIC THERAPY

Biologic medications are immunomodulators that regulate inflammation via specifically targeted pathways involving cell signaling, immune cell development, recruitment, and apoptosis. The safety and efficacy data of various classes are rapidly accumulating for pediatric patients, for whom their use is becoming much more commonly considered among other first-line systemic agents. No biologics were licensed by the FDA for pediatric psoriasis at the time of publication of the 2009 guidelines. Since that time, evidence has accumulated, and 2 agents, etanercept and ustekinumab, are now FDA approved for patients with psoriasis 4 years and older and 12 years and older, respectively. In Europe, these agents are also approved, as is adalimumab for patients 4 years

of age and older. Although several other biologic agents are used off label for pediatric psoriasis treatment, current literature is limited to single case reports.

Most of the literature regarding biologic treatment for pediatric psoriasis shows efficacy in moderate to severe plaque psoriasis. Successful use of biologics has been described for pustular and erythrodermic psoriasis in children but has not been tested in clinical trials. The failure of one biologic therapy does not preclude a successful response to another biologic, even of the same class. Although there is little formal evidence in the pediatric population regarding the use of biologic therapies for severe palmoplantar, nail, or scalp disease or inverse or guttate psoriasis, these treatments have been used off label for these indications and anecdotally have been effective. Treatment choices should be individualized to the clinical situation.

The efficacy of etanercept for pediatric psoriasis relative to placebo was measured in a double-blind randomized controlled trial by Paller and colleagues.[135] A total of 211 children ages 6 through 17 years with moderate to severe plaque psoriasis were given 0.8 mg/kg of etanercept per week (max dose, 50 mg/wk) for 12 weeks. Etanercept showed a significant effect relative to placebo, with achievement of PASI 75 or greater in 57% versus 11%, respectively. Only 4 patients had adverse events (1 surgical, 3 infections), all of which resolved without sequelae. A related study of this patient population showed that CDLQI scores improved significantly in patients after 12 weeks of etanercept therapy relative to placebo (52.3% vs 17.5%, respectively), with the greatest impact on QOL noticed in patients who achieved a PASI 75 or greater during treatment.[136]

The long-term safety of etanercept use in pediatric patients with psoriasis was studied in 181 patients with plaque psoriasis ages 4 through17 years out to weeks 96 (1.8 years) and 264 (5.07 years).[137,138] At weeks 96 and 264, 8% and 89% of patients, respectively, reported an adverse event, none of which were judged to be treatment related. Eight patients reported serious adverse events by week 264, 1 of which was thought to be treatment related (cellulitis). There were no cases of opportunistic infection or malignancy reported during the follow-up period.

The only comparative trial of methotrexate versus a biologic was a randomized, double-blind, phase 3 trial of 114 children with severe plaque psoriasis 4 through 17 years old, described by Papp et al.[139] PASI 75 was achieved by week 16 in 58% and 44% of children treated with adalimumab 0.8 mg/kg (full dose) or 0.4 mg/kg (half dose) every other week, respectively, in contrast to 32% treated with weekly oral methotrexate (0.1-0.4 mg/kg). Consistently, 61% with full-dose and 41% with half-dose adalimumab versus 41% with methotrexate achieved a clear or almost clear score by physician global assessment. Infections were the most frequent adverse events and were not significantly different among the 3 patient groups. Although this study suggested better efficacy of adalimumab standard dose versus methotrexate with similar safety, it should be noted that the average dose of methotrexate (0.15 mg/kg/week) is well below the 0.3 to 0.6 mg/kg/week dosing that is typically used for pediatric psoriasis. Landells et al[140] randomly assigned 110 children to receive either ustekinumab standard dosing, half-standard dosing, or placebo at weeks 0 and 4 and every 12 weeks. In this study, standard dosing was considered 0.75 mg/kg for those less than 60 kg, 45 mg for those 60 through 100 kg, and 90 mg for those greater than 100 kg. At week 12, 80.6% of those receiving the standard dose and 78.4% of those receiving the half dose achieved PASI 75 versus 10.8% of those receiving placebo, and 61.1% of those receiving the standard dose and 54.1% of those receiving the half dose achieved a 90% or greater improvement in PASI score versus 5.4% of those receiving placebo. Similarly, at 12 weeks, 67.6% and 69.4% of patients receiving ustekinumab at standard and half doses, respectively, achieved Physician Global Assessment of 0/1, in contrast to 5.4% for placebo. The report of adverse events was similar among the patient groups (44% for the standard dose, 51% for the half dose, and 57% for placebo).

A retrospective case series of 51 patients with pediatric psoriasis ages 7 through 18 years by Klufas and colleagues[141] described patients treated with etanercept, adalimumab, or ustekinumab from initiation to 1 year of follow-up. Patients had a successful response (defined as a statistically significant improvement in Physician Global Assessment score at 5 months) to all 3 medications, with low adverse risk effect. There were no serious adverse events. Injection site pain and fatigue were the most common symptoms, reported at 8.6% and 7.5%, respectively. Patients who did not respond to one biologic agent remitted with an alternate biologic. Five patients (33%) had concomitant PSA and received a biologic in combination with methotrexate. Cutaneous and joint disease improved, with minimal adverse effects. The researchers concluded that biologic therapies are a safe, effective means of treating refractory plaque psoriasis in children for whom first- and second-line treatment options fail.

The primary risk of biologic treatment in children is injection site reaction. Injection site reactions may

occur with all biologics and occurred in 18.9% of patients in a retrospective chart review that included 106 children treated with primarily etanercept and adalimumab.[101]

Patients and their households should be monitored for infection during treatment and should be current on their vaccinations before the initiation of treatment. The safety and efficacy of live immunizations administered to children receiving biologic treatment is unknown; therefore, if live vaccination is needed, the physician should weigh the known risk with potential benefit. It is reasonable to temporarily hold biologic therapy during a severe infection that requires antibiotic treatment, resuming therapy upon resolution of the illness. It is unknown if biologic therapies alter the risk of solid tumor or lymphoreticular malignancies in children.

There is little evidence to guide recommendations regarding surgical procedures during biologic therapy in children with psoriasis. The section of the guideline on this topic pertaining to adults may provide insight but is not evidence based for children. Please reference the adult section of this guideline for recommendations regarding safety during pregnancy and lactation and for adolescent male patients receiving biologics who attempt conception.[142]

Baseline monitoring for biologic therapy includes testing for latent tuberculosis by purified protein derivative test (PPD) or interferon-gamma release assay, especially in high-risk geographic locations. Repeat testing for tuberculosis annually during the use of TNF inhibitors is recommended (expert opinion), but its value for other biologics is currently unclear. Children with a positive tuberculosis test result should be referred for consultation with an infectious disease specialist (Table XLV). Hepatitis and HIV screening in children should be performed based on the presence of relevant risk factors. Baseline and repeated history and physical examination are recommended during treatment, especially to monitor for infection. The frequency of such evaluations (ranging from every 3 months to annually) should be individualized. No additional laboratory monitoring is required for children receiving biologic therapy (such as blood count, liver function tests, etc) but should be individualized based on the specific clinical context (ie, in the presence of risk factors and comorbidities).

Psoriasiform eruptions while receiving TNF inhibitor therapies for other indications (eg, Crohn's disease) can occur in the pediatric population.[21] The suggested approach for the treatment of such eruptions is to use topical agents first. If this fails, switching to another biologic medication (in the same class or different) may afford resolution, with approximately 50% success[21] (an expert opinion).

Biologics may be safely combined with topical therapies. There are no evidence-based recommendations for the pediatric population related to strategies to achieve safe and efficacious transitioning from nonbiologic therapy to biologic therapy, from one biologic medication to another, or from a biologic therapy to nonbiologic therapy. Given the relatively limited experience and trials testing biologics in children and adolescents relative to adults, adult recommendations may provide guidance but are not evidence-based for pediatric patients. Combination therapy has been described in several case reports, including biologics with cyclosporine, methotrexate, and UV light therapy. Although some experts use biologic therapy in combination with methotrexate to attempt to reduce antibody development, increase efficacy, and reduce infusion reactions, data to support the combination in children toward a formal recommendation are lacking.

The use of biologics, such as first-line agents, is increasing based on growing evidence of safety and efficacy. Similar to adults, the very high cost relative to methotrexate and the unknown long-term safety of biologic therapies are factors that might reduce their use in the pediatric population. Dosing for pediatric patients is listed in Table XLVI.[133,139,143] Obese patients, particularly adolescents, may require a higher dose of medication than the maximum suggested pediatric dose. Autoinjectors are available for etanercept (50 mg) and adalimumab (40 mg), which may be preferable to prefilled syringes if the dosing is appropriate for weight.

Strength of recommendations and levels of evidence for pediatric psoriasis and biologic therapy are summarized in Tables XLVII and XLVIII.[101,135-138,140,141,144-146] Additional information about monitoring for tuberculosis in patients receiving biologics is provided in Table XLV.[147-149]

ROLE OF THE DERMATOLOGIST

Dermatologists play a key role in managing pediatric patients with psoriasis but should do so in communication and collaboration with the patient's primary care provider and other specialists as the need arises. Discussions with our primary care colleagues could relate to the complexity of the disease, the potentially associated comorbidities, and the therapeutic options and their risks. Dermatologists should be mindful of the unique aspects of the emotional development of children and the social dynamics of having a visible difference. Shared decision making with the patient (if age appropriate) and the caregivers is a useful approach,

particularly as related to the use of off-label medications to treat severe disease.

PATIENT EDUCATION

The importance of patient education for patients with psoriasis and their families cannot be overemphasized. Psoriasis is a complex, multisystem disease that affects the skin and joints, has numerous potential comorbidities, and may affect not only health but the overall QOL. Educating the patient and caregivers regarding the etiology, natural history, triggers, potential comorbidities, treatment options and their risk profiles and precautions, and impact of lifestyle factors (eg, greater disease severity with obesity) on the disease strengthens the therapeutic alliance, facilitates shared decision making, and may positively affect patient satisfaction and compliance. Education should be provided regardless of the level of disease involvement and can be given via verbal discussion, pamphlets, and trusted Internet resources. Many education tools have versions adapted for children (cartoon models, pictures, simple language). Patients and their caregivers should be made aware of psoriasis support groups, including the National Psoriasis Foundation (www.psoriasis.org) and the International Federation for Psoriasis (www.IPFA-pso.org).

GAPS IN RESEARCH

There is much to be learned about psoriasis, particularly in pediatric patients. Significant knowledge gaps include mechanisms of disease onset; etiology; development of comorbidities; systemic treatment options, their ideal dosage and adverse effect profiles, and their effect on future risk of disease-associated comorbidities; the use of combination therapy; and transition between treatment options. It is hoped that, with additional knowledge of the pathophysiology of psoriasis, particularly addressing disease onset and comorbidities, patients and providers will be afforded more patient-specific treatment options and will have the opportunity to modify lifestyle factors that positivity affect morbidity and quality of life.

Work group members disclosures

Authors (listed alphabetically) with relevant conflicts with respect to this guideline are noted with an asterisk*. April W. Armstrong,* MD, MPH, served as an investigator for AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly and Company, Janssen-Ortho Inc, Leo Pharma Inc, National Institutes of Health, Novartis, Regeneron, and UCB, receiving grants and/or research funding; as an investigator for Regeneron and Sanofi, receiving no compensation; as an advisory board member for AbbVie, Amgen, Janssen-Ortho Inc, Merck & Co, Inc, Novartis, Pfizer, Inc, and UCB, receiving honoraria; as a consultant for AbbVie, Bristol-Myers Squibb, Celgene, Dermavant, Eli Lilly and Company, Genentech, Sanofi Genzyme, GlaxoSmithKline, Janssen-Ortho Inc, Janssen Pharmaceuticals, Inc, Leo Pharma, Inc. Menlo Therapeutics, Modernizing Medicine, Novartis Pharmaceuticals Corp, Ortho Dermatologics, Pfizer Inc, Regeneron, Science 37, Inc, and Valeant, receiving honoraria; as a speaker for AbbVie, Eli Lilly and Company, Janssen Pharmaceuticals, Inc, Regeneron Pharmaceuticals, Inc, and Sanofi, receiving honoraria; and as a data safety member for Boehringer Ingelheim and Merck & Co, Inc, receiving honoraria.

Cody Connor, MD, has no relationships to disclose.

Kelly M. Cordoro,* MD, served as a consultant for Valeant, receiving honoraria; as a consultant for Pfizer, Inc, receiving fees; as an advisory board member for Anacor Pharmaceuticals, Inc, receiving honoraria; and in another position as a member of the Scientific Steering Committee for Celgene, receiving fees.

Dawn M. R. Davis, MD, served as an investigator for Regeneron, receiving no compensation.

Boni E. Elewski,* MD, served as a consultant for Boehringer Ingelheim, Celgene Corporation, Leo Pharma, Lilly ICOS LLC, Menlo Therapeutics, Novan (receiving no fees), Novartis Pharmaceuticals Corp, Pfizer, Inc, Sun Pharmaceutical Industries, Ltd, Valeant Pharmaceuticals International, and Verrica Pharmaceuticals, receiving honoraria; as a principal investigator for AbbVie, Amgen, AnaptysBio, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene Corporation, Eli Lilly and Company, Incyte Corporation, InflaRX GmbH, Janssen-Ortho Inc, LEO Pharma, Menlo Therapeutics, Merck & Co, Inc, Novartis Pharmaceuticals Corp, Pfizer, Inc, Regeneron, Sun Pharmaceuticals, Ltd, Valeant Pharmaceuticals International, Vanda Pharmaceuticals, and Vioment, receiving grants/research funding; as an advisory board member for the Foundation for Research & Education of Dermatology, LEO Pharma, and Verrica Pharmaceuticals Inc, receiving honoraria; and in another role for Hoffman-La Roche Ltd, receiving fees.

Craig A. Elmets, MD, served as a consultant for Ferndale Laboratories, Inc, receiving honoraria; as a consultant/advisory board member for Vertex pharmaceuticals, receiving fees and/or honoraria; as a principal investigator for the California Association of Winegrape Growers, receiving grants and/or research funding; as an investigator for

Elorac, Inc, Idera Pharmaceuticals, Inc, Kyowa Hakko USA, and Solgenix LLC, receiving grants/research funding; as a data safety monitoring board member for Astellas Pharma US, Inc, and LEO Laboratories Ltd, receiving fees; as a stockholder for Medgenics, Inc, receiving no fees; and as a stockholder for Aevi Genomic Medicine (receiving stock) and Immunogen (paid to spouse).

Joel M. Gelfand,* MD, MSCE, served as a consultant for AbbVie, BMS, Boehringer Ingelheim, Dermira, Dr. Reddy, GlaxoSmithKline, Janssen Pharmaceuticals, Inc, Menlo Therapeutics, Novartis Pharmaceuticals Corp, Pfizer, Inc, Regeneron, Sanofi US Services, UCB (DSMB), and Valeant Pharmaceuticals North America LLC, receiving honoraria; as a consultant for BMS, receiving fees; as a speaker for the AAD, receiving honoraria; as speaker and/or faculty education for continuing medical education supported by Eli Lilly, receiving fees; as a principal investigator for AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly and Company, Janssen Pharmaceuticals, Inc, Novartis Pharmaceuticals Corp, Ortho Dermatologics, Pfizer, Inc, Regeneron, and Sanofi/Sanofi US Services, receiving grants/research funding; as an investigator for Sanofi, receiving grants and/or research funding; as an advisory board member for Sanofi US Services, receiving honoraria; as a data safety monitoring board member for Coherus Biosciences and Merck & Co, Inc, receiving honoraria. In addition, Dr Gelfand has received payment for continuing medical education work related to psoriasis that was supported indirectly by Lilly, Ortho Dermatologics, and Novartis; served in another role for the Society for Investigative Dermatology, receiving honoraria; served in another role for Elsevier, Inc, and SID, receiving no compensation; served in another role for Eli Lilly and UCB, receiving fees; and served in another role for resiquimod, receiving patent royalties or other compensation for intellectual rights.

Kenneth B. Gordon,* MD, served as a consultant for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Demira, Dermavant Sciences, Kyowa Hakko Kirin Pharma, Inc, Leo Pharma, Ortho Dermatologics, Sun Pharmaceuticals Ltd, and UCB, receiving honoraria; as a consultant for Genzyme, receiving fees; as a principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene Corporation, Eli Lilly and Company, Janssen Pharmaceuticals, Inc, Merck & Co, Inc, and Novartis Pharmaceuticals Corp, receiving grants and/or research funding; and as an advisory board member for Celgene Corporation, Janssen Pharmaceuticals Inc, Lilly ICOS LLC, Novartis Pharmaceuticals Corp, and Pfizer, Inc, receiving honoraria.

Alice B. Gottlieb,* MD, PhD, served as a consultant for Abbott Laboratories, AbbVie, Akros Pharma, Inc, Allergan, Amgen, Amicus Therapeutics, Baxalta Incorporated, Bristol-Myers Squibb, Can-Fite, Celgene Corporation, CSL Behring, Dermira, Dr. Reddy, DUSA Pharmaceuticals, Inc, GlaxoSmithKline, Incyte Corporation, KPI Therapeutics, Lilly ICOS LLC, Meiji Seika Pharma Co, Ltd, Merck & Co, Inc, Mitsubishi Pharma, Novartis Pharmaceuticals Corp, Sanofi-Aventis, Sienna Biopharmaceuticals, Sun Pharmaceutical Industries, Takeda Pharmaceuticals USA, Inc, Teva, UCB, Valeant Pharmaceuticals International, Valeant Pharmaceuticals North America LLC, XBiotech, and Xenoport, Inc, receiving honoraria; as a consultant for Aclaris Therapeutics, Inc, Avotres Inc, Merck & Co Inc, and XBiotech, receiving no compensation; as a speaker for AbbVie, Eli Lilly, and Janssen Biotech, receiving honoraria; as a principal investigator for Abbott Laboratories, AbbVie, Allergan, Amgen, Celgene Corporation, Coronado Biosciences, Immune Control, Incyte Corporation, Janssen-Ortho, Inc, LEO Pharma, Lerner Medical Devices, Inc, Lilly ICOS LLC, Merck & Co, Inc, Novartis Pharmaceuticals Corp, Novo Nordisk A/S, Pfizer Inc, UCB, Xbiotech, and Xenoport, Inc, receiving grants/research funding; as a principal investigator for Janssen-Ortho, Inc, receiving honoraria; as an advisory board member for Abbott Laboratories, Actelion, Allergan, Amgen, Astellas Pharma US, Inc, Beiersdorf, Inc, BMS, Celgene Corporation, Coronado Biosciences, Dermira, Dr. Reddy, Genentech, Janssen-Ortho, Inc, Janssen Biotech, Leo Pharma US, Lilly ICOS LLC, Novartis Pharmaceuticals Corp, Novo Nordisk A/S, Pfizer, Inc, UCB, and Valeant, receiving honoraria; in another role for Amgen, receiving grants and/or research funding; in another role for Crescendo Bioscience and Karyopharm Therapeutics, receiving no compensation; in another role (data safety) for Catabasis Pharmaceuticals, Inc, receiving honoraria; and in another role for DermiPsor, receiving honoraria.

Daniel H. Kaplan, MD, PhD, served as a consultant for Eli Lilly and Company, receiving no compensation and as a member of the data safety monitoring board for Hapten Sciences, receiving fees.

Arthur Kavanaugh,* MD, served as a principal investigator for AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly and Company, Janssen Biotech, Novartis, Pfizer, Inc, and UCB, receiving grants/research funding.

Matthew Kiselica has no relationships to disclose.

Dario Kivelevitch, MD, has a first-degree relative employed by Boehringer Ingelheim.

Neil J. Korman,* MD, PhD, served as a consultant for Novartis Pharmaceuticals Corp, receiving honoraria; as a consultant for Dr. Reddy's Laboratory, receiving fees;

as a speaker for AbbVie, Celgene, Eli Lilly, Genentech, Janssen, Novartis, Regeneron, and Sanofi, receiving honoraria; as a principal investigator for AbbVie, Amgen, Celgene Corporation, Chugai, Dermira, Eli Lilly and Company, Kyowa Hakko Kirin Pharma, Inc, LEO Pharma, Menlo Therapeutics, Merck, Pfizer, Prothena, Regeneron, Rhizen, Inc, Syntimmune, Trevi, and UCB, receiving grants and/or research funding; as an advisory board member for Amgen, Celgene Corporation, Eli Lilly and Company, Genentech, GlaxoSmithKline, Janssen Pharmaceuticals, Inc, Novartis Pharmaceuticals Corp, Pfizer, Inc, and Principia Biopharma, receiving honoraria; as an advisory board member for Dr. Reddy's Laboratory, Immune Pharmaceuticals, Regeneron, Sanofi, Sun Pharma, and Valeant, receiving fees; as an advisory board member/consultant for AbbVie, Eli Lilly, GlaxoSmithKline, Pfizer Inc, and Principa, receiving honoraria/fees; and in another role for Janssen Pharmaceuticals, Inc, receiving grants and/or research funding.

Daniela Kroshinsky, MD, MPH, has no relationships to disclose.

Mark Lebwohl,* MD, served as a consultant for Allergan, Almirall, Arcutis, Inc, Boehringer Ingelheim, Bristol-Myers Squibb, Castle Biosciences Inc, Leo Pharma, Menlo Therapeutics, Mitsubishi Pharma, Neuroderm LTD, Pfizer, Promius/Dr. Reddy, Theravance Biopharma, and Verrica Pharmaceuticals Inc, receiving honoraria; as a principal investigator or investigator for AbbVie, Amgen, Inc. AstraZeneca, Boehringer Ingelheim, Celgene Corporation, Eli Lilly and Company, Incyte Corporation, Janssen Research and Development LLC/Johnson & Johnson, Leo Pharma, Medimmune, Novartis Pharmaceuticals Corp, Ortho Dermatologics, Pfizer, Inc, SCIDerm, UCB, and ViDac Pharma, receiving grants and/or research funding; and in another role for Corrona, Inc, Facilitation of International Dermatology Education, and Foundation for Research and Education in Dermatology, receiving honoraria.

Craig L. Leonardi,* MD, served as a consultant/advisory board member for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly and Company, Janssen Pharmaceuticals, Inc, Leo Pharma A/S, Ortho Dermatologics, Pfizer, Inc, Sandoz (a Novartis Company), UCB, and Vitae, receiving honoraria; as a speaker for AbbVie, Amgen, Celgene Corporation, Eli Lilly and Company, Novartis, Sun Pharmaceuticals, Ltd, and UCB, receiving honoraria; and as a principal investigator for Actavis, Amgen, Boehringer Ingelheim, Celgene Corporation, Cellceutix, Coherus Biosciences, Corrona, Dermira, Eli Lilly and Company, Galderma Laboratories, LP, Glenmark Generics, Inc, Janssen Pharmaceuticals, Inc, Leo Pharma, Inc, Merck, Novartis, Novella, Pfizer, Inc, Sandoz (a Novartis Company), Sienna Biopharmaceuticals, Stiefel (a GSK company), UCB, and Warner Chillcott, receiving other financial benefits (fee for service).

Jason Lichten, MD, has no relationships to disclose.

Henry W. Lim, MD, served as a principal or coinvestigator for Estee Lauder, Ferndale Laboratories, Inc, Incyte, and Unigen, receiving grants and/or research funding; and as a speaker and/or faculty education for Pierre Fabre Dermatologie, receiving honoraria.

Nehal N. Mehta,* MD, MSCE, is a full-time US government employee and has served as a consultant for Amgen, Eli Lilly, and Leo Pharma, receiving grants and/or other payments; as a principal investigator and/or investigator for AbbVie, Celgene, Janssen Pharmaceuticals, Inc, and Novartis, receiving grants and/or research funding; and as a principal investigator for the National Institutes of Health, receiving grants and/or research funding.

Alan Menter,* MD, served as a consultant for Abbott Labs, AbbVie, Amgen, Eli Lilly and Company, Galderma USA, Janssen Pharmaceuticals Inc, LEO Pharma US, Menlo Therapeutics, Novartis, Sienna Biopharmaceuticals, and Wyeth Labs, receiving honoraria; as a consultant for New Enterprise Associates, Promius Pharma LLC, Spherix Global Insights US, UCB, and Valeant Pharmaceuticals North America, receiving fees; as a consultant for Afecta Pharmaceuticals, receiving no compensation; as a speaker for Abbott Labs, AbbVie, Amgen, Janssen Biotech, LEO Pharma, US, Pfizer, Inc, Promius Pharma LLC, Sienna Pharmaceuticals, UCB, and Wyeth Labs, receiving honoraria; as a principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene Corporation, Eli Lilly and Company, Janssen Pharmaceuticals, Inc, Medimetriks Pharmaceuticals, Inc, Merck & Co, Inc, Novartis Pharmaceutical Corp, and Pfizer, Inc, receiving grant and/or research funding; as an investigator for Eli Lilly and Company and UCB, receiving honoraria; as an investigator for Abbott Labs, Leo Pharma US, and Sienna Biopharmaceuticals, receiving grants; as an advisory board member for Abbott Labs, AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen Pharmaceuticals, Inc, LEO Pharma US, Medscape, Pfizer, Inc, and Sienna Biopharmaceuticals, receiving honoraria; as an advisory board member for Amgen, receiving grant and/or research funding; as an advisory board member for Afecta Pharmaceuticals, receiving no compensation; and as an independent contractor for Prime Education, receiving fees.

Amy S. Paller,* MD, served as a consultant for Amgen, Amicus Therapeutics, Anacor Pharmaceuticals, Inc, Aqua Pharmaceuticals, Boehringer Ingelheim International GmbH, BridgeBio Pharma, Castle Creek Pharma, Celgene Corporation, Dermavant Sciences, Dermira, Eli Lilly and Company, Galderma Laboratories, LP, Leo Pharma Inc, Genentech, Menlo Therapeutics, MorphoSys AG, Novartis Pharmaceuticals Corp, Pfizer Inc, Pierre Fabre Dermatologie, Proctor and Gamble, Regeneron, Sanofi, Scioderm, Shire, Sol-Gel Technologies, Stiefel (a GSK company), Theravance Biopharma, UCB, Union Therapeutics, Valeant Pharmaceuticals North America LLC, Vitae Pharmaceuticals, and Verrica, receiving honoraria; as a speaker/educator for Expanscience, receiving honoraria; and as a principal investigator for AbbVie, Amgen, Anacor Pharmaceuticals, Inc, AnaptysBio, Celgene Corporation, Eli Lilly, Galderma, Janssen Pharmaceuticals, Inc, Leo Pharma, Regeneron, and Scioderm, receiving no compensation.

Sylvia L. Parra, MD, has no relationships to disclose.

Arun L. Pathy, MD, has no relationships to disclose.

Elizabeth A. Farley Prater, MD, has no relationships to disclose.

Reena N. Rupani, MD, served as speaker for Nutrafol, receiving no honoraria.

Michael Siegel, PhD, has no relationships to disclose.

Benjamin Stoff, MD, MA, served as an investigator for Celtaxsys, Inc, receiving fees.

Bruce E. Strober,* MD, PhD, served as a consultant for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene Corporation, Dermira, Eli Lilly and Company, GlaxoSmithKline, Janssen-Ortho, Inc, Leo Pharma, Inc, Maruho Co, Ltd, Medac Pharma, Inc, Menlo Therapeutics, Novartis Pharmaceuticals Corp, Ortho Dermatologics, Pfizer, Inc, Sanofi-Regeneron, Sun Pharmaceuticals Industries, and UCB, receiving honoraria; as a consultant for Affibody, Arena, Bristol-Myers Squibb, Dermavant, Meiji Seika Pharma Co, Ltd, Sebela Pharmaceuticals, Sirtris, and UCB, receiving fees; as a principal investigator for AbbVie, Boehringer Ingelheim, Celgene Corporation, Eli Lilly and Company, Galderma, Janssen-Ortho, Inc, Merck & Co, Pfizer, Inc, Sienna, and Sun Pharmaceutical Industries, receiving no compensation; as an advisory board member for AbbVie, Amgen, Bristol-Myers Squibb, Celgene Corporation, Dermira, Eli Lilly and Company, Janssen-Ortho, Inc, Novartis Pharmaceuticals Corp, Pfizer, Inc, Sanofi-Regeneron, Sun Pharmaceuticals Industries, and UCB, receiving honoraria; as consultant/advisory board for AstraZeneca Pharmaceuticals LP, receiving fees/honoraria; and in another role for AbbVie and Janssen-Ortho, Inc, receiving no compensation.

Emily B. Wong, MD, has no relationships to disclose.

Jashin J. Wu,* MD, served as a consultant for AbbVie, Allergan, Almirall, Amgen, Bristol-Myers Squibb, Celgene, Dermira, Dr. Reddy's Laboratories, Eli Lilly and Company, Janssen Biotech, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Inc, Promius Pharma, Regeneron, Sun Pharmaceutical Industries, Ltd, UCB, and Valeant Pharmaceuticals North America, LLC, receiving fees and/or honoraria; as a speaker for AbbVie, Celgene, Novartis, Regeneron, Sanofi Genzyme, Sun Pharmaceutical Industries Ltd, UCB, and Valeant Pharmaceuticals North America LLC, receiving honoraria; and as a principal/investigator for AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Coherus Biosciences, Dermira, Eli Lilly and Company, Janssen Pharmaceuticals, Inc, Merck & Co, Inc, Novartis, Pfizer, Inc, Regeneron, Sandoz (a Novartis company), and Sun Pharmaceutical Industries Ltd, receiving research and/or grant funding.

Vidhya Hariharan, PhD, has no relationships to disclose.

We thank our medical librarian, Charniel McDaniels, MS, and our specialist, David A. Castillo, BS, for helping with search strings, evidence table generation and the manuscript publication process. During the development of this guideline, Michael Siegel served as a patient representative for the National Psoriasis Foundation.

REFERENCES

1. Kaushik SB, Lebwohl MG. Psoriasis: which therapy for which patient: psoriasis comorbidities and preferred systemic agents. *J Am Acad Dermatol*. 2019;80(1):27-40.
2. Kaushik SB, Lebwohl MG. Psoriasis: which therapy for which patient: focus on special populations and chronic infections. *J Am Acad Dermatol*. 2019;80(1):43-53.
3. American Academy of Dermatology. 410—Psoriasis: clinical response to oral systemic or biologic medications. Available at: https://www.aad.org/practicecenter/quality/quality-measures/mips-measures/410. Accessed January 24, 2019.
4. Pearl RL, Wan MT, Takeshita J, Gelfand JM. Stigmatizing attitudes toward persons with psoriasis among laypersons and medical students. *J Am Acad Dermatol*. 2018;80(6):1556-1563.
5. Salek MS, Jung S, Brincat-Ruffini LA, et al. Clinical experience and psychometric properties of the Children's Dermatology Life Quality Index (CDLQI), 1995-2012. *Br J Dermatol*. 2013;169(4):734-759.
6. Holme SA, Man I, Sharpe JL, Dykes PJ, Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index: validation of the cartoon version. *Br J Dermatol*. 2003;148(2):285-290.
7. Tripodi S, Panetta V, Pelosi S, Pelosi U, Boner AL. Measurement of body surface area in atopic dermatitis using specific PC software (ScoradCard). *Pediatr Allergy Immunol*. 2004;15(1):89-92.

8. de Jager ME, van de Kerkhof PC, de Jong EM, Seyger MM. A cross-sectional study using the Children's Dermatology Life Quality Index (CDLQI) in childhood psoriasis: negative effect on quality of life and moderate correlation of CDLQI with severity scores. *Br J Dermatol*. 2010;163(5):1099-1101.
9. Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. *Br J Dermatol*. 1995;132(6):942-949.
10. Ozden MG, Tekin NS, Gurer MA, et al. Environmental risk factors in pediatric psoriasis: a multicenter case-control study. *Pediatr Dermatol*. 2011;28(3):306-312.
11. Paller AS, Mercy K, Kwasny MJ, et al. Association of pediatric psoriasis severity with excess and central adiposity: an international cross-sectional study. *JAMA Dermatol*. 2013;149(2):166-176.
12. Becker L, Tom WL, Eshagh K, Benjamin LT, Paller AS. Excess adiposity preceding pediatric psoriasis. *JAMA Dermatol*. 2014;150(5):573-574.
13. Raychaudhuri SP, Gross J. A comparative study of pediatric onset psoriasis with adult onset psoriasis. *Pediatr Dermatol*. 2000;17(3):174-178.
14. Naldi L, Peli L, Parazzini F, Carrel CF, Psoriasis Study Group of the Italian Group for Epidemiological Research in Dermatology. Family history of psoriasis, stressful life events, and recent infectious disease are risk factors for a first episode of acute guttate psoriasis: results of a case-control study. *J Am Acad Dermatol*. 2001;44(3):433-438.
15. Telfer NR, Chalmers RJ, Whale K, Colman G. The role of streptococcal infection in the initiation of guttate psoriasis. *Arch Dermatol*. 1992;128(1):39-42.
16. Yoon S, Oh ST, Lee JY, Cho BK. Plaque type psoriasiform eruption following Kawasaki disease. *Pediatr Dermatol*. 2007;24(3):336-337.
17. Liao YC, Lee JY. Psoriasis in a 3-month-old infant with Kawasaki disease. *Dermatol Online J*. 2009;15(11):10.
18. Haddock ES, Calame A, Shimizu C, Tremoulet AH, Burns JC, Tom WL. Psoriasiform eruptions during Kawasaki disease (KD): a distinct phenotype. *J Am Acad Dermatol*. 2016;75(1):69-76.
19. Cullen G, Kroshinsky D, Cheifetz AS, Korzenik JR. Psoriasis associated with anti-tumour necrosis factor therapy in inflammatory bowel disease: a new series and a review of 120 cases from the literature. *Aliment Pharmacol Ther*. 2011;34(11-12):1318-1327.
20. Perman MJ, Lovell DJ, Denson LA, Farrell MK, Lucky AW. Five cases of anti-tumor necrosis factor alpha-induced psoriasis presenting with severe scalp involvement in children. *Pediatr Dermatol*. 2012;29(4):454-459.
21. Eickstaedt JB, Killpack L, Tung J, Davis D, Hand JL, Tollefson MM. Psoriasis and psoriasiform eruptions in pediatric patients with inflammatory bowel disease treated with anti-tumor necrosis factor alpha agents. *Pediatr Dermatol*. 2017;34(3):253-260.
22. Tsankov N, Angelova I, Kazandjieva J. Drug-induced psoriasis. Recognition and management. *Am J Clin Dermatol*. 2000;1(3):159-165.
23. Elmets CA, Leonardi CL, Davis DMR, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities. *J Am Acad Dermatol*. 2019;80(4):1073-1113.
24. Egeberg A, Khalid U, Gislason GH, Mallbris L, Skov L, Hansen PR. Risk of psoriasis in patients with childhood asthma: a Danish nationwide cohort study. *Br J Dermatol*. 2015;173(1):159-164.
25. Augustin M, Radtke MA, Glaeske G, et al. Epidemiology and comorbidity in children with psoriasis and atopic eczema. *Dermatology*. 2015;231(1):35-40.
26. Ogdie A, Weiss P. The epidemiology of psoriatic arthritis. *Rheum Dis Clin North Am*. 2015;41(4):545-568.
27. Osier E, Wang AS, Tollefson MM, et al. Pediatric psoriasis comorbidity screening guidelines. *JAMA Dermatol*. 2017;153(7):698-704.
28. Stoll ML, Punaro M. Psoriatic juvenile idiopathic arthritis: a tale of two subgroups. *Curr Opin Rheumatol*. 2011;23(5):437-443.
29. Lewkowicz D, Gottlieb AB. Pediatric psoriasis and psoriatic arthritis. *Dermatol Ther*. 2004;17(5):364-375.
30. Augustin M, Glaeske G, Radtke MA, Christophers E, Reich K, Schafer I. Epidemiology and comorbidity of psoriasis in children. *Br J Dermatol*. 2010;162(3):633-636.
31. Mahe E, Maccari F, Beauchet A, et al. Childhood-onset psoriasis: association with future cardiovascular and metabolic comorbidities. *Br J Dermatol*. 2013;169(4):889-895.
32. Eichenfield LF, Paller AS, Tom WL, et al. Pediatric psoriasis: evolving perspectives. *Pediatr Dermatol*. 2018;35(2):170-181.
33. Goldminz AM, Buzney CD, Kim N, et al. Prevalence of the metabolic syndrome in children with psoriatic disease. *Pediatr Dermatol*. 2013;30(6):700-705.
34. Zhu KJ, He SM, Zhang C, Yang S, Zhang XJ. Relationship of the body mass index and childhood psoriasis in a Chinese Han population: a hospital-based study. *J Dermatol*. 2012;39(2):181-183.
35. Boccardi D, Menni S, La Vecchia C, et al. Overweight and childhood psoriasis. *Br J Dermatol*. 2009;161(2):484-486.
36. Hagan JF, Shaw JS, Duncan PM, et al. Bright Futures/American Academy of Pediatrics. Bright Futures: Guidelines for Health Supervision of Infants, Children, and Adolescents. Recommendations for Preventive Pediatric Health Care. 4th ed. Elk Grove Village, IL: American Academy of Pediatritcs; 2017.
37. Bryld LE, Sorensen TI, Andersen KK, Jemec GB, Baker JL. High body mass index in adolescent girls precedes psoriasis hospitalization. *Acta Derm Venereol*. 2010;90(5):488-493.
38. Kelati A, Baybay H, Najdi A, Zinoune S, Mernissi FZ. Pediatric psoriasis: should we be concerned with comorbidity? Cross-sectional study. *Pediatr Int*. 2017;59(8):923-928.
39. Koebnick C, Black MH, Smith N, et al. The association of psoriasis and elevated blood lipids in overweight and obese children. *J Pediatr*. 2011;159(4):577-583.
40. Kwa L, Kwa MC, Silverberg JI. Cardiovascular comorbidities of pediatric psoriasis among hospitalized children in the United States. *J Am Acad Dermatol*. 2017;77(6):1023-1029.
41. Boehncke WH, Boehncke S, Tobin AM, Kirby B. The 'psoriatic march': a concept of how severe psoriasis may drive cardiovascular comorbidity. *Exp Dermatol*. 2011;20(4):303-307.
42. Gottlieb AB, Chao C, Dann F. Psoriasis comorbidities. *J Dermatolog Treat*. 2008;19(1):5-21.
43. Tom WL, Playford MP, Admani S, et al. Characterization of lipoprotein composition and function in pediatric psoriasis reveals a more atherogenic profile. *J Invest Dermatol*. 2016;136(1):67-73.
44. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017;140(3):1-73.
45. Di Costanzo L, Fattorusso V, Mozzillo E, et al. Psoriasis in children with type 1 diabetes: a new comorbidity to be considered? *Acta Diabetol*. 2017;54(8):803-804.

46. de Jager ME, De Jong EM, Evers AW, Van De Kerkhof PC, Seyger MM. The burden of childhood psoriasis. *Pediatr Dermatol*. 2011;28(6):736-737.
47. Gelfand JM, Weinstein R, Porter SB, Neimann AL, Berlin JA, Margolis DJ. Prevalence and treatment of psoriasis in the United Kingdom: a population-based study. *Arch Dermatol*. 2005;141(12):1537-1541.
48. Todberg T, Egeberg A, Jensen P, Gislason G, Skov L. Psychiatric comorbidities in children and adolescents with psoriasis: a population-based cohort study. *Br J Dermatol*. 2017;177(2):551-553.
49. Bilgic A, Bilgic O, Akis HK, Eskioglu F, Kilic EZ. Psychiatric symptoms and health-related quality of life in children and adolescents with psoriasis. *Pediatr Dermatol*. 2010;27(6):614-617.
50. Kimball AB, Wu EQ, Guerin A, et al. Risks of developing psychiatric disorders in pediatric patients with psoriasis. *J Am Acad Dermatol*. 2012;67(4):651-657.
51. Centers for Disease Control and Prevention. What is IBD? Available at: https://www.cdc.gov/ibd/what-is-IBD.htm. Accessed August 1, 2019.
52. de Jager ME, de Jong EM, van de Kerkhof PC, Seyger MM. Efficacy and safety of treatments for childhood psoriasis: a systematic literature review. *J Am Acad Dermatol*. 2010;62(6):1013-1030.
53. Frangos JE, Kimball AB. Clobetasol propionate emollient formulation foam in the treatment of corticosteroid-responsive dermatoses. *Expert Opin Pharmacother*. 2008;9(11):2001-2007.
54. Herz G, Blum G, Yawalkar S. Halobetasol propionate cream by day and halobetasol propionate ointment at night for the treatment of pediatric patients with chronic, localized plaque psoriasis and atopic dermatitis. *J Am Acad Dermatol*. 1991;25(6 Pt 2):1166-1169.
55. Brune A, Miller DW, Lin P, Cotrim-Russi D, Paller AS. Tacrolimus ointment is effective for psoriasis on the face and intertriginous areas in pediatric patients. *Pediatr Dermatol*. 2007;24(1):76-80.
56. Clayton TH, Harrison PV, Nicholls R, Delap M. Topical tacrolimus for facial psoriasis. *Br J Dermatol*. 2003;149(2):419-420.
57. Steele JA, Choi C, Kwong PC. Topical tacrolimus in the treatment of inverse psoriasis in children. *J Am Acad Dermatol*. 2005;53(4):713-716.
58. Amichai B. Psoriasis of the glans penis in a child successfully treated with Elidel (pimecrolimus) cream. *J Eur Acad Dermatol Venereol*. 2004;18(6):742-743.
59. Mansouri P, Farshi S. Pimecrolimus 1 percent cream in the treatment of psoriasis in a child. *Dermatol Online J*. 2006;12(2):7.
60. Siegfried EC, Jaworski JC, Kaiser JD, Hebert AA. Systematic review of published trials: long-term safety of topical corticosteroids and topical calcineurin inhibitors in pediatric patients with atopic dermatitis. *BMC Pediatr*. 2016;16:75.
61. Prograf (tacrolimus) [package insert]. Toyama, Japan: Astellas Pharma Tech Co. Ltd. 2019.
62. US Food and Drug Administration. *ELIDEL® (pimecrolimus) cream, 1% for topical use initial*. U.S. Approval: 2001. 2014.
63. Lovato P, Norsgaard H, Tokura Y, Ropke MA. Calcipotriol and betamethasone dipropionate exert additive inhibitory effects on the cytokine expression of inflammatory dendritic cell-Th17 cell axis in psoriasis. *J Dermatol Sci*. 2016;81(3):153-164.
64. Darley CR, Cunliffe WJ, Green CM, Hutchinson PE, Klaber MR, Downes N. Safety and efficacy of calcipotriol ointment (Dovonex) in treating children with psoriasis vulgaris. *Br J Dermatol*. 1996;135(3):390-393.
65. Oranje AP, Marcoux D, Svensson A, et al. Topical calcipotriol in childhood psoriasis. *J Am Acad Dermatol*. 1997;36(2 Pt 1):203-208.
66. Patrizi A, Neri I, Rizzoli L, Varotti C. Topical calcipotriol in childhood psoriasis. *Acta Derm Venereol*. 1999;79(6):477.
67. Park SB, Suh DH, Youn JI. A pilot study to assess the safety and efficacy of topical calcipotriol treatment in childhood psoriasis. *Pediatr Dermatol*. 1999;16(4):321-325.
68. Eichenfield LF, Ganslandt C, Kurvits M, Schlessinger J. Safety and efficacy of calcipotriene plus betamethasone dipropionate topical suspension in the treatment of extensive scalp psoriasis in adolescents ages 12 to 17 years. *Pediatr Dermatol*. 2015;32(1):28-35.
69. van Geel MJ, Mul K, Oostveen AM, van de Kerkhof PC, de Jong EM, Seyger MM. Calcipotriol/betamethasone dipropionate ointment in mild-to-moderate paediatric psoriasis: long-term daily clinical practice data in a prospective cohort. *Br J Dermatol*. 2014;171(2):363-369.
70. Fabrizi G, Vultaggio P. Calcipotriol and psoriasis in children. *J Dermatolog Treat*. 2009;8(4):221-223.
71. Choi YJ, Hann SK, Chang SN, Park WH. Infantile psoriasis: successful treatment with topical calcipotriol. *Pediatr Dermatol*. 2000;17(3):242-244.
72. Ashcroft DM, Po AL, Williams HC, Griffiths CE. Systematic review of comparative efficacy and tolerability of calcipotriol in treating chronic plaque psoriasis. *BMJ*. 2000;320(7240):963-967.
73. Lebwohl M, Siskin SB, Epinette W, et al. A multicenter trial of calcipotriene ointment and halobetasol ointment compared with either agent alone for the treatment of psoriasis. *J Am Acad Dermatol*. 1996;35(2 Pt 1):268-269.
74. Lebwohl M, Yoles A, Lombardi K, Lou W. Calcipotriene ointment and halobetasol ointment in the long-term treatment of psoriasis: effects on the duration of improvement. *J Am Acad Dermatol*. 1998;39(3):447-450.
75. Diluvio L, Campione E, Paterno EJ, Mordenti C, El Hachem M, Chimenti S. Childhood nail psoriasis: a useful treatment with tazarotene 0.05%. *Pediatr Dermatol*. 2007;24(3):332-333.
76. de Jager ME, van de Kerkhof PC, de Jong EM, Seyger MM. Dithranol therapy in childhood psoriasis: unjustifiably on the verge of falling into oblivion. *Dermatology*. 2010;220(4):329-332.
77. Zvulunov A, Anisfeld A, Metzker A. Efficacy of short-contact therapy with dithranol in childhood psoriasis. *Int J Dermatol*. 1994;33(11):808-810.
78. Oostveen AM, Beulens CA, van de Kerkhof PC, de Jong EM, Seyger MM. The effectiveness and safety of short-contact dithranol therapy in paediatric psoriasis: a prospective comparison of regular day care and day care with telemedicine. *Br J Dermatol*. 2014;170(2):454-457.
79. Guerrier CJ, Porter DI. An open assessment of 0.1% dithranol in a 17% urea base ('Psoradrate' 0.1%) in the treatment of psoriasis of children. *Curr Med Res Opin*. 1983;8(6):446-450.
80. Menter MA, Whiting DA, McWilliams J. Resistant childhood psoriasis: an analysis of patients seen in a day-care center. *Pediatr Dermatol*. 1984;2(1):8-12.
81. Kortuem KR, Davis MD, Witman PM, McEvoy MT, Farmer SA. Results of Goeckerman treatment for psoriasis in children: a 21-year retrospective review. *Pediatr Dermatol*. 2010;27(5):518-524.
82. Borska L, Andrys C, Krejsek J, et al. Genotoxic hazard and cellular stress in pediatric patients treated for psoriasis with the Goeckerman regimen. *Pediatr Dermatol*. 2009;26(1):23-27.

83. Borska L, Smejkalova J, Cerna M, et al. Urinary mutagenicity and genotoxic risk in children with psoriasis after therapeutic exposure to polycyclic aromatic hydrocarbons and ultraviolet radiation. *Mutat Res*. 2010;696(2):144-147.
84. Borska L, Fiala Z, Krejsek J, et al. Immunologic changes in TNF-alpha, sE-selectin, sP-selectin, sICAM-1, and IL-8 in pediatric patients treated for psoriasis with the Goeckerman regimen. *Pediatr Dermatol*. 2007;24(6):607-612.
85. Borska L, Andrys C, Krejsek J, et al. Oxidative damage to nucleic acids and benzo(a)pyrene-7,8-diol-9,10-epoxide-DNA adducts and chromosomal aberration in children with psoriasis repeatedly exposed to crude coal tar ointment and UV radiation. *Oxid Med Cell Longev*. 2014;2014:302528.
86. Goeckerman W. Treatment of psoriasis. *Northwest Med*. 1925; 24:229-231.
87. Walters IB, Burack LH, Coven TR, Gilleaudeau P, Krueger JG. Suberythemogenic narrow-band UVB is markedly more effective than conventional UVB in treatment of psoriasis vulgaris. *J Am Acad Dermatol*. 1999;40(6 Pt 1):893-900.
88. Ersoy-Evans S, Altaykan A, Sahin S, Kolemen F. Phototherapy in childhood. *Pediatr Dermatol*. 2008;25(6):599-605.
89. Pavlovsky M, Baum S, Shpiro D, Pavlovsky L, Pavlotsky F. Narrow band UVB: is it effective and safe for paediatric psoriasis and atopic dermatitis? *J Eur Acad Dermatol Venereol*. 2011;25(6):727-729.
90. Jain VK, Aggarwal K, Jain K, Bansal A. Narrow-band UV-B phototherapy in childhood psoriasis. *Int J Dermatol*. 2007; 46(3):320-322.
91. Jain VK, Bansal A, Aggarwal K, Jain K. Enhanced response of childhood psoriasis to narrow-band UV-B phototherapy with preirradiation use of mineral oil. *Pediatr Dermatol*. 2008;25(5): 559-564.
92. Eustace K, Dolman S, Alsharqi A, Sharpe G, Parslew R. Use of phototherapy in children. *Pediatr Dermatol*. 2017;34(2):150-155.
93. Garber C, Creighton-Smith M, Sorensen EP, Dumont N, Gottlieb AB. Systemic treatment of recalcitrant pediatric psoriasis: a case series and literature review. *J Drugs Dermatol*. 2015;14(8):881-886.
94. Jury CS, McHenry P, Burden AD, Lever R, Bilsland D. Narrowband ultraviolet B (UVB) phototherapy in children. *Clin Exp Dermatol*. 2006;31(2):196-199.
95. Kumar B, Soni A, Saraswat A, Kaur I, Dogra S. Hair in psoriasis: a prospective, blinded scanning electron microscopic study. *Clin Exp Dermatol*. 2008;33(4):491-494.
96. Pahlajani N, Katz BJ, Lozano AM, Murphy F, Gottlieb A. Comparison of the efficacy and safety of the 308 nm excimer laser for the treatment of localized psoriasis in adults and in children: a pilot study. *Pediatr Dermatol*. 2005;22(2):161-165.
97. Pasic A, Ceovic R, Lipozencic J, et al. Phototherapy in pediatric patients. *Pediatr Dermatol*. 2003;20(1):71-77.
98. Tay YK, Morelli JG, Weston WL. Experience with UVB phototherapy in children. *Pediatr Dermatol*. 1996;13(5):406-409.
99. Wong Y, Koh MJ, Chong WS. Role of narrowband ultraviolet B phototherapy in the treatment of childhood psoriasis in Asian children. *Pediatr Dermatol*. 2015;32(5):e221-e223.
100. Zamberk P, Velazquez D, Campos M, Hernanz JM, Lazaro P. Paediatric psoriasis—narrowband UVB treatment. *J Eur Acad Dermatol Venereol*. 2010;24(4):415-419.
101. Bronckers I, Seyger MMB, West DP, et al. Safety of systemic agents for the treatment of pediatric psoriasis. *JAMA Dermatol*. 2017;153(11):1147-1157.
102. Kaur I, Dogra S, De D, Kanwar AJ. Systemic methotrexate treatment in childhood psoriasis: further experience in 24 children from India. *Pediatr Dermatol*. 2008;25(2):184-188.
103. Collin B, Vani A, Ogboli M, Moss C. Methotrexate treatment in 13 children with severe plaque psoriasis. *Clin Exp Dermatol*. 2009;34(3):295-298.
104. van Geel MJ, Oostveen AM, Hoppenreijs EP, et al. Methotrexate in pediatric plaque-type psoriasis: long-term daily clinical practice results from the Child-CAPTURE registry. *J Dermatolog Treat*. 2015;26(5):406-412.
105. Ergun T, Seckin Gencosmanoglu D, Alpsoy E, et al. Efficacy, safety and drug survival of conventional agents in pediatric psoriasis: a multicenter, cohort study. *J Dermatol*. 2017;44(6): 630-634.
106. van Geel MJ, Mul K, de Jager ME, van de Kerkhof PC, de Jong EM, Seyger MM. Systemic treatments in paediatric psoriasis: a systematic evidence-based update. *J Eur Acad Dermatol Venereol*. 2015;29(3):425-437.
107. Kumar B, Dhar S, Handa S, Kaur I. Methotrexate in childhood psoriasis. *Pediatr Dermatol*. 1994;11(3):271-273.
108. Bulbul Baskan E, Yazici S, Tunali S, Saricaoglu H. Clinical experience with systemic cyclosporine A treatment in severe childhood psoriasis. *J Dermatolog Treat*. 2016; 27(4):328-331.
109. Dogra S, Mahajan R, Narang T, Handa S. Systemic cyclosporine treatment in severe childhood psoriasis: a retrospective chart review. *J Dermatolog Treat*. 2017;28(1):18-20.
110. Kilic SS, Hacimustafaoglu M, Celebi S, Karadeniz A, Ildirim I. Low dose cyclosporin A treatment in generalized pustular psoriasis. *Pediatr Dermatol*. 2001;18(3):246-248.
111. Cyclosporine [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation. 2015.
112. Mahe E, Bodemer C, Pruszkowski A, Teillac-Hamel D, de Prost Y. Cyclosporine in childhood psoriasis. *Arch Dermatol*. 2001;137(11):1532-1533.
113. Berth-Jones J, Voorhees JJ. Consensus conference on cyclosporin A microemulsion for psoriasis, June 1996. *Br J Dermatol*. 1996;135(5):775-777.
114. Perrett CM, Ilchyshyn A, Berth-Jones J. Cyclosporin in childhood psoriasis. *J Dermatolog Treat*. 2003;14(2):113-118.
115. Pereira TM, Vieira AP, Fernandes JC, Sousa-Basto A. Cyclosporin A treatment in severe childhood psoriasis. *J Eur Acad Dermatol Venereol*. 2006;20(6):651-656.
116. Heydendael VM, Spuls PI, Ten Berge IJ, Opmeer BC, Bos JD, de Rie MA. Cyclosporin trough levels: is monitoring necessary during short-term treatment in psoriasis? A systematic review and clinical data on trough levels. *Br J Dermatol*. 2002;147(1):122-129.
117. Di Lernia V, Stingeni L, Boccaletti V, et al. Effectiveness and safety of cyclosporine in pediatric plaque psoriasis: a multicentric retrospective analysis. *J Dermatolog Treat*. 2016;27(5): 395-398.
118. Mockli G, Kabra PM, Kurtz TW. Laboratory monitoring of cyclosporine levels: guidelines for the dermatologist. *J Am Acad Dermatol*. 1990;23(6 Pt 2):1275-1279.
119. Chao PH, Cheng YW, Chung MY. Generalized pustular psoriasis in a 6-week-old infant. *Pediatr Dermatol*. 2009;26(3): 352-354.
120. Popadic S, Nikolic M. Pustular psoriasis in childhood and adolescence: a 20-year single-center experience. *Pediatr Dermatol*. 2014;31(5):575-579.
121. Chen P, Li C, Xue R, et al. Efficacy and safety of acitretin monotherapy in children with pustular psoriasis: results from 15 cases and a literature review. *J Dermatolog Treat*. 2018; 29(4):353-363.
122. Rosinska D, Wolska H, Jablonska S, Konca I. Etretinate in severe psoriasis of children. *Pediatr Dermatol*. 1988;5(4): 266-272.

123. Shelnitz LS, Esterly NB, Honig PJ. Etretinate therapy for generalized pustular psoriasis in children. *Arch Dermatol*. 1987;123(2):230-233.
124. Kopp T, Karlhofer F, Szepfalusi Z, Schneeberger A, Stingl G, Tanew A. Successful use of acitretin in conjunction with narrowband ultraviolet B phototherapy in a child with severe pustular psoriasis, von Zumbusch type. *Br J Dermatol*. 2004; 151(4):912-916.
125. Absorica (isotretinoin) [package insert]. Humaco, PR: Galephar Pharmaceuticals Research, Inc. 2018.
126. Nesher G, Zuckner J. Rheumatologic complications of vitamin A and retinoids. *Semin Arthritis Rheum*. 1995;24(4): 291-296.
127. Halverstam CP, Zeichner J, Lebwohl M. Lack of significant skeletal changes after long-term, low-dose retinoid therapy: case report and review of the literature. *J Cutan Med Surg*. 2006;10(6):291-299.
128. Soriatane (acitretin) capsules [package insert]. Research Triangle Park, NC: Stiefel Laboratories, Inc. 2017.
129. Posso-De Los Rios CJ, Pope E, Lara-Corrales I. A systematic review of systemic medications for pustular psoriasis in pediatrics. *Pediatr Dermatol*. 2014;31(4):430-439.
130. Steinz K, Gerdes S, Domm S, Mrowietz U. Systemic treatment with fumaric acid esters in six paediatric patients with psoriasis in a psoriasis centre. *Dermatology*. 2014;229(3):199-204.
131. van Geel MJ, van de Kerkhof PC, Oostveen AM, de Jong EM, Seyger MM. Fumaric acid esters in recalcitrant pediatric psoriasis: a prospective, daily clinical practice case series. *J Dermatolog Treat*. 2016;27(3):214-220.
132. Balak DM, Oostveen AM, Bousema MT, et al. Effectiveness and safety of fumaric acid esters in children with psoriasis: a retrospective analysis of 14 patients from the Netherlands. *Br J Dermatol*. 2013;168(6):1343-1347.
133. Marqueling AL, Cordoro KM. Systemic treatments for severe pediatric psoriasis: a practical approach. *Dermatol Clin*. 2013; 31(2):267-288.
134. Takemoto CK, Hodding JH, Donna KM. *Lexicomp Pediatric & Neonatal Dosage Handbook*. 25th ed. Hudson, OH: Wolters Kluwer Clinical Drug Information; 2019.
135. Paller AS, Siegfried EC, Langley RG, et al. Etanercept treatment for children and adolescents with plaque psoriasis. *N Engl J Med*. 2008;358(3):241-251.
136. Langley RG, Paller AS, Hebert AA, et al. Patient-reported outcomes in pediatric patients with psoriasis undergoing etanercept treatment: 12-week results from a phase III randomized controlled trial. *J Am Acad Dermatol*. 2011;64(1):64-70.
137. Paller AS, Siegfried EC, Eichenfield LF, et al. Long-term etanercept in pediatric patients with plaque psoriasis. *J Am Acad Dermatol*. 2010;63(5):762-768.
138. Paller AS, Siegfried EC, Pariser DM, et al. Long-term safety and efficacy of etanercept in children and adolescents with plaque psoriasis. *J Am Acad Dermatol*. 2016;74(2):280-287.
139. Papp K, Thaci D, Marcoux D, et al. Efficacy and safety of adalimumab every other week versus methotrexate once weekly in children and adolescents with severe chronic plaque psoriasis: a randomised, double-blind, phase 3 trial. *Lancet*. 2017;390(10089):40-49.
140. Landells I, Marano C, Hsu MC, et al. Ustekinumab in adolescent patients age 12 to 17 years with moderate-to-severe plaque psoriasis: results of the randomized phase 3 CADMUS study. *J Am Acad Dermatol*. 2015;73(4):594-603.
141. Klufas DM, Wald JM, Strober BE. Treatment of moderate to severe pediatric psoriasis: a retrospective case series. *Pediatr Dermatol*. 2016;33(2):142-149.
142. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
143. Luu M, Cordoro KM. The evolving role of biologics in the treatment of pediatric psoriasis. *Skin Therapy Lett*. 2013; 18(2):1-4.
144. Landells I, Paller AS, Pariser D, et al. Efficacy and safety of etanercept in children and adolescents aged > or = 8 years with severe plaque psoriasis. *Eur J Dermatol*. 2010;20(3):323-328.
145. Siegfried EC, Eichenfield LF, Paller AS, Pariser D, Creamer K, Kricorian G. Intermittent etanercept therapy in pediatric patients with psoriasis. *J Am Acad Dermatol*. 2010;63(5):769-774.
146. Hawrot AC, Metry DW, Theos AJ, Levy ML. Etanercept for psoriasis in the pediatric population: experience in nine patients. *Pediatr Dermatol*. 2006;23(1):67-71.
147. Costa L, Caso F, Atteno M, et al. Long-term safety of anti-TNF-alpha in PsA patients with concomitant HCV infection: a retrospective observational multicenter study on 15 patients. *Clin Rheumatol*. 2014;33(2):273-276.
148. Ndzi EN, Nkenfou CN, Gwom LC, Fainguem N, Fokam J, Pefura Y. The pros and cons of the QuantiFERON test for the diagnosis of tuberculosis, prediction of disease progression, and treatment monitoring. *Int J Mycobacteriol*. 2016;5(2):177-184.
149. Gamsky TE, Lum T, Hung-Fan M, Green JA. Cumulative false-positive QuantiFERON-TB interferon-gamma release assay results. *Ann Am Thorac Soc*. 2016;13(5):660-665.
150. Singh JA, Guyatt G, Ogdie A, et al. Special article: 2018 American College of Rheumatology/National Psoriasis Foundation guideline for the treatment of psoriatic arthritis. *Arthritis Rheumatol*. 2019;71(1):5-32.
151. Kimball AB, Gladman D, Gelfand JM, et al. National Psoriasis Foundation clinical consensus on psoriasis comorbidities and recommendations for screening. *J Am Acad Dermatol*. 2008; 58(6):1031-1042.
152. Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *J Am Board Fam Pract*. 2004;17(1):59-67.
153. *Administrative Regulation—Evidence-Based Clinical Practice Guidelines*. Washington, DC: American Academy of Dermatology; 2014.

APPENDIX 1

Method

A multidisciplinary workgroup (WG) of recognized psoriasis experts consisting of dermatologists (including private practitioners), a rheumatologist, a cardiologist, and representatives from a patient advocacy organization were convened to identify important clinical questions with regard to pediatric psoriasis. WG members completed a disclosure of interests that was updated and reviewed for potential relevant conflicts of interest throughout guideline development. If a potential conflict was noted, the WG member recused himself or herself from discussion and drafting of recommendations pertinent to the topic area of the disclosed interest.

An evidence-based model was used, and evidence was obtained by using a search of the PubMed and MEDLINE databases from January 2011 through December 31, 2017, for clinical questions addressed in the previous version of this guideline published in 2008 through 2011 and from 1960 through 2017 for all newly identified clinical questions. Searches were limited to publications in the English language. Medical Subject Headings terms/search terms used in various combinations in the literature search included *psoriasis*, *pediatric*, *biologic*, *adalimumab*, *etanercept*, *infliximab*, *ixekizumab*, *secukinumab*, *ustekinumab*, *brodalumab*, *tildrakizumab*, *guselkumab*, *BI655066*, *tofacitinib*, *biosimilar non-biologic systemic*, *apremilast*, *methotrexate*, *cyclosporine*, *acitretin*, *azathioprine*, *fumaric acid esters*, *hydroxyurea*, *leflunomide*, *mycophenolate mofetil*, *sulfasalazine*, *calcineurin inhibitors* (*tacrolimus*, *pimecrolimus*), *6-thioguanine*, *complementary alternative medicine*, *aloe vera*, *St John's wort*, *fish oil*, *vitamin D*, *turmeric* (*curcumin*), *zinc*, *hypnosis*, *meditation*, *stress reduction*, *gluten free diet*, *topical agents*, *topical corticosteroids*, *topical steroids*, *tazarotene*, *tacrolimus*, *pimecrolimus*, *moisturizers*, *salicylic acid*, *anthralin*, *coal tar*, *anti*-Candida *agents*, *phototherapy*, *BB-UVB*, *NB-UVB*, *targeted phototherapy*, *PUVA* (*topical*, *oral*), *Grenz-ray*, *climatotherapy*, *photodynamic therapy*, *BB-UVA*, *UVB-LED*, *turbo UVB*, *intense pulsed light*, *Goeckerman therapy* and comorbidities including *psoriatic arthritis*, *inflammatory bowel disease*, *cardiovascular disease*, *psychological and psychiatric disorders*, *metabolic syndrome*, *atherosclerosis*, *nonalcoholic fatty liver disease*, *lymphomas*, *sleep apnea*, *chronic obstructive pulmonary disease*, *osteoporosis*, *depression*, *suicidal ideation*, *sexual dysfunction*, *uveitis*, *renal disease*, *smoking*, *alcoholism*, *anxiety*, *interpersonal relationships*, *work productivity*, *combination*, *alternate*, *failure* (*primary*, *secondary*), *switch*.

After removal of duplicate data, 134 were retained for final review based on relevancy and the highest level of available evidence for the outlined clinical questions. Evidence tables were generated for these studies and used by the WG in developing recommendations. The Academy's prior published guidelines on psoriasis were evaluated, as were other current published guidelines on psoriasis.[150,151]

The available evidence was evaluated by using a unified system called the Strength of Recommendation Taxonomy (SORT), which was developed by editors of the US family medicine and primary care journals (ie, *American Family Physician*, *Family Medicine*, *Journal of Family Practice*, and *BMJ USA*).[152] Evidence was graded using a 3-point scale based on the quality of methodology (eg, randomized controlled trial, case-control, prospective/retrospective cohort, case series, etc) and the overall focus of the study (ie, diagnosis, treatment/prevention/screening, or prognosis) as follows:

I. Good-quality patient-oriented evidence (ie, evidence measuring outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life).
II. Limited-quality patient-oriented evidence.
III. Other evidence, including consensus guidelines, opinion, case studies, or disease-oriented evidence (ie, evidence measuring intermediate, physiologic, or surrogate endpoints that may or may not reflect improvements in patient outcomes).

Clinical recommendations were developed on the best available evidence tabled in the guideline. These are ranked as follows:

A. Recommendation based on consistent and good-quality patient-oriented evidence.
B. Recommendation based on inconsistent or limited-quality patient-oriented evidence.
C. Recommendation based on consensus, opinion, case studies, or disease-oriented evidence.

In those situations in which evidence-based data were not available, expert opinion was used to generate our clinical recommendations.

This guideline has been developed in accordance with the American Academy of Dermatologists (AAD)/AAD Association Administrative Regulations for Evidence-Based Clinical Practice Guidelines (May 2014),[153] which includes the opportunity for review and comment by the entire AAD membership and final review and comment by the AAD Board of Directors. Additionally, this guideline has been developed in collaboration with the National Psoriasis Foundation and as part of the review

process, the National Psoriasis Foundation medical board members provided their feedback. This guideline will be considered current for a period of 5 years from the date of publication unless reaffirmed, updated, or retired before that time.

Definitions

Psoriasis vulgaris is a chronic inflammatory skin disease that classically presents with well-demarcated, pink plaques with silvery scale. Although commonly involving the scalp, elbows, knees, and presacral region in adolescents and adults, any area of skin may be involved, including the palms and soles. Children with psoriasis can present with unique distribution patterns, including isolated facial or genital involvement, particularly in infancy.

Psoriasis has many cutaneous forms, including plaque (psoriasis vulgaris), guttate, palmoplantar, inverse, and pustular, which will be discussed as a collective whole unless otherwise specified.

Psoriasis is an inflammatory, immune-mediated condition stemming from inappropriate activation of cutaneous T cells and dendritic cells with subsequent release of inflammatory cytokines such as interleukin (IL) 1, IL-6, IL-12, IL-17, IL-23, and tumor necrosis factor α. These chemical signals are responsible for keratinocyte hyperproliferation, the influx of neutrophils, and further propagation of inflammation. This inflammation is also thought to contribute to a number of systemic disease associations, including metabolic syndrome and arthritis.