Joint AAD–NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures

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Psoriasis is a chronic, inflammatory, multisystem disease that affects up to 3.2% of the United States population. This guideline addresses important clinical questions that arise in psoriasis management and care and provides recommendations based on the available evidence. The treatment of psoriasis with topical agents and with alternative medicine will be reviewed, emphasizing treatment recommendations and the role of dermatologists in monitoring and educating patients regarding benefits as well as risks that may be associated. This guideline will also address the severity assessment methods of psoriasis in adults. (J Am Acad Dermatol 2021;84:432-70.)

Key words: alternative medicine (AM); clinical guidelines for psoriasis; dermatology; guidelines; psoriasis; severity assessment; skin disease; topical agents.

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Abbreviations used:

AAD:	American Academy of Dermatology
AM:	alternative medicine
AV:	*Aloe vera*
BSA:	body surface area
DLQI:	Dermatology Life Quality Index
FDA:	Food and Drug Administration
HM:	herbal medicine
LCD:	liquor carbonis detergens
NB-UVB:	narrow band ultraviolet B
NPF:	National Psoriasis Foundation
PASI:	Psoriasis Area Severity Index
PGA:	Physician's Global Assessment
PSI:	Psoriasis Symptom Inventory
RCT:	randomized controlled trial
UVA:	ultraviolet A
UVB:	ultraviolet B
US:	United States
WG:	workgroup

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 and the patient 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.

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 information below represents the authors who disclosed a relationship with industry during guideline development. Authors (listed alphabetically) with relevant conflicts with respect to this

Table I. Clinical questions

1. What are the efficacy, effectiveness, and adverse events of the following therapies used as monotherapy and/or combination therapy to treat psoriasis in adults?
   a. Topical corticosteroids
   b. Calcineurin inhibitors (Topical tacrolimus and pimecrolimus)
   c. Vitamin D analogues
   d. Tazarotene
   e. Moisturizers
   f. Salicylic acid
   g. Anthralin
   h. Coal tar
   i. Biologic agent combination
   j. Nonbiologic combination
      i. Methotrexate
      ii. Cyclosporine
      iii. Acitretin
2. What are the efficacy, effectiveness, and adverse events of the following alternative medicines used for adult psoriasis?
   a. Traditional Chinese medicine
   b. Herbal therapies
      i. *Aloe vera*
      ii. St John's wort
   c. Diet/dietary supplements
      i. Fish oil
      ii. Vitamin D
      iii. Curcumin (Turmeric)
      iv. Zinc
      v. Gluten-free diet
   d. Mind/body
      i. Hypnosis
      ii. Stress reduction/meditation
3. What is the accuracy, clinical utility, and treatment parameters for using the following severity measures to measure psoriasis severity and response to treatment?
   a. Body surface area (BSA)
   b. Psoriasis Area and Severity Index (PASI)
   c. Physician Global Assessment (PGA)
   d. PGA × BSA
   e. Psoriasis Symptom Inventory (PSI)
   f. Dermatology of Life Quality Index (DLQI)
   g. Pruritus assessment

Table II. Classification of topical corticosteroid[6-8]*

WHO potency group	Classification	Topical corticosteroid
Super-potent Ultrahigh	Class 1	1. Augmented betamethasone dipropionate 0.05%[a,b] 2. Clobetasol propionate 0.05%[a,b,c,d,e,f,g,h,i] 3. Desoximetasone 0.25%[h] 4. Augmented diflorasone diacetate 0.05%[a] 5. Fluocinonide 0.1%[c] 6. Flurandrenolide 4 μg/cm^2[j] 7. Halobetasol propionate 0.05%[a,c]
High	Class 2	1. Amcinonide 0.1%[a] 2. Betamethasone dipropionate 0.05%[a] 3. Augmented betamethasone dipropionate 0.05%[c,d] 4. Desoximetasone 0.25%[a,c] 5. Desoximetasone 0.05%[b] 6. Augmented diflorasone diacetate 0.05%[c] 7. Diflorasone diacetate 0.05%[a] 8. Fluocinonide 0.05%[a,b,c,f] 9. Halcinonide 0.1%[a,c] 10. Mometasone furoate 0.1%[a] 11. Triamcinolone acetonide 0.5%[a]
	Class 3	1. Amcinonide 0.1%[c,d] 2. Betamethasone dipropionate 0.05%[c,k] 3. Betamethasone valerate 0.1%[a] 4. Betamethasone valerate 0.12%[l] 5. Diflorasone diacetate 0.05%[c] 6. Fluticasone propionate 0.005%[a] 7. Triamcinolone acetonide 0.1%[a] 8. Triamcinolone acetonide 0.5%[c]
Moderate (medium)	Class 4	1. Betamethasone valerate 0.12%[l] 2. Desoximetasone 0.05%[c] 3. Fluocinolone acetonide 0.025%[a] 4. Flurandrenolide 0.05%[a] 5. Hydrocortisone valerate 0.2%[a] 6. Mometasone furoate 0.1%[c,d] 7. Triamcinolone acetonide 0.1%[c,m] 8. Triamcinolone acetonide 0.2%[h]
	Class 5	1. Betamethasone dipropionate 0.05%[k] 2. Betamethasone valerate 0.1%[c,d] 3. Clocortolone pivalate 0.1%[c] 4. Fluocinolone acetonide 0.025%[c] 5. Fluocinolone acetonide 0.01%[n,o] 6. Fluticasone propionate 0.05%[c,d] 7. Flurandrenolide 0.05%[c,d] 8. Hydrocortisone butyrate 0.1%[a,c,d,f] 9. Hydrocortisone probutate 0.1%[c] 10. Hydrocortisone valerate 0.2%[c] 11. Prednicarbate 0.1%[a,c] 12. Triamcinolone acetonide 0.025%[a] 13. Triamcinolone acetonide 0.01%[d]

Continued

Table II. Cont'd

WHO potency group	Classification	Topical corticosteroid
Low	Class 6	1. Alclometasone dipropionate 0.05%[a,c] 2. Betamethasone valerate 0.05%[d] 3. Desonide 0.05%[a,b,c,d,e] 4. Fluocinolone acetonide 0.01%[c,f] 5. Triamcinolone acetonide 0.025%[c,d]
	Class 7	1. Dexamethasone sodium phosphate 0.1%[c] 2. Hydrocortisone 0.5%-2.5%[a,b,c,d,f] 3. Methylprednisolone acetate 0.25%[c]

WHO, World Health Organization.
*Reprinted from *Dermatology*: 2-Volume Set, 4th Edition, Jean Bolognia, Julie Schafer, and Lorenzo Cerroni, Glucocorticosteroids, Page No. 2190, Copyright 2018, with permission from Elsevier.
[a]Ointment.
[b]Gel.
[c]Cream.
[d]Lotion.
[e]Foam.
[f]Solution.
[g]Scalp solution application, in some classifications class 2.
[h]Spray.
[i]Shampoo 0.05%.
[j]Tape.
[k]Lotion, depending upon classification, class 3 or 5.
[l]Foam, depending upon classification, class 3 or 4.
[m]Kenalog ointment (manufactured by APOTHECON, a Bristol-Myers Squibb Company; Princeton, NJ).
[n]Oil.
[o]Shampoo.

guideline are noted with an asterisk (*). In accordance with the AAD policy, fewer than 51% of workgroup members had any relevant conflicts of interest.

Participation in one or more of the below-listed activities constitutes a relevant conflict:

- service as a member of a speaker bureau, consultant, advisory board, for pharmaceutical companies on the psoriasis disease state or psoriasis drugs in development or United States (US) Food and Drug Administration (FDA) approved;
- 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 FDA approved.

Draft guideline recommendations were developed through a collaborative approach between conflicted and nonconflicted section leaders. Initial recommendations were presented to the full workgroup for finalization.

SCOPE

This guideline will cover the use of topical agents and alternative medicine (AM) in the treatment of psoriasis in adults as well as the assessment of disease severity; psoriasis in the pediatric population will be covered in a separate guideline section, "Joint American Academy of Dermatology-National Psoriasis Foundation (NPF) guidelines of care for the management and treatment of psoriasis in pediatric patients."[1]

METHOD

For a full description of the methodology used herein, please refer to the Appendix section.

DEFINITION OF REVIEW

See the Appendix for full definition statement.

INTRODUCTION

Psoriasis is a common inflammatory disease, affecting approximately 3.2% of the population.[2] While skin involvement is the most prominent manifestation of this disease, recognition of psoriasis as a chronic, multisystem inflammatory disorder is imperative to optimize management and reduce comorbidities.

Topical medications are the most common agents used to treat patients with mild to moderate psoriasis. They are frequently used as adjunctive therapies for patients on phototherapy, systemic, or biologic therapy. Alternative medicine (AM) is not typically part of conventional medical care. It may have

origins outside of usual Western practice and may be desired by and benefit a subset of patients.[3,4]

This section will review the assessment of psoriasis severity and the management and treatment of psoriasis with topical therapy and AM modalities in adult psoriasis patients (Table I).

I. TOPICAL AGENTS

Topical corticosteroids

Efficacy. Topical corticosteroids, which provide high efficacy and good safety, play a key role in the treatment of psoriasis, especially for localized disease. Topical corticosteroids have anti-inflammatory, antiproliferative, immunosuppressive, and vasoconstrictive effects. These effects are exerted via intracellular corticosteroid receptors, which regulate gene transcription, including several that code for proinflammatory mediators. Topical corticosteroids are classified into 7 categories based on their skin vasoconstrictive activity, ranging in strength from ultra-high (class 1) to low (class 6 and 7; Table II).[5-8]

Choosing a corticosteroid with appropriate potency plus the appropriate vehicle should be based on the disease severity, disease location, patient preference, and the age of the patient. Lower potency corticosteroids should be used on the face, intertriginous areas, and areas that are susceptible to steroid atrophy (eg, forearms) and other adverse effects. In adults, corticosteroids in classes 2 through 5 (moderate to high potency; Table II) are generally recommended as initial therapy. Areas with thick, chronic plaques often require treatment with class 1 (ultrahigh-potency) corticosteroids. In numerous randomized controlled trials (RCTs), different potency topical corticosteroids were effective and safe at 2 to 4 weeks in the treatment of mild to severe plaque psoriasis.[9-11] Evidence on the efficacy of topical corticosteroids from RCTs varies due to the differences in study designs, patient populations, and end points, making it difficult to do an accurate statistical comparison of the majority of published studies.

For ultrahigh-potency (class 1) corticosteroids, the efficacy rates in several RCTs vary from 58% to 92%.[9,10,12,13] In a double-blind, vehicle-controlled trial of 204 patients with moderate to severe psoriasis, after 2 weeks of treatment, the halobetasol propionate ointment (class 1) group improved the Physician's Global Assessment (PGA) scores by 92% compared with 39% in vehicle-treated patients ($P < .0003$).[9] An RCT of 279 patients with mild to moderate psoriasis found that after 2 weeks of treatment with clobetasol foam (class 1), 68% of patients achieved a Physician's Static Global Assessment (PSGA) score of 0 or 1 compared with 21% of patients treated with vehicle ($P < .0001$).[10] Another double-blind RCT of 81 patients used the Investigator Global Assessment scale to assess patients with mild to moderate psoriasis and demonstrated that after 2 weeks of treatment with clobetasol foam (class 1), 58% of patients achieved moderate or marked improvement, or almost or completely clear psoriasis compared with 15% in vehicle-treated patients ($P < .0005$).[11]

For high-potency (class 2 and 3) corticosteroids, the efficacy rates in several RCTs vary from 68% to 74%. In a double blind-RCT of 35 patients with psoriasis treated with 0.25% desoximetasone cream (class 2) for 3 weeks, 68% of the desoximetasone group compared with 23% of the vehicle group achieved improvement in their mean overall evaluation scores ($P < .001$).[14] Two RCTs with fluticasone propionate 0.005%, a class 3 corticosteroid, showed 68% to 69% of patients with moderate to severe psoriasis in the treatment group achieved, good, excellent, or clear skin after 4 weeks compared with 29% to 30% in the vehicle group ($P = .00001$).[15]

For moderate-potency (class 4 and 5) corticosteroids, the efficacy rates in several RCTs vary from 70% to 83%.[16,17] An RCT of 40 patients with nonscalp psoriasis revealed that 70% of patients treated with betamethasone valerate foam 0.12% (class 4) achieved greater than 50% improvement compared with 24% of patients in the placebo group after 12 weeks of treatment ($P < .001$).[17] In an RCT of patients with moderate to severe scalp psoriasis, the group treated with fluocinolone acetonide 0.01% oil (class 5 corticosteroid) had a higher proportion of patients achieving good or better improvement from baseline compared with the vehicle-treated group after 3 weeks of treatment (83% vs 36%; $P < .001$).[16] Additionally, an RCT showed that fluticasone propionate 0.05% cream (class 5) was superior to hydrocortisone butyrate 0.1% cream (class 7) in achieving clearance, excellent, or good treatment response after 3 weeks of treatment (79% vs 68%; $P < .05$).[18]

Owing to the inconsistent criteria in RCT design, comparisons between different corticosteroids and classes are complex. Nevertheless, a systematic review of topical corticosteroids for the treatment of psoriasis revealed that potent and super-potent topical corticosteroids were more efficacious than mild or moderately potent corticosteroids.[19]

Treatment of psoriasis in intertriginous areas, such as the groin, or hair-bearing skin, such as the scalp, can be challenging due to the difficulty of applying a topical product to these areas based on the vehicle selection. Therefore, appropriate selection of the vehicle depending on hair density and individual hairstyles and preferences is essential for the efficacy

Table III. Recommendations and strength of recommendation for topical corticosteroids

Reference number	Recommendations	Strength of recommendation
1.1	The use of class 1, class 2, and class 3-5 topical corticosteroids for up to 4 weeks is recommended for the treatment of plaque psoriasis not involving intertriginous areas	A
1.2	The use of class 1-7 topical corticosteroids for a minimum of up to 4 weeks is recommended as initial and maintenance treatment of scalp psoriasis	A
1.3	The use of topical corticosteroids for >12 weeks can be considered if done under the careful supervision of a physician	C

Table IV. Level of evidence for topical corticosteroids

Recommendation	Reference number	Level of evidence	Studies
Topical corticosteroid for plaque psoriasis not involving intertriginous areas	1.1	I	9-11,13,15,45-47
Topical corticosteroid for scalp psoriasis	1.2	I	16,17,20
Long-term use of topical corticosteroid	1.3	III	Expert opinion

of the treatment. Several RCTs and systematic reviews of scalp psoriasis treatment demonstrate the safety and efficacy of various potency topical corticosteroids used for 3 to 12 weeks.[16,17,20] The duration of the therapy depends on factors such as the strength of topical corticosteroids, the severity of the disease, anatomic location, and age of the patient. Similarly, a steroid-sparing agent can be considered to avoid adverse effects.

Additionally, intralesional corticosteroids can be used for localized nonresponding or very thick lesions on glabrous skin, scalp, nails, palms, and soles. Several studies and reports have shown that intralesional corticosteroids can be effective for the treatment of psoriasis.[21-23] Triamcinolone acetonide in a dose up to 20 mg/mL can be used every 3 to 4 weeks.[24] The injection volume varies pending lesional size and the area affected.

Risks/harms and benefits. The most common local skin adverse effects of topical corticosteroid use include skin atrophy, striae, folliculitis, telangiectasia, and purpura.[25] Face and intertriginous areas, as well as chronically treated areas, especially forearms, are at greatest risk to develop these adverse effects. Topical corticosteroids may exacerbate acne, rosacea, perioral dermatitis, and tinea infections and may occasionally cause contact dermatitis. Rebound (ie, when the disease recurs and is more severe than before treatment) can occur from abrupt withdrawal of topical corticosteroids, although the frequency and severity of this phenomenon are unknown. The daily use of ultrahigh- and high-potency (class 1-3) corticosteroids for up to 4 weeks is generally safe with minimal risk of skin atrophy.[26]

Risk of hypothalamic pituitary adrenal axis suppression from the use of topical corticosteroids for extensive plaque or scalp psoriasis has been reported to be low.[26] In a systematic review of 13 randomized studies, studies performed for up to 4 weeks found the percentage of patients with a reduction in the morning cortisol level was 0% with halobetasol or fluocinonide, 0% to 48% with clobetasol propionate, and 0% to 18% with betamethasone dipropionate. Nevertheless, results of adrenocorticotropic hormone stimulation tests, the gold standard for assessing hypothalamic-pituitary-adrenal axis suppression, were always within normal reference ranges, even when assessed after 6 to 12 months of topical corticosteroid use.[26] Rare systemic adverse effects include Cushing syndrome and osteonecrosis of the femoral head.[27,28] Topical products that contain corticosteroid should not be used for more than 12 weeks for nail disease, because there are isolated reports of bone atrophy with persistent use.[29,30] Increased intraocular pressure, glaucoma, and cataracts have been rarely reported with the use of topical corticosteroids around the eye.[31,32] In rare cases, type 2 diabetes has been reported with topical corticosteroid use.[33]

Despite the safety data,[26] caution is advised, because the greatest risk for systemic adverse effects occurs when ultrahigh- or high-potency corticosteroids are used over a large surface (>20% body surface area [BSA]) or under occlusion for a prolonged period (>4 weeks). Clinicians should consider limiting the use of class 1 corticosteroids to no more than twice daily for up to 4 weeks, when possible.[34] In the event of a flare, repeated courses of a class 1 corticosteroid can be administered. Longer durations of class 1 corticosteroid therapy for psoriasis of the palms and soles are acceptable with close

attention to the development of potential adverse effects. Gradual reduction in the frequency of use after clinical improvement is recommended, but the exact details of this tapering are not well established. Topical corticosteroids can be tapered off by reducing use to every other day, then eventually 2 times a week, and finally discontinuation if psoriasis is well controlled and stable during the whole process. To minimize the adverse effects of topical corticosteroids, transitioning to lower-potency agents after improvement, using intermittent therapy, and combining treatment with noncorticosteroidal agents can also be considered.

Topical corticosteroids are safe during pregnancy when low cumulative doses (<60 g/wk) are used (expert consensus). In rare cases, low fetal birth weight has been reported with prolonged potent topical corticosteroid use during pregnancy.[35] Further, there is a single case report of a nursing mother who applied a potent topical corticosteroid on the nipple and the infant developed hypertension.[36] Therefore, the use of a super potent corticosteroid in the nipple and the areola area should be avoided in nursing mothers.[37,38]

General comments. Because psoriasis generally recurs after discontinuation of topical corticosteroid treatment, it is important to consider using steroid-sparing agents that have been developed to supplement and reduce over-reliance on topical corticosteroids as monotherapy, decreasing the risk of corticosteroid adverse effects.[26] Agents such as vitamin D analogues, topical retinoids, and calcineurin inhibitors can be used as a maintenance treatment. For example, a therapeutic regimen for mild psoriasis flares could include 2 to 4 weeks of treatment with a topical corticosteroid twice daily, followed by maintenance with a steroid-sparing agent twice daily on weekdays, and a corticosteroid agent twice daily on weekends.[39] Treatment as discussed above can be reinstituted when a new flare occurs.

"Proactive treatment" is another strategy for optimal topical management of psoriasis during maintenance that is helpful. Proactive treatment refers to topical treatment of areas that are clinically quiescent but are usually involved in recurrence. It typically involves twice-weekly treatment of these clinically quiescent areas to reduce the frequency of flares.[40,41] Proactive treatment can be implemented with any of the topical agents discussed in these guidelines.

Tachyphylaxis is defined as the loss of effectiveness of topical corticosteroids with continued use. Tachyphylaxis may compromise the effectiveness in certain patients when used for an extended period >12 weeks. Whether tachyphylaxis represents a true loss of effectiveness of the medication or a loss of adherence on the part of patients is controversial. Current suggestions are based on extrapolation from animal studies, and further research into this subject is needed. Recommendations on the use of topical corticosteroids and its supporting evidence can be found in Tables III and IV.[9-11,13,15-17,20,39,42-47]

Calcineurin inhibitors

Efficacy. Topical calcineurin inhibitors bind to calcineurin, blocking its phosphorylation and thus, inhibiting T-cell activation and the synthesis of several proinflammatory cytokines that play a critical role in the pathogenesis of psoriasis. Although not FDA approved for psoriasis, the topical calcineurin inhibitors tacrolimus and pimecrolimus are often used in the treatment of psoriasis. They are especially helpful on thinner skin, such as facial and intertriginous areas, and are used as steroid-sparing agents for prolonged use (>4 weeks). Most of the data regarding these medications are derived from their extensive use in atopic dermatitis.

Several RCTs support the use of pimecrolimus for the treatment of intertriginous psoriasis.[48,49] In a double-blind RCT of 57 patients with intertriginous psoriasis, after 8 weeks of twice-daily treatment, 71% of the patients in the pimecrolimus 0.1% cream group were clear or almost clear compared with 21% of patients in the placebo group (treatment difference in target area score was −1.810; 95% confidence interval −2.801 to −0.819).[49] Several RCTs also support the use of tacrolimus for the treatment of facial and intertriginous psoriasis.[50] In a double-blind RCT of 167 patients with facial and intertriginous psoriasis, after 8 weeks of therapy, 65% of patients in the tacrolimus 0.1% ointment group were clear or almost clear compared with 31% of patients in the placebo group.[51] Recommendations on the use of topical calcineurin inhibitors and its supporting evidence can be found in Tables V and VI.[48-52,61]

The off-label combination of tacrolimus and 6% salicylic acid for 12 weeks may be used for the treatment of plaque psoriasis.[52]

Risks/harms and benefits. Studies from atopic dermatitis have reported that tacrolimus and pimecrolimus can both cause burning and pruritus.[53-56] These adverse events generally improve with continued use and can be mitigated by avoiding application to moist skin.[53,54]

In 2005, the FDA issued a boxed warning citing concerns that long-term, intermittent use of pimecrolimus or tacrolimus could lead to an increased incidence of lymphoma. This warning was due to a theoretical increased risk of lymphoma with the systemic use of these agents based on animal data, isolated case reports, and the mechanism of action of

Table V. Recommendations and strength of recommendation for topical pimecrolimus and tacrolimus

Reference number	Recommendations	Strength of recommendation
2.1	The off-label use of 0.1% tacrolimus for psoriasis involving the face as well as inverse psoriasis for up to 8 weeks can be considered	B
2.2	The off-label use of pimecrolimus for inverse psoriasis for 4-8 weeks is recommended	B
2.3	Long-term use of tacrolimus or pimecrolimus can be considered for inverse psoriasis treatment as off-label use	C
2.4	The off-label combination of tacrolimus and 6% salicylic acid for 12 weeks may be used for the treatment of plaque psoriasis	B

Table VI. Level of evidence for topical pimecrolimus and tacrolimus

Recommendation	Reference number	Level of evidence	Studies
Use of 0.1% tacrolimus for psoriasis involving the face/ inverse psoriasis	2.1	I	50,51
Use of pimecrolimus for inverse psoriasis	2.2	I	48,49
Long-term use of tacrolimus or pimecrolimus for inverse psoriasis	2.3	III	61
Combination of tacrolimus and 6% salicylic acid for plaque psoriasis	2.4	II	52

these drugs. Although both agents carry a boxed warning related to the potential risk for malignancy (eg, skin and lymphoma), there is no evidence showing an increased risk of malignancy with the topical use of either agent.[53,54,57-59] A common adverse effect of calcineurin inhibitors includes flushing with the ingestion of alcohol.[53,54]

The effects in humans of tacrolimus and pimecrolimus on the fetus are unknown. If they are used during pregnancy, they should, therefore, be used cautiously. Breastfeeding mothers should avoid use on the nipple but can use them on other areas, because maternal systemic absorption is minimal.[53,54,60] Additionally, no signs of reduced fertility were found in men and women using tacrolimus.[54] Similarly, in animal studies, no signs of reduced fertility were associated with pimecrolimus.[53]

Contraindication. There are no specific contraindications, but much of the data (except that given above for facial and intertriginous psoriasis) regarding these medications are derived from their extensive use in atopic dermatitis.

Vitamin D analogues

Efficacy. Vitamin D analogs exert their effect in psoriasis by binding to vitamin D receptors, which inhibit keratinocyte proliferation and enhance keratinocyte differentiation. Calcipotriene (also known as calcipotriol) and calcitriol are the 2 commonly used synthetic vitamin D analogues. Calcipotriene is available in several formulations in the US, but topical calcitriol is only available as an ointment. Tacalcitol and maxacalcitol are vitamin D analogues available worldwide, but not currently in the US. Additionally, calcipotriene and tacalcitol are available in combination with topical corticosteroids.

Several studies have shown that 4 to 8 weeks' treatment of calcipotriene, calcitriol, tacalcitol, and maxacalcitol is safe and efficacious for treating mild to moderate psoriasis.[62-64] Two double-blind RCT compared calcipotriene foam to the vehicle for the treatment of plaque psoriasis. In the first study, 14% of patients in the calcipotriene foam group vs 7% in the vehicle foam group achieved treatment success after 8 weeks (P = .058). In the second study, treatment success and the primary end point, defined as achieving an Investigator's Static Global Assessment score of 0 (clear) or 1 (almost clear), was achieved by more participants in the calcipotriene foam group (27% vs 16%; P = .016).[65]

A 6-week double-blind RCT in 258 patients with plaque psoriasis showed that calcitriol ointment had comparable efficacy, defined as a mean reduction of Psoriasis Area and Severity Index (PASI), to betamethasone dipropionate 0.05% ointment (10.6% and 9.67%, respectively).[12] During the follow-up after treatment, 48% of patients who applied calcitriol and 25% of patients who applied betamethasone dipropionate remained in remission ($P < .01$). Treatment with calcipotriene foam for 8 weeks and calcipotriene plus betamethasone dipropionate gel for 4 to 12 weeks compared with placebo was safe and effective for the treatment of mild to moderate scalp psoriasis.[66,67]

An 8-week double-blind RCT with 363 patients with psoriasis used the Investigator's Static Global Assessment to measure its primary outcome. After 8 weeks, calcipotriene foam (40.9%) was more effective in achieving an Investigator's Static Global Assessment score of 0 (clear) or 1 (almost clear) compared with vehicle (24.2%) for the treatment of scalp psoriasis ($P < .001$).[68] The efficacy of vitamin D analogues was noted at 8 weeks but not at 4 weeks. This can be considered and addressed with patients when planning appropriate topical treatment.

The use of calcipotriene or tacalcitol ointment combined with hydrocortisone is efficacious for the treatment of facial psoriasis.[69] Topical calcipotriene has displayed greater efficacy than 6% coal tar or salicylic acid but less efficacy than liquor carbonis detergens (LCD) 15% solution.[70,71] An 8-week double-blind RCT (n = 409) with 4 treatment arms compared calcipotriene 25 μg/g, calcipotriene 25 μg/g plus hydrocortisone 10 mg/g, calcipotriene 50 μg/g, and calcipotriene 50 μg/g plus hydrocortisone 10 mg/g.[72] All treatments were equally effective on the body, but the treatments containing hydrocortisone were more effective on the face, as determined by a score of 0 or 1 in the Investigator Global Assessment of the face (odds ratio, 2.01; 95% confidence interval, 1.33-3.05, $P = .001$).[72]

The use of combination treatments with vitamin D analogues and potent topical corticosteroids from 3 to 52 weeks is more effective than either agent alone for the treatment of psoriasis.[73-84] A systematic review of RCTs concluded that when given for 3 to 8 weeks, ultrapotent or potent corticosteroid treatments outperform calcipotriene. The outcome measures assessed in the review included Investigator Global Assessment, PASI, and PGA which were translated to a 6-point improvement scale. Nevertheless, calcipotriene combined with potent betamethasone dipropionate was slightly more efficacious than betamethasone as a monotherapy.[85] In a 52-week study with 828 patients, 69% to 74% of patients in the group treated with calcipotriene 0.005% plus betamethasone 0.064% once or twice daily achieved clear or almost clear status compared with 27% of the patients treated with vehicle control ($P < .001$). No serious adverse events, including striae or hypothalamic-pituitary-adrenal axis suppression, were observed over the 52-week treatment period with calcipotriene 0.005% and betamethasone 0.064%.[81]

There is evidence supporting the application of vitamin D analogues twice daily on weekdays in conjunction with high-potency topical corticosteroids twice daily on weekends.[39] An open-label study in 70 patients showed treatment with calcipotriene ointment on weekdays and clobetasol spray on weekends applied twice daily for 4 weeks is an effective treatment regimen for moderate plaque psoriasis.[39] Additionally, the application of morning high-potency topical corticosteroids and evening topical vitamin D analogues is an effective combination regimen for the treatment of psoriasis.[86] In an open-label study, 68 patients applied an morning/evening regimen of clobetasol propionate spray 0.05% and calcipotriene ointment 3 μg/g. At 4 weeks, 85.5% of patients were clear, almost clear, or had mild involvement.[86]

Risks/harms and benefits. Vitamin D analogues are considered safe for the treatment of plaque psoriasis. No clinical or experimental evidence has been found relating to tachyphylaxis with topical vitamin D analogue use in psoriasis. Other local adverse effects can affect up to 35% of patients and include burning, pruritus, edema, peeling, dryness, and erythema. They may occur both on lesional and perilesional skin. With continued treatment, these adverse effects usually subside or disappear. Systemic adverse effects due to topical vitamin D analogues include hypercalcemia and parathyroid hormone suppression. These effects are quite rare unless more than 30% BSA is treated, the recommended dose is exceeded, or the patient has an underlying renal disease or impaired calcium metabolism. When using calcipotriene, applications of more than 100 g/wk should be avoided to minimize this risk.[87] Calcipotriene over 52 weeks was well tolerated in an open-label study of 132 patients. Mild hypercalcemia occurred in 3.1% of patients that did not correlate with the length of treatment or pretreatment BSA.[22] Vitamin D analogues may be used during pregnancy and lactation if the benefit outweighs the risk. The use of vitamin D combination products containing corticosteroids on more than 15% BSA once daily rarely induces adrenal suppression.[88]

General comments. Ultraviolet A (UVA) radiation can decrease the concentration of calcipotriene on the skin. Conversely, thick layers of calcipotriene can block ultraviolet B (UVB), thereby increasing the minimal erythema dose.[89] Vitamin D analogues can be used in conjunction with phototherapy but should be applied after the phototherapy treatment to avoid inactivation by UVA and blocking UVB radiation.[90] Combining separate vitamin D and corticosteroid preparations into specific easy-to-follow regimens can be used to reduce both the adverse effects of topical corticosteroids and the cost for some patients, as discussed above in the topical corticosteroid section. Additionally, the

Table VII. Recommendations and strength of recommendation for vitamin D analogues

Reference number	Recommendations	Strength of recommendation
3.1	The long-term use of topical vitamin D analogues (up to 52 weeks), including calcipotriene/calcipotriene, calcitriol, tacalcitol, and maxacalcitol, is recommended for the treatment of mild to moderate psoriasis	A
3.2	Use of calcipotriene foam and calcipotriene plus betamethasone dipropionate gel is recommended for 4-12 weeks for the treatment of mild to moderate scalp psoriasis	A
3.3	Topical tacalcitol ointment or calcipotriene combined with hydrocortisone for 8 weeks can be used for the treatment of facial psoriasis	B
3.4	Use of combination treatments with vitamin D analogues and potent class II and class III topical corticosteroids up to 52 weeks is recommended for the treatment of psoriasis	A
3.5	Use of combination products with calcipotriol and corticosteroids is recommended for the treatment of psoriasis	A
3.6	The application of vitamin D analogues twice daily on weekdays in conjunction with high-potency topical corticosteroids twice daily on weekends can be considered for maintenance treatment for psoriasis	B
3.7	The application of morning high-potency topical corticosteroids and evening topical vitamin D analogues is an effective treatment regimen that can be considered for the treatment of psoriasis	B

simultaneous use of salicylic acid with calcipotriene should be avoided because the acid pH of salicylic acid will inactivate calcipotriene and reduce its effectiveness.

Topical vitamin D analogues combined with betamethasone dipropionate can be used for the treatment of nail psoriasis to reduce nail thickness, hyperkeratosis, onycholysis, and pain.[30] These agents have limitations in treating severe nail disease due to poor penetration, particularly of the nail matrix.[91] Topical maxcalcitol (not available in the US) ointment can be considered as an initial treatment for palmoplantar psoriasis, including palmoplantar pustulosis.[92,93]

Other combination treatments. Calcipotriene ointment combined with topical tacrolimus is more efficacious than tacrolimus alone.[94] Combination products with calcipotriene and topical nicotinamide are effective for the treatment of mild to moderate psoriasis. Recommendations on the use of vitamin D analogues and its supporting evidence can be found in Tables VII and VIII.*

Tazarotene

Efficacy. Tazarotene is a topical retinoid available for the treatment of psoriasis since 1997. It exerts its therapeutic effects by acting on keratinocyte differentiation and proliferation and by downregulating the expression of proinflammatory genes. The use of topical tazarotene for 8 to 12 weeks is recommended for the treatment of mild to moderate psoriasis, with several studies demonstrating its efficacy.[102-105] In 2 RCT of 1303 patients with plaque psoriasis, 40% and 51% of patients treated with tazarotene (0.1% cream and 0.05% cream, respectively) compared with 25% of patients treated with the vehicle once daily for 12 weeks achieved treatment success, defined as overall lesional assessment of none, minimal, or mild psoriasis activity (P for trend = .04).[106] A 12-week RCT showed that the efficacy of tazarotene 0.1% gel for the treatment of plaque psoriasis was comparable to fluocinonide cream. The efficacy was assessed by measuring plaque elevation, scaling, and erythema (grading each from 0 to 4) of target lesions at baseline and at each follow-up visit. Treatment success was defined as 50% to 74% improvement.[103]

An RCT showed that the combination of tazarotene 0.1% gel plus clobetasol propionate 0.05% ointment was more effective than tazarotene gel alone in maintaining clearance after 20 weeks.[107] Tazarotene can also be combined with phototherapy. An RCT showed tazarotene plus narrowband UVB (NB-UVB) therapy improved the efficacy of phototherapy and decreased the amount of UV radiation needed to achieve 50% or better improvement from baseline using the 6-point global improvement scale.[108]

A double-blind RCT compared the efficacy of tazarotene 0.1% cream with clobetasol 0.05% cream, both under occlusion, for 12 weeks for nail psoriasis. The efficacy was assessed using the Nail Psoriasis Severity Index. At 12 weeks, both groups showed significant improvement in the Nail Psoriasis Severity Index with respect to onycholysis, pitting,

*References 12,20,22,39,65-69,72-80,82-84,86,95-101.

Table VIII. Level of evidence for vitamin D analogues

Recommendation	Reference number	Level of evidence	Studies
Topical vitamin D analogues therapy	3.1	I-II	12,20,22,65,96
Treatment with calcipotriene foam and calcipotriene plus betamethasone dipropionate gel for scalp psoriasis	3.2	I	66-68,97
Topical tacalcitol ointment or calcipotriene combined with hydrocortisone for facial psoriasis	3.3	I-II	69,72
Combination treatments with vitamin D analogues and potent topical corticosteroids for psoriasis	3.4	I-II	73-80,85,98
Combination products with calcipotriene and corticosteroids for psoriasis	3.5	I-III	82-84,99-101
Application of vitamin D analogues twice daily on weekdays in conjunction with high-potency topical corticosteroids twice daily on weekends	3.6	II	39
Morning high-potency topical corticosteroids and evening topical vitamin D analogues	3.7	II	86

hyperkeratosis, and oil spots (salmon patches). Additionally, the difference in efficacy between both groups was not statistically significant.[109] A smaller double-blind, placebo-controlled clinical trial with 31 patients assessed the efficacy of tazarotene for the treatment of nail psoriasis. After 24 weeks of treatment, tazarotene 0.1% gel showed a significantly greater reduction of onycholysis (in occluded and nonoccluded nails) and pitting (in occluded nails) compared with placebo ($P \leq .05$).[110]

Risks/harms and benefits. Potential adverse effects include erythema, burning, and pruritus and are more prominent at higher concentrations.[111] Avoid the application of the formulation to uninvolved skin to minimize irritation. These adverse effects can be reduced by using a cream formulation or lower concentration formulation, combining tazarotene with moisturizers, applying it on alternate days, or short-contact (30 to 60 minutes) treatment, and combining it with topical corticosteroids.[112] The combination of tazarotene with halobetasol is beneficial because it reduces the irritation caused by tazarotene. Additionally, the combination reduces the amount of topical corticosteroids needed, thereby limiting atrophy produced by halobetasol.[113]

Tazarotene should be avoided in pregnant women. In women of childbearing age, a negative pregnancy test should be obtained 2 weeks before starting tazarotene, according to the package insert.[112] Women of childbearing age should be counseled to discontinue tazarotene if they become pregnant. No human data are available on excretion in human milk. No signs of fertility reduction based on animal studies have been reported.[112]

Contraindication. Tazarotene should not be used in pregnant women.

Topical corticosteroids and tazarotene. The use of a medium- or high-potency topical corticosteroid in combination with tazarotene for 8 to 16 weeks is recommended for the treatment of mild to moderate psoriasis.[114] There may be a synergistic effect when topical corticosteroids are used along with tazarotene, and this combination also increases the duration of treatment effect as well as the time of remission.[107,115] A multicenter RCT of 300 patients with stable plaque psoriasis with 20% BSA or less involved treated with tazarotene 0.1% gel once daily, alone or combined with low-, medium-, or high-potency topical corticosteroids, demonstrated the combination of tazarotene with medium- or high-potency topical corticosteroid increased efficacy while reducing local adverse events.[116] For details related to the treatment of psoriasis with tazarotene monotherapy as well as potential risk/harm, refer to the respective section below. Tazarotene is contraindicated during pregnancy and should be discontinued if pregnancy is recognized.[112]

General comments. Topical tazarotene can be particularly helpful for palmar-plantar psoriasis and nail psoriasis. Topical tazarotene studies have reported similar efficacy to fluocinonide cream, crude coal tar 5% ointment, and calcipotriene 0.005% ointment.[103-105] Topical corticosteroids can be added to topical tazarotene to increase efficacy. Recommendations on the use of topical tazarotene and its supporting evidence can be found in Tables IX and X.[102-108,114-118]

Moisturizers

Efficacy. Nonmedicated moisturizers are available in several formulations (ie, creams, ointments, lotions, gels, etc). They can be used as part of a general treatment regimen for patients with psoriasis to help reduce itching and desquamation.

Table IX. Recommendations and strength of recommendation for topical tazarotene

Reference number	Recommendations	Strength of recommendation
4.1	Topical tazarotene can be used for the treatment of mild to moderate psoriasis	B
4.2	Topical tazarotene can be used for the treatment of nail psoriasis	B
4.3	The combination of topical tazarotene and NB-UVB has been shown to be effective and allow a reduction in total use of NB-UVB	B
4.4	The use of mid- or high-potency topical corticosteroid in combination with tazarotene for 8-16 weeks is more effective than monotherapy with tazarotene and is recommended for the treatment of mild to moderate psoriasis	A
4.5	The use of topical corticosteroids along with tazarotene is recommended to decrease the duration of treatment as well as increase the length of remission	A

NB-UVB, Narrowband ultraviolet B.

Table X. Level of evidence for topical tazarotene

Recommendation	Reference number	Level of evidence	Studies
Tazarotene for mild to moderate psoriasis	4.1	I-III	102-107
Tazarotene for nail psoriasis	4.2	I-II	114,117,118
Tazarotene and NB-UVB combination	4.3	II	108
Monotherapy (tazarotene) vs combination with mid- to high-potency topical corticosteroid for psoriasis	4.4	I	114,116
Synergistic effect of combination therapy	4.5	I	107,115

NB-UVB, Narrowband ultraviolet B.

Emollients, one type of moisturizer, exert their action by retaining moisture in the stratum corneum. An RCT showed the combination of mometasone plus emollient improved the area of palmoplantar skin affected, desquamation, and symptoms compared with mometasone alone after 4 weeks of treatment.[119] Emollients have no known contraindications unless there is hypersensitivity to their ingredients. Recommendations on the use of moisturizers and its supporting evidence can be found in Tables XI and XII.[119,120]

Risks/harms and benefits. There is a small risk of contact dermatitis with some emollients. Emollients, like any other topical agents, may be inconvenient to regularly apply for patients with a large BSA of involvement. Moisturizers are considered safe during pregnancy and lactation.

General comments. Moisturizers can be safely applied several times a day.

Salicylic acid

Efficacy. Salicylic acid is used as a topical keratolytic agent in the treatment of psoriasis. Its mechanism of action is believed to involve the reduction of the binding between keratinocytes; it minimizes scaling and softens psoriatic plaques.[121] Topical salicylic acid use for 8 to 16 weeks is recommended for the treatment of mild to moderate psoriasis. Salicylic acid is effective for the treatment of psoriasis, alone or combined with other topical therapies, including corticosteroids and topical immunomodulators.[52,70,122,123] The improvements in efficacy seen with combination therapy compared with corticosteroid alone is likely due to the increased skin penetration caused by salicylic acid. An open-label study of 10 patients assessed the efficacy of 6% salicylic acid in an ammonium lactate vehicle for the treatment of scalp psoriasis. After 4 weeks of monotherapy, the mean Psoriasis Scalp Severity Index decreased from 15 to 3.[123] An RCT with 408 patients with psoriasis revealed that mometasone 0.1% with salicylic acid was superior to mometasone 0.1% ointment after 21 days of twice-daily use for plaques on upper and lower extremities.[124] Additionally, the combination of tacrolimus with 6% salicylic acid was more effective than salicylic acid plus vehicle.[52]

Risks/harms and benefits. Systemic absorption and increased risk for salicylate toxicity are higher in patients with renal disease and patients with hepatic disease when treating large BSAs (>20%); therefore, its use should be avoided or used with caution in these groups. Topical salicylic acid should not be applied before UVB phototherapy because it reduces its efficacy.[125,126] There are inadequate human data available for the use of salicylic acid during pregnancy/lactation.

Topical corticosteroids and salicylic acid. The combination of salicylic acid with topical corticosteroids can be used for the treatment of moderate to severe psoriasis (BSA ≤20%) as well as palmar-plantar psoriasis. Two randomized multicenter studies demonstrated the addition of salicylic acid to mometasone furoate is safe

Table XI. Recommendations and strength of recommendation for emollient

Reference number	Recommendations	Strength of recommendation
5.1	The use of an emollient in conjunction with topical corticosteroids for 4 to 8 weeks can be used to help reduce itching, desquamation, and total body surface area and prevent quick relapse of psoriasis when topical corticosteroids are discontinued	B

and more effective than mometasone alone.[124,127] High-potency topical corticosteroids can be used in combination with salicylic acid, but caution must be used to ensure only small quantities of the high-strength corticosteroid are used to reduce the potential risk of systemic absorption of the corticosteroid. Recommendations on the use of topical salicylic acid and its supporting evidence can be found in Tables XIII and XIV.[52,70,122-124,127]

Anthralin (dithranol)

Efficacy. Anthralin (dithranol) is a polycyclic aromatic hydrocarbon derivative. The exact mechanism of action of anthralin is not fully understood, although it is thought to be mediated by preventing T-lymphocyte activation and promoting keratinocyte differentiation.[128]

Topical anthralin is effective in the treatment of psoriasis.[129-132] The recommended treatment for mild to moderate psoriasis is 8 to 12 weeks of topical anthralin starting at 0.1% concentration, with increasing concentration over time as tolerated. Short contact (up to 2 hours per once-daily application) anthralin therapy is recommended to limit adverse effects. Two small RCTs with 12 and 25 psoriasis patients assessed the efficacy of an aqueous gel formulation of anthralin and an anthralin ointment, respectively. After 4 weeks of twice-daily 1-minute treatments, anthralin demonstrated significantly better results than placebo and similar efficacy to topical calcipotriene.[129,130] An RCT of 106 patients that compared calcipotriene and short-contact dithranol showed no statistically significant difference in the quality of life over 12 weeks between the 2 treatments.[131]

Combination treatment of anthralin with excimer laser showed better results than anthralin alone and similar results to the combination of 308-nm laser plus topical calcipotriene.[132] Recommendations on the use of topical anthralin and its supporting evidence can be found in Tables XV and XVI.[129-132]

Table XII. Level of evidence for emollient

Recommendation	Reference number	Level of evidence	Studies
Emollients in conjunction with topical corticosteroid therapy	5.1	II	119,120

Risks/harms and benefits. Adverse effects include perilesional erythema, burning, and mild-to-severe staining of the skin. These are improved by using the short-contact application method (up to 2 hours). Application to the face or other highly visible areas should be avoided. There is no evidence of any topical or systemic toxicities related to prolonged anthralin use. No data are available on human milk excretion.

Precaution. Anthralin can temporarily stain the skin, and application to the face or other highly visible areas should be avoided. The use of anthralin on the face and flexures should be avoided.

Coal tar/LCD

Efficacy. Coal tar/LCD, a distillation product from coal, is a heterogeneous mixture of thousands of chemical compounds. Its composition differs between preparations. Coal tar has been used for the treatment of psoriasis for more than a century. The polyaromatic hydrocarbons bind to the aryl hydrocarbon receptor, and tar is known to decrease keratinocyte proliferation by suppressing DNA synthesis. It also suppresses inflammation and may affect immunologic function. Several clinical trials and a systematic review have shown the efficacy of coal tar in the treatment of psoriasis.[77,78,111,133-138] The use of coal tar preparations is recommended for the treatment of mild to moderate psoriasis. An RCT compared 1% coal tar lotion with 5% coal tar extract among 324 patients with mild to moderate psoriasis. The improvement in Total Sign Score was better in patients treated with 1% lotion than with 5% extract (−10.6%; 95% CI, −20.6% to −0.5%; $P = .04$).[133] Another RCT of 60 patients compared LCD 15% solution and calcipotriene 0.005% cream. The LCD group had greater mean reductions in PASI scores than the calcipotriene group at 12 weeks (58% vs 37%; $P < .05$).[78] Coal tar can also be combined with NB-UVB, resulting in reduction of the time to clearance and improved therapeutic outcome compared with NB-UVB alone.[137,138] An example of that is Goeckerman therapy, which consists of the application of coal tar and exposure to NB-UVB light.

Table XIII. Recommendation and strength of recommendation for salicylic acid

Reference number	Recommendations	Strength of recommendation
6.1	Topical salicylic acid can be used for 8-16 weeks for the treatment of mild to moderate psoriasis	B
6.2	The combination of salicylic acid with topical corticosteroids can be used for the treatment of moderate to severe psoriasis (body surface area ≤20%)	B

Table XIV. Level of evidence for salicylic acid

Recommendation	Reference number	Level of evidence	Studies
Topical salicylic acid for mild to moderate psoriasis	6.1	I-II	52,70,122-124
Salicylic acid plus topical corticosteroid for psoriasis	6.2	I	124,127

Risks/harms and benefits. The risks of coal tar application include local irritation, folliculitis, contact dermatitis, and phototoxicity. Possible carcinogenicity has remained controversial, but not proven. Dermatologic studies on topical preparations have not revealed an increased risk, but animal and occupational studies document carcinogenicity with prolonged exposures over many years.[139,140] A retrospective analysis of human use of coal tar preparations during pregnancy has not shown any adverse effects on the fetus, although in animal studies, large doses have been observed to increase the risk of cleft palates, small lungs, and perinatal mortality.[141,142] Thus, it may be advisable to avoid the use of coal tar preparations during pregnancy and lactation.[36,143] Coal tar preparations have frequently been used in conjunction with phototherapy. While the application of coal tar 1 day before phototherapy may be helpful, the application just before phototherapy can cause tar pigmentation. Refer to the joint AAD-NPF guideline on phototherapy in reference to Goeckerman therapy.[90] Recommendations on the use of coal tar and its supporting evidence can be found in Tables XVII[90] and XVIII.[77,78,111,133-138,144,145]

Precaution. Coal tar products can stain clothes, and tar odor is present in most preparations, thus reducing patient adherence.

Table XV. Recommendation and strength of recommendation for topical anthralin

Reference number	Recommendation	Strength of recommendation
7.1	Topical anthralin for 8-12 weeks can be used for the treatment of mild to moderate psoriasis. Short contact (up to 2 hours per day) anthralin is recommended to limit adverse side effects	B

Table XVI. Level of evidence for topical anthralin

Recommendation	Reference number	Level of evidence	Studies
Topical anthralin for mild to moderate psoriasis	7.1	I-III	129-132

Topical agents in combination with systemic therapies

Topical agents in combination with biologics. All topical corticosteroids can be used with biologic agents for the treatment of psoriasis. The addition of an ultrahigh-potency (class 1) topical corticosteroid to standard-dose etanercept led to improved efficacy without any increased safety concerns.[146] This advantageous effect of combination therapy at 12 weeks disappeared by 24 weeks.[146] The addition of calcipotriene/betamethasone to standard-dose adalimumab resulted in higher efficacy than adalimumab monotherapy at 4 weeks, but at 16 weeks, there was no difference in efficacy between the 2 groups (Tables XIX and XX).[146,147]

Topical agents in combination with nonbiologic therapies

Topical calcipotriene and methotrexate. The addition of topical calcipotriene to standard-dose methotrexate leads to lower cumulative doses of methotrexate and increased time to relapse after its discontinuation.[148] A multicenter RCT (vehicle-controlled) demonstrated that when calcipotriene was added to weekly methotrexate, calcipotriene decreased the necessary dosing of methotrexate from 9.9 to 6.5 mg per week (P = .002) (Tables XXI and XXII).[148]

Topical agents and cyclosporine. The addition of calcipotriene/betamethasone dipropionate ointment to low-dose cyclosporine (2 mg/kg/d) enhances the clinical response of cyclosporine. An open-label RCT of patients with moderate to severe

Table XVII. Recommendations and strength of recommendation for coal tar

Reference number	Recommendation	Strength of recommendation
8.1	Coal tar preparations are recommended for the treatment of mild to moderate psoriasis	A
8.2	According to the joint AAD-NPF phototherapy guideline,[90] there is sufficient evidence to recommend the use of Goeckerman therapy for the treatment of psoriasis	B

AAD, American Academy of Dermatology; *NPF*, National Psoriasis Foundation.

Table XVIII. Level of evidence for coal tar

Recommendation	Recommendation number	Level of evidence	Studies
Use of coal tar for psoriasis	8.1	I-II	70,71,104,133-138
Goeckerman therapy for psoriasis	8.2	II-III	144,145

psoriasis demonstrated that 30 patients given 2 mg/kg/d cyclosporine along with calcipotriene/betamethasone had a significantly higher PASI 75 at 8 weeks of treatment than 30 patients treated with 2 mg/kg/d cyclosporine with emollient placebo ointment (87% vs 37%; $P = .0001$) (Tables XXIII and XXIV).[149]

Topical calcipotriene and acitretin. The addition of calcipotriene ointment to the standard dose of acitretin can improve the efficacy of acitretin. A multicenter RCT of 135 adults with severe psoriasis demonstrated a greater rate of clearance and marked improvement in the combination group compared with acitretin alone (67% vs 41%; $P = .006$).[4] There were no differences in safety between the 2 groups (Tables XXV and XXVI).[4]

Role of patient preferences—with topical agents. The optimal vehicle choice is often the one the patient is most likely to use. For example, hair-bearing areas, such as the scalp, are often successfully treated with solutions, shampoos, foams, oils, gels, or sprays. In general, creams are more cosmetically acceptable than ointments for glabrous skin. Nevertheless, some patients do prefer ointments.

It is recommended that clinicians take into account patient preference when selecting the most appropriate vehicle, recognizing different vehicles may have a different clinical impact on patients and their adherence to treatment. It is important for the health care provider to be aware of the different vehicles available to provide the best option for each patient on a case-by-case basis.

Compounding of topical agents. Compounding by reputable pharmacies of topical agents is frequently used in clinical practice and is beneficial in certain patients pending the quality of the ingredients and the quality of the compounding.

This concludes the portion of the AAD-NPF Joint Guideline on care for the management of psoriasis with topical therapy. The following section of this joint guideline will focus on the use of alternative medicine (AM) for the treatment of psoriasis. The workgroup provided their expert opinion on AM therapy and is not part of evidence-based recommendations. Furthermore, the joint guideline also discusses the severity measures of psoriasis used in clinical practice and trials as well as patient-reported outcomes.

II. ALTERNATIVE MEDICINE

AM can be defined as a set of products and practices that are believed to have similar or better healing effects than allopathic medicine. Nevertheless, in many cases, their effectiveness may not have been established using scientific methods or may have not shown similar or superior results compared with conventional medications. AM is not typically part of conventional medical care or has origins outside of usual Western practice and may be desired by, and be of benefit to, a subset of patients. Complementary AM consists of the use of AM together with conventional medical treatment, based on the belief that it improves the effect of medical treatments.

Traditional Chinese medicine

Efficacy. Traditional Chinese medicine is an approach commonly used in China for patients of varying psoriasis severity and includes topical and oral herbs as well as acupuncture and other therapeutic modalities. Herbal methods should only be considered and incorporated if the ingredients within the herbal blends are known and well understood. Acupuncture has been used for the therapy of psoriasis, especially mild to moderate with responses relatively minor.

Several clinical trials have assessed the efficacy of herbal medicine (HM) for the treatment of psoriasis.

Table XIX. Recommendations and strength of recommendation for the combination of topical agents with biologics

Recommendation number	Recommendation	Strength of recommendation
9.1	The addition of an ultrahigh potency (class 1) topical corticosteroid to standard dose etanercept for 12 weeks is recommended for the treatment of moderate to severe psoriasis	A
9.2	The addition of calcipotriene/betamethasone to standard dose adalimumab for 16 weeks is recommended for the treatment of moderate to severe psoriasis to accelerate clearance of psoriatic plaques.	B
9.3	All topical corticosteroids can be used in combination with any biologics for the treatment of moderate to severe psoriasis	C

Table XX. Level of evidence for the combination of topical agents with biologics

Recommendation	Recommendation number	Level of evidence	Studies
Addition of class 1 topical corticosteroid to standard dose etanercept for psoriasis	9.1	I	[146]
Addition of calcipotriene/betamethasone to standard dose adalimumab for psoriasis	9.2	III	Expert opinion
Topical corticosteroid with biologic for treatment of psoriasis	9.3	III	Expert opinion

Table XXI. Recommendation and strength of recommendation for the combination of topical calcipotriene and methotrexate

Recommendation number	Recommendation	Strength of recommendation
10.1	The addition of topical calcipotriene to standard dose methotrexate therapy is recommended for the treatment of moderate to severe psoriasis. It may lead to lower cumulative doses of methotrexate and increased time to relapse after methotrexate discontinuation	A

Table XXII. Level of evidence for the combination of topical calcipotriene and methotrexate

Recommendation	Recommendation number	Level of evidence	Studies
Calcipotriene and methotrexate for psoriasis	10.1	I	[148]

A systematic review of topical HM for the treatment of psoriasis found that *Mahonia aquifolium*, indigo naturalis, and *Camptotheca* sp showed anti-inflammatory benefits compared with the vehicle. Adding these topical HMs to conventional pharmacotherapy appeared to produce additional clinical benefits. Nevertheless, the author mentions the lack of standardization as a weakness of the included studies and states further research is needed to assess the efficacy and safety of these HMs as adjunct therapies for psoriasis.[150] An RCT assessed the efficacy of indigo naturalis extract in oil (lindioil) vs olive oil for the treatment of nail psoriasis. After 12 weeks of twice-daily treatment, there was a significant difference in Nail Psoriasis Severity Index reduction for 1 hand of 48.9% for the lindioil group vs 22.9% for the olive oil group.[151]

A RCT with 56 patients with psoriasis assessed the efficacy of electrostimulation by intramuscularly placed needles plus ear acupuncture or placebo (minimal acupuncture) twice weekly for 10 weeks. After 10 weeks of treatment, the mean PASI had

Table XXIII. Recommendation and strength of recommendation for combination of topical agents and cyclosporine

Recommendation number	Recommendation	Strength of recommendation
11.1	The addition of calcipotriene/betamethasone dipropionate ointment to low dose (2 mg/kg/d) cyclosporine can be used for the treatment of moderate to severe psoriasis	B

Table XXIV. Level of evidence for the combination of topical agents and cyclosporine

Recommendation	Recommendation number	Level of evidence	Studies
Cyclosporine and calcipotriene/betamethasone dipropionate for psoriasis	11.1	I	[149]

Table XXV. Recommendation and strength of recommendation for the combination of calcipotriene and acitretin

Recommendation number	Recommendation	Strength of recommendation
12.1	The addition of calcipotriene to standard dose acitretin is recommended for the treatment of moderate to severe psoriasis.	A

decreased from 9.6 to 8.3 in the active group and from 9.2 to 6.9 in the placebo group ($P < .05$ for both groups), with no statistically significant differences between the 2 groups. The benefit seen with minimal acupuncture may indicate a positive placebo effect from the perception of attention paid to the patient and mere interest in a holistic approach on the part of a practitioner.[152]

Table XXVI. Level of evidence for the combination of calcipotriene and acitretin

Recommendation	Recommendation number	Level of evidence	Studies
Calcipotriene and acitretin for psoriasis	12.1	I	[4]

A single-blind RCT compared "auricular therapy" (pressure and blood-letting puncture of the auricular points on the back of the ear) plus optimized Yinxieling formula with Yinxieling formula alone in 84 patients with psoriasis. Optimized Yinxieling formula is composed of *Radix paeoniae rubra*, *Rhizoma curcumae*, sarcandra, *Radix glycyrrhizae*, *Fructus mume*, *Radix arnebiae*, and *Rhizoma smilacis glabrae*. After 8 weeks of treatment, the PASI reduction in the combination treatment group was 74.4% (32 of 43) compared with the optimized Yinxieling formula alone group (36.6%, $P < .01$).[153]

An open-label RCT with 60 patients with psoriasis using Yin Xie Ping granules vs Xiao Yin Pian (known HM to treat psoriasis as control) found no significant difference between the 2 groups.[154] The clinical improvement determined as cured and markedly effective was achieved by 61.67% and 50% patients in Yin Xie Ping and control group, respectively. Yin Xie Ping is compounded with *Radix rehmanniae*, *Radix angelicae formosanae*, powder of *Carapax eretmochelys*, *Radix paeoniae rubra*, *Calculus bovis artificial*, and *Herba schizonepetae tenuifoliae*. Xiao Yin Pian is compounded with *Radix rehmanniae*, *Cortex moutan*, *Radix paeoniae rubra*, *Sophora flavescens*, honeysuckle, *Radix sappan*, *Arctium lappa*, *Folium isatidis*, and safflower.

A systematic review of studies comparing UVA and UVB phototherapy with and without herbal baths showed that herbal baths appeared to improve response to phototherapy, but the lack of standardization makes results difficult to interpret and replicate.[155] The HM formula used for the bath varied across the 13 studies analyzed. The most frequently used herbs were *Salvia miltiorrhiza* root, *Dictamnus dasycarpus* bark, *Sophora flavescens* root, and *Kochia scoparia* fruit. The HM bath was taken for 20 to 30 minutes before each phototherapy session.

Risks/harms and benefits. Constituent herbs can be difficult to elucidate in Chinese herbal blends, thereby making allergy and toxicity risk difficult to predict. Some formulations of herbal remedies have been found to contain corticosteroids.[156,157] Topical indigo naturalis must be carefully formulated by a

compounding or integrative pharmacist to minimize the natural purple staining effect of the crude extract.

Exclusions. There is little information on the effects of HM for psoriasis treatment during pregnancy or lactation. Because of the unknown effects on the fetus or infant, they should be avoided during pregnancy and breastfeeding and if there is a known allergy to prevent potential toxicity from herbal blends.

Role of patient preferences. Many patients undergo acupuncture for a variety of health reasons. Several insurance companies reimburse for acupuncture. Interest on the part of patients is high.[158]

General comments. Traditional Chinese medicine is by definition an individualized medical practice based on each patient's constitution and therefore is difficult to study in an aggregate model. Additionally, the lack of standardized clinical trials makes it very difficult to clearly assess the efficacy of these treatments. Understanding traditional Chinese medicine requires an intense background in herbology, which is lacking in traditional allopathic medical curricula.

Aloe vera

Efficacy. *Aloe vera* (AV) is a succulent plant species of the genus *Aloe*. Its use has been documented in medicine for centuries. In patients who are not allergic to AV, topical AV may be efficacious for mild psoriasis. An RCT with 60 patients with psoriasis comparing thrice-daily application of AV vs placebo for 4 weeks reported 83.3% cure rate (complete clearance) in the AV group vs 6.6% in the placebo group.[159] A double-blind RCT with 40 patients assessing AV vs placebo showed no difference between the 2 groups after 4 weeks of twice-daily application.[160] Furthermore, the clinical score sum of erythema, infiltration, and desquamation decreased in 72.5% in the AV-treated areas compared with 82.5% in placebo-treated areas after 12 weeks.[160] Despite the placebo effect being elevated and higher than that of AV, the clinical effect of AV was not negligible. Nevertheless, it should be noted that AV might not be better than just an emollient. Additionally, topical and oral use of AV can cause skin irritation, hives, cramping, and diarrhea to those who are allergic to other plants related to the lily family, for example, onion and tulips.[161,162]

Risks/harms and benefits. There is a risk of contact dermatitis with AV use.

Contraindication. Treatment should not be used in patients who are allergic to AV.

Role of patient preferences. For patients who are interested in trying a plant-based treatment for their mild psoriasis, AV may be a reasonable consideration.

St John's wort

Efficacy. Topical St John's wort may improve mild psoriasis, but its compounding is not standardized or well-studied enough to recommend its use. There is limited literature on this subject. A split-body study with compounded topical St John's wort cream showed a significant modified PASI reduction at 4 weeks compared with vehicle alone ($P < .04$).[163] This study demonstrated a reduction in erythema, lesional thickness, and scaling over 4 weeks.

Risks/harms and benefits. Owing to St John's wort photosensitizing effect, caution exists for burns and sunburns, especially for psoriasis patients undergoing phototherapy.

Exclusions. St John's wort is photosensitizing when administered topically and orally. Caution should be exercised in patients with a history of skin cancer or continued heavy sun exposure, or both, including phototherapy. Safety in pregnant and nursing women is unknown.

Role of patient preferences. Considering an increasing number of patients asking about nonprescription and natural options for psoriasis, further studies are required to better assess the role of St John's wort in psoriasis.

General comments. Because St John's wort is a supplement that is generally used for potential antidepressive effects, a potential therapeutic role in psoriasis may also exist in the area of stress reduction if taken orally.

Fish/omega-3 oil

Efficacy. Fish oil may exert an anti-inflammatory effect via inhibition of inflammatory eicosanoid formation. Fish oil/omega-3 fatty acid oral supplementation has been useful as a monotherapy for psoriasis.[164,165] Oral fish oil supplementation may augment the effects of topical, oral-systemic, and phototherapy for chronic plaque psoriasis. It can be considered as an additional supplement in patients with chronic plaque psoriasis.[166-170] Fish oil can be useful as adjuvant therapy for treatments, including acitretin, cyclosporine, and NB-UVB.[171,172] A randomized 12-week open study revealed that etretinate and eicosapentaenoic acid supplementation for patients with chronic stable plaque psoriasis had better and more rapid improvement compared with etretinate alone.[173]

Risks/harms and benefits. Owing to contaminants, fish oil supplementation can cause mercury

poisoning or accumulation of other toxins such as dioxins and polychlorinated biphenyls.[174-176]

Exclusions. Caution should be exercised in pregnant women. Patients should be instructed to select supplements that are free of mercury, dioxin, and polychlorinated biphenyls. Fish oil can reduce platelet aggregation, but this effect did not increase bleeding risk during or after surgery in RCTs.[177,178]

Role of patient preferences. Considering an increasing number of patients frequently asking about nonprescription and natural treatment options for psoriasis, further studies are required to better assess the role of fish oil supplementation/omega-3 fatty acids in psoriasis.

Vitamin D supplementation

Efficacy. While topical vitamin D analogues have benefit in psoriasis, oral supplementation does not directly improve disease activity at dosages that avoid hypercalcemia and calciuria.[179-183] Therefore, oral vitamin D supplementation is not recommended for the treatment of psoriasis.[183]

Risks/harms and benefits. Excess vitamin D supplementation may lead to hypercalcemia.

Precaution. The studies reviewed here do not include pregnant or lactating women, or children.

Role of patient preferences. Many patients ask about the overall role of vitamin D in skin health. Rather than adding oral vitamin D supplementation, topical therapy with vitamin D agents is effective for the treatment of psoriasis.

Curcumin

Efficacy. Curcumin is the active chemical in the spice turmeric. Curcumin modulates T-helper type 22 cell activity and decreases epidermal proliferation via inhibition of adenosine-5'-triphosphate—phosphorylase b phosphotransferase activity, similar to topical vitamin D_3 analogues.[184] Piperine derived from black pepper greatly enhances the absorption of dietary curcumin.[185] While there is limited literature on this subject, oral curcumin supplementation may benefit patients with psoriasis as adjunctive therapy.

Risks/harms and benefits. Curcumin has low toxicity but poor bioavailability.

Role of patient preferences. Patients increasingly ask about nonprescription or natural options for psoriasis. Further studies are required to better assess the role of curcumin in psoriasis.

Zinc

Efficacy. There is limited literature on the efficacy of zinc for the treatment of psoriasis. Oral zinc supplementation did not independently improve psoriasis severity (PASI scores) and therefore is not recommended.[186]

Risks/harms and benefits. Oral zinc has been associated with headaches, nausea, vomiting, decreased appetite, diarrhea, and abdominal cramps.[187] In high doses with prolonged use, oral zinc can have more severe adverse effects such as low copper, anemia, leukopenia, neutropenia, and gastrointestinal ulcers.[187]

Role of patient preferences. Patients are increasingly interested in taking oral supplements. Further studies are required to better assess the role of zinc supplementation in psoriasis.

Gluten-free diet

Efficacy. Gluten is a group of proteins present in various cereal grains that are associated with hypersensitivity and celiac disease in certain patients. A small percentage (4%-14%) of patients with moderate to severe plaque psoriasis have a higher incidence of celiac disease and therefore should be asked about gastrointestinal symptoms of celiac disease.[188-191] If patients have a positive serology for the disease or have gastrointestinal symptoms of celiac disease, consultation with a gastrointestinal physician to confirm celiac disease with small intestine biopsy and manage the disease is advised. Adherence to a gluten-free diet is part of the treatment plan only for patients with confirmed celiac disease.[191-193]

Patients testing positive to celiac antibodies may not benefit from a strict gluten-free diet in terms of PASI improvement, because they may not have actual celiac disease. The diagnosis of celiac disease is not just based on symptoms and serology, and patients should be referred to a gastroenterologist for diagnosis and management. For patients who are already following restricted diets (vegetarian, vegan, nut-free, etc.) due to personal choice or other medical conditions (including food allergies) and are now planning to eliminate gluten, consultation with a nutritionist is strongly suggested to optimize nutrition and assist in meal planning. A gluten-free diet is inadvisable from a psoriasis treatment perspective unless the patient has a confirmed diagnosis of celiac disease.

Role of patient preferences. Patients often ask about the role of diet in skin health, and many would be interested in incorporating a gluten-free diet if applicable and potentially beneficial. Others would find this diet a detriment to their quality of life.

Hypnosis

Efficacy. Hypnosis is a state characterized by focused attention and an increased capacity to

respond to suggestions. Hypnosis should be considered a therapeutic adjunct for highly hypnotizable patients with mild to moderate psoriasis. However, there is limited literature on this subject. A small pilot trial in 11 patients with psoriasis showed a significant improvement in the PASI score and attainment of PASI 75 compared with neutral hypnosis after 3 months of weekly hypnosis ($P < .001$).[194]

General comments. These recommendations would not apply to patients who are not highly hypnotizable. Access to a trained hypnotherapist would limit the ability to incorporate this therapy.

Role of patient preferences. Patients must be interested in and amenable to hypnosis for optimal benefit. Further studies are required to better assess the role of hypnosis in psoriasis.

Stress reduction

Efficacy. Stress reduction includes a wide spectrum of techniques aimed at controlling a person's stress level. Meditation as a form of stress reduction can have a positive impact on the severity of symptoms in some patients with psoriasis. Therefore, it can be discussed as adjunctive therapy with interested patients. A small study assessing different meditation techniques as adjunctive therapy in patients with mild to moderate psoriasis treated with topical therapies showed improvement of psoriasis symptoms after 12 weeks compared with no adjunctive treatment.[195] There is evidence that guided mindfulness meditation improves outcomes in patients with moderate psoriasis qualifying for phototherapy.[196] Biofeedback and relaxation techniques (progressive and suggestive) may improve symptoms in some patients with mild psoriasis and should also be considered for adjunctive therapy.[197] Psychologic interventions in the form of stress reduction techniques, cognitive behavioral therapy, and guided imagery can improve psoriasis severity and should be discussed with all interested patients.[198] Data are limited on this subject, and further research is needed.

Risks/harms and benefits. While studies are limited and data are lacking, individual treatment responses are positive, with little to no adverse effect of these adjunctive recommendations (expert opinion).

Work and other time constraints may be a limiting factor for some patients to engage in a guided meditation or relaxation strategies, but interested patients can be taught a self-guided practice that can be tailored to any schedules.

Biofeedback is time-consuming and requires specialized equipment.

Role of patient preferences. Patients' interest in, and receptiveness to, mindfulness meditation practices may influence the degree of therapeutic efficacy. Further studies are required to assess the role of stress reduction in psoriasis. Supplementary statements for complimentary alternative medicine can be found in Table XXVII.[†]

This concludes the portion of the AAD-NPF joint guideline on AM. The following section of this joint guideline will focus on severity measures for psoriasis.

III. PSORIASIS SEVERITY MEASURES

Body surface area

Recommendations. BSA, one of the most commonly used measures in clinical and research dermatology, is recommended to assess the severity of psoriasis as well as the response to treatment in the clinical setting.[213-217] It is calculated by using the area from the wrist to the fingers and thumb of the hand closed together to represent ~1% of the patient's BSA.[218] Its use can be simplified by rounding up the percentage of BSA corresponding to different parts of the body. The head and neck, upper extremities, trunk, and lower extremities (including buttocks) correspond to approximately 10%, 20%, 30%, and 40% of the BSA, respectively. Refer to *AAD pay-for-performance Measure 410* for further details.[218]

Patient preferences play a primary role in determining the final treatment target and treatment. A full discussion should be offered to the patient regarding the treatment options and expected benefits, risks, and outcomes in order to facilitate a shared decision-making approach.

The reassessment of disease severity and response to therapy can be performed regularly and adjustments to therapy made as necessary. In particular, if the patient is dissatisfied with clinical responses, a different therapy should be considered. Individual patient preferences and comorbidities are important in the final treatment plan. If a patient is satisfied with their results, they should continue treatment even if it does not meet the target or recommended improvement. Recommendations on the use of BSA and its supporting evidence can be found in Tables XXVIII and XXIX.

Pitfalls (or limitations) in assessment. BSA can be overestimated, particularly by untrained providers.[219-223] Nevertheless, BSA assessment has good

[†]References 150-155,159,160,163,164,166-168,170-173,179,182,184,186,188-212.

Table XXVII. Supplementary statements for complementary alternative medicine*

Therapy	Statement	Studies
Traditional Chinese medicine (TCM)*	Herbal methods should only be considered and incorporated if herbal blends are well understood and if working with practitioners experienced in dermatology and in TCM Acupuncture may have a therapeutic effect on chronic plaque psoriasis and can be considered as adjunctive therapy in psoriasis based on patient interest and practice availability **Risk/harm and benefits** • Topical indigo naturalis must be carefully formulated by a compounding or integrative pharmacist to avoid the natural purple staining effect of the crude extract • Constituent herbs can be difficult to elucidate in Chinese herbal blends, thereby making allergy and toxicity difficult to predict • The benefit seen with "sham" acupuncture may indicate a positive placebo effect from the perception of attention paid to the patient and mere interest in a holistic approach on the part of a practitioner **Exclusions** • Safety in pregnancy and breastfeeding are unknown. Potential allergy and toxicity risk exist from undifferentiated herbal blends	150-155,199-202
*Aloe vera**	In patients who are not allergic, topical *Aloe vera* may have efficacy in the treatment of mild psoriasis **Risk/harms and benefits** • There is a risk of contact dermatitis in patients who use *Aloe vera* **Exclusions** • Treatment should not be used in patients who are allergic to *Aloe vera*	159,160
St John's wort*	Topical St John's wort may lower the PASI score but is not standardized, commercially available, or well studied enough to recommend its use **Risk/harms and benefit** • Owing to the photosensitizing effect, caution exists for burns and sunburns, especially for psoriasis patients undergoing phototherapy **Exclusions** • St John's wort is known to be photosensitizing if taken orally, and this same consideration exists for topical administration. Caution should be exercised in patients with a history of skin cancer and/or continued heavy sun exposure, including phototherapy. Safety in pregnant and nursing women is unknown	163
Fish oil*	Fish oil/omega-3 fatty acid supplementation is not useful as monotherapy, but may augment the effects of other topical and oral or systemic therapies and phototherapy for chronic plaque psoriasis and may be considered in those patient populations **Risk/harms and benefits** • Owing to contaminants, fish oil supplementation can cause mercury poisoning or accumulation of other toxins such as dioxins and polychlorinated biphenyls (PCBs) **Exclusions** • Caution should be exercised in pregnant women. Patients should be instructed to select supplement sources that are free of mercury, dioxin, and PCBs. The risk of bleeding with fish oil has been generally determined to be not real	164,166-168, 170-173,203,204

Continued

Table XXVII. Cont'd

Therapy	Statement	Studies
Vitamin D supplementation*	Although it is established that topical vitamin D analogues have benefit in psoriasis, oral supplementation does not directly improve disease activity at dosages that avoid hypercalcemia and calciuria **Risk/harms and benefits** • Excess vitamin D supplementation may lead to toxicity in the form of hypercalcemia **Exclusions** • Role of vitamin D oral supplementation in pregnant/lactating women or children not included	179,182,205,206
Curcumin*	Oral curcumin supplementation may benefit patients with psoriasis of varying severity, as adjunctive therapy	184,207-209
Zinc*	Oral zinc supplementation does not improve PASI scores	186
Gluten-free diet*	Patients with moderate to severe plaque psoriasis may, but not always, have a higher incidence of celiac disease and therefore should be asked about GI symptoms of celiac disease. If identified positive, consultation with GI physician for treatment and management of the disease is advised. Further, adherence to a gluten-free diet is suggested to be part of the treatment plan only for patients diagnosed with celiac disease **Risk/harm and benefits** • Patients testing positive to celiac antibodies may benefit from a strict gluten-free diet in terms of PASI improvement, but also may not. A trial period of 3 months should be considered. Gluten-free diets are restrictive and can impact the quality of life **Exclusions** • For patients who are already following restricted diets (vegetarian, vegan, nut-free, etc) due to personal choice or food allergies and are now planning to eliminate gluten, a nutritionist should be consulted in order to best plan meals and avoid nutritional deficiencies	188-193,210-212
Hypnosis*	Hypnosis can be discussed with and incorporated as a therapeutic adjunct for highly hypnotizable patients with mild to moderate psoriasis	194
Stress reduction*	Meditation as a form of stress reduction can have a positive impact of severity of symptoms in some patients with psoriasis and therefore could be discussed as adjunctive therapy with interested patients Mindfulness meditation (guided) improves outcomes in patients with moderate psoriasis qualifying for phototherapy Biofeedback and relaxation techniques (progressive and suggestive) may improve symptoms in some patients with mild psoriasis and should be considered for adjunctive therapy Psychologic interventions in the form of stress reduction techniques, cognitive behavioral therapy, and guided imagery can improve psoriasis severity and should be discussed with all interested patients **Risk/harm and benefits** • Work and other time constraints may be a limiting factor for some patients to engage in a guided meditation or relaxation strategies but interested patients can be taught a self-guided practice which can be tailored to any schedule • Biofeedback is time consuming and requires specialized equipment	195-198
Other AM therapies	Cannabis and cannabinoids are not infrequently used by patients. Not enough literature is available to justify their use	

AM, Alternative medicine; *GI*, gastrointestinal; *PASI*, Psoriasis Area and Severity Index.
*Supporting suggestions are not evidence based.

Table XXVIII. Recommendation and strength of recommendation for body surface area (*BSA*) severity measure

Recommendation number	Recommendation	Strength of recommendation
13.1	BSA measurement of involved skin is recommended as an important measure of psoriasis severity to risk stratify patient for future comorbidities and to assess response to treatment	B

Table XXIX. Level of evidence for body surface area (*BSA*) severity measure

Recommendation	Recommendation number	Level of evidence	Studies
BSA for severity assessment of psoriasis	13.1	III	Expert opinion

intra-rater reliability.[214,224] The BSA measurement is a provider assessment tool. It does not take into account location on the body, clinical characteristics of the plaques, symptoms, or quality of life issues.

Psoriasis area and severity index

Recommendations. PASI assesses 3 plaque issues—erythema, induration, and scaling—plus the BSA affected and provides a severity score ranging from 0 to 72. In general, a score of ≥10 is considered moderate to severe psoriasis.[218] Refer to *AAD pay-for-performance Measure 410* for further details.[218] PASI is recommended as a measure of psoriasis severity and response to treatment for moderate to severe psoriasis primarily in clinical trials. PASI is primarily a research tool, and its use in clinical practice is infrequent.[215,216,225-229]

Pitfalls (or limitations) in assessment. Various studies have revealed that PASI has reproducible inter-rater and intra-rater reliability.[230-232] Rater experience reduces the variation in the scores.[233,234] The delta of mean PASI and the delta of mean Dermatology Life Quality Index (DLQI), a quality of life assessment tool designed for dermatologic conditions, are highly correlated and showed improvement over a prolonged period of time (6.5 years) when treated with biologics.[235] PASI is responsive to varying degrees of improvement in psoriasis.[236] Additionally, PASI is more strongly correlated with clinical response to initiating biologic therapy than DLQI.[237,238] Nevertheless, PASI is not accurate for mild psoriasis, defined as below 3% BSA affected. The average patient with psoriasis will not have BSA measurements as high as those in clinical trials and research. Furthermore, PASI is not ideal for measuring certain aspects of the disease such as nail, palmoplantar, and genital psoriasis. PASI is not an easily accessible tool to use due to time intensiveness. Thus, PASI is not a frequently used tool in clinical practice.

Table XXX. Recommendation and strength of recommendation for Psoriasis Area and Severity Index (*PASI*) severity measure

Recommendation number	Recommendation	Strength of recommendation
14.1	PASI is a commonly used outcome measure in clinical trials. However, it is seldom used in clinical practice to assess psoriasis severity	B

Table XXXI. Level of evidence for the Psoriasis Area and Severity Index (*PASI*) severity measure

Recommendation	Recommendation number	Level of evidence	Studies
PASI severity assessment tool	14.1	III	215,216, 225-228

General comments. The PASI is a provider assessment tool. PASI has significant evidence as a useful tool in research settings but does not take into account symptoms or quality of life issues. Recommendations on the use of PASI and its supporting evidence can be found in Tables XXX and XXXI.[215,216,225-228]

Physician Global Assessment

Recommendations. The PGA is a scoring system that uses erythema, induration, and scaling. It is suggested as an important measure to assess psoriasis severity and response to treatment.[215,232,233,236,239,240] There are several different PGA versions, with most severity scores ranging from 0 to 4 or 0 to 5.[218] In many clinical trials and research, PGA is used as a primary end point, but

Table XXXII. Recommendation and strength of recommendation for the Physician Global Assessment (*PGA*) severity measure

Recommendation number	Recommendation	Strength of recommendation
15.1	PGA measurement of psoriasis is recommended as an important measure to assess psoriasis severity	B

Table XXXIII. Level of evidence for Physician Global Assessment (*PGA*) severity measure

Recommendation	Recommendation number	Level of evidence	Studies
PGA for severity assessment of psoriasis	15.1	I-III	215,232,233, 236,239,240

Table XXXIV. Recommendation and strength of recommendation for Physician Global Assessment (*PGA*) × body surface area (*BSA*) severity measure

Recommendation number	Recommendation	Strength of recommendation
16.1	PGA × BSA is recommended as an important measure of psoriasis severity	B

Table XXXV. Level of evidence for Physician Global Assessment (*PGA*) × body surface area (*BSA*) severity measure

Recommendation	Recommendation number	Level of evidence	Studies
PGA × BSA for the assessment of psoriasis severity	16.1	II	241-243

its use in clinical practice, while potentially valuable, is infrequent.

The reassessment of disease severity and response to therapy can be performed at intervals and adjustments to therapy as necessary. Refer to *AAD pay-for-performance Measure 410* for further details.[218]

Individual patient preferences and comorbidities are important regarding the final treatment plan. If a patient is satisfied with their results, they should be allowed to continue treatment even if it does not meet the target or recommended improvement.

Pitfalls (or limitations) in assessment. PGA has reproducible inter-rater and intra-rater reliability and validity.[232,233,240] PGA is responsive to varying degrees of clinical improvement.[238] Additionally, PGA and Lattice System-PGA do not require significant experience to achieve reliable results.[233] Plaque quality/morphology does not account for the BSA or the widespread nature of the disease. This is a limitation of the PGA systems.

General comments. The PGA assessment tool is a relatively simple tool to grade and use. It may represent a static measure of the physician's impression at a single point or a dynamic measure in which the physician assesses global improvement from baseline. The PGA does not take into account symptoms or quality of life issues. Recommendations on the use of PGA and its supporting evidence can be found in Tables XXXII and XXXIII.[215,232,233,236,239,240]

PGA × BSA

Recommendations. PGA × BSA can be used as a measure of psoriasis severity and response to treatment. It is not commonly used, although a few dermatologists do use it in clinical practice.

Individual patient preferences and comorbidities are important regarding the final treatment plan. As such, if a patient is satisfied with their results, they should be allowed to continue treatment even if it does not meet the target or recommended improvement. Recommendations on the use of PGA × BSA and its supporting evidence can be found in Tables XXXIV and XXXV.[241-243]

Pitfalls (or limitations) in assessment. BSA can be overestimated, particularly by untrained providers.[219-223] Nevertheless, BSA assessment has good intra-rater reliability.[214,224] PGA has reproducible inter-rater and intra-rater reliability and validity.[232,233,240] PGA is responsive to varying degrees of clinical improvement.[236] The BSA measurement is a provider assessment tool. It does not take into account location on the body, clinical characteristics of the plaques, symptoms, or quality of life issues. Furthermore, the combination of 2 measures adds an extra step that could be detrimental for the practical use of this tool in the clinical setting.

Psoriasis Symptom Inventory

Recommendations. The Psoriasis Symptom Inventory (PSI) is a new patient-reported outcome that has been validated in clinical studies and has the potential to be used in clinical practice.[244-248] The PSI

Table XXXVI. Recommendation and strength of recommendation for Psoriasis Symptom Inventory (*PSI*) severity measure

Recommendation number	Recommendation	Strength of recommendation
17.1	The PSI is recommended as an important patient-reported measure of psoriasis severity with utility in clinical trials. PSI is a new quality of life instrument and has potential to be used in clinical practice and clinical trials	C

measures the severity of 8 psoriasis signs and symptoms: itch, redness, scaling, burning, stinging, cracking, flaking, and pain. Each item is rated on a scale of 0 to 4, yielding a total score ranging from 0 to 32.

Pitfalls (or limitations) in assessment. As a patient-reported outcome, the PSI relies on patients being willing and able to complete the assessment. For patients with cognitive impairment, the PSI may not be feasible or reliable.

General comments. There are paper versions of the PSI available for patient use. Recommendations on the use of PSI and its supporting evidence can be found in Tables XXXVI and XXXVII.[244,247]

Dermatology Life Quality Index

Recommendations. The DLQI is a 10-question questionnaire used to measure the impact of skin disease on the quality of life of an affected person. The DLQI score ranges from 0 to 30. It is a self-reported measure of psoriasis that is recommended to assess psoriasis severity and response to treatment with utility in clinical trials.[218] Refer to the *AAD pay-for-performance Measure 410* for further details.[218] DLQI is used in more than 40 different skin conditions and is not a specific measurement tool for psoriasis.[215,216,225-228,249-253]

Pitfalls (or limitations) in assessment. As a patient-reported outcome, the DLQI relies on patients being willing and able to complete the assessment. For patients with cognitive impairment, the DLQI may not be feasible or reliable.

General comments. The DLQI is a patient-reported severity measure used in more than 40 different skin conditions and in the majority of clinical trials in moderate-severe psoriasis.[218] It is readily used in more than 80 countries and available in more than 85 languages. Recommendations on the use of DLQI and its supporting evidence can be found in Tables XXXVIII and XXXIX.[218,225,226,249-253]

Table XXXVII. Level of evidence for Symptom Inventory (*PSI*) severity measure

Recommendation	Recommendation number	Level of evidence	Studies
PSI for severity assessment of psoriasis	17.1	I-II	244-247

Table XXXVIII. Recommendation and strength of recommendation for the Dermatology Life Quality Index (*DLQI*) severity measure

Recommendation number	Recommendation	Strength of recommendation
18.1	DLQI measurement of psoriasis is recommended as an important measure of psoriasis severity with utility in clinical trials and is seldom used in clinical practice	B

Pruritus assessment

Recommendations. Pruritus is a significant symptom of psoriasis and is often under-recognized. Itch severity assessment is recommended for patients whose psoriasis causes significant pruritus because it can have a major impact on a patient's quality of life. Several tools are available to assess this subjective symptom.[254-270] Nevertheless, at this time there is no recommendation on which tool should be used due to limited evidence. The visual analog scale (VAS) and numeric rating scale (NRS) are 2 of the most commonly used pruritus assessment tools. When assessing patients with these 2 scales, the minimal clinically important difference should be 3 to 4 points for a change to be considered meaningful. Recommendations on the use of pruritus assessment and its supporting evidence can be found in Tables XXXX and XXXXI.[254-273]

CONCLUSION

There is no one measure to completely determine a patient's quality of life. Some patients may have a

Table XXXIX. Level of evidence for the Dermatology Life Quality Index (*DLQI*) severity measure

Recommendation	Recommendation number	Level of evidence	Studies
DLQI is a research tool used in clinical trials	18.1	II-III	225,226, 249-253

Table XXXX. Recommendation and strength of recommendation for pruritus assessment severity measure

Recommendation number	Recommendation	Strength of recommendation
19.1	Pruritus is a significant symptom of psoriasis. An itch severity assessment is recommended to appropriately assess the degree of pruritus when present	B

Table XXXXI. Level of evidence for pruritus assessment severity measure

Recommendation	Recommendation number	Level of evidence	Studies
Itch severity assessment for patients with psoriasis	19.1	II-III	254-270

low severity score, but the affected area may be in a very sensitive location such as the face or hands. This may require escalating the treatment used to treat psoriasis depending on patient preference. Therefore, it is important to work with the patient to determine their satisfaction with the treatment. Similarly, some patients may not be comfortable with certain methods of administration. In these cases, it is also important to work with the patient to determine a treatment modality they are comfortable with. Some patients, for example, may not like using needles; therefore, any treatment relying on needles for self-administration may not be as effective for the patient. Working with the patient will increase adherence to the treatment protocol. There may also be cases in which the patient is satisfied with a less than "clear" outcome. In these cases, it would be necessary to work with the patient to determine what outcome they are satisfied with based on their preferences.

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APPENDIX

Methods

A multidisciplinary workgroup (WG) of psoriasis experts consisting of dermatologists (including private practitioners), a rheumatologist, a cardiologist, and representatives from a patient advocacy organization, was convened to update and expand on the previously published 2008 American Academy of Dermatology (AAD) psoriasis guideline.[127] The WG determined the scope of the guideline and identified important clinical questions with regard to psoriasis treatment with topical agents and alternative medicine (AM) (Table I). WG members completed a disclosure of interests that was periodically updated and reviewed for potentially relevant conflicts of interests throughout guideline development. If a relevant conflict was noted, a balance of conflicted and nonconflicted WG members was used to draft initial recommendations.

An evidence-based model was used, and evidence was obtained using a search of the PubMed and MEDLINE databases from January 1, 2008, to December 31, 2017, for clinical questions addressed in the previous version of this guideline published in 2008-2011, and for all newly identified clinical questions. Searches were limited to publications in the English language. Medical Subject Heading terms used in various combinations in the literature search included psoriasis (vulgaris, plaque, guttate, erythrodermic, pustular, palmoplantar, inverse, nail); topical corticosteroids, calcipotriol, calcineurin inhibitors (tacrolimus, pimecrolimus), combination, switch, failure (primary, secondary), alternate, cessation, emollients, salicylic acid, anthralin, body surface area (BSA), psoriasis area and severity index (PASI), physician global assessment (PGA), psoriasis symptom inventory (PSI), dermatology of life quality index (DLQI), pruritus assessment, traditional Chinese medicine, *Aloe vera*, St John's wort, fish oil, vitamin D, turmeric (curcumin), zinc, hypnosis, meditation, and stress reduction.

After removal of duplicate data, 287 (157 [topical], 66 [severity measures], 64 [AM]) articles 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 as part of the evidence review.

The available evidence was evaluated using a unified system called the Strength of Recommendation Taxonomy 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*). 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 end points 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 where documented evidence-based data is not available, we have used expert opinion to generate our clinical recommendations or opted not to issue a recommendation.

This guideline has been developed in accordance with the AAD/AAD Association Administrative Regulations for Evidence-based Clinical Practice Guidelines (May 2014),[274] 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 is developed in collaboration with the National Psoriasis Foundation (NPF) and as part of the review process; the NPF 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.

Definition

Psoriasis vulgaris is a chronic inflammatory skin disease that classically presents with well-demarcated, red plaques with silvery scale, commonly involving the scalp, elbows, knees, and presacral region, though any area of skin may be involved, including the palms, soles, nails, and genitalia. While the severity of psoriasis is defined in part 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% considered severe disease, psoriasis can be severe irrespective of BSA, when it has serious emotional consequences or when it occurs in select locations, including, but not restricted to, the hands, feet, scalp, face, genital area, or when it causes intractable pruritus. The Psoriasis Area Severity Index (PASI) is a more specific means of quantifying the extent and severity of psoriasis, because it takes into account not only BSA but also the intensity of redness, scaling, and plaque thickness, ultimately producing a score from 0 (no disease) to 72 (maximal disease severity). The PASI is used for monitoring response to treatments in clinical trials and as a research tool to judge the severity of psoriasis. It is rarely used by dermatologists in clinical practice to guide management.

Psoriasis is an inflammatory, immune-mediated condition involving cutaneous T-cells, dendritic cells, and keratinocytes with subsequent release of a variety of cytokines and other soluble mediators. These chemical signals are responsible for keratinocyte hyperproliferation manifesting as characteristic scaly plaques, and they also contribute to the augmented inflammation underlying a number of systemic disease associations, including metabolic syndrome, cardiovascular disease, and psoriatic arthritis. To inhibit the inflammation underpinning this condition, a number of topical and systemic medications have been created with varying success. Topical treatments refer to agents that are applied directly on the skin in order to exert their therapeutic action. AM is a group of diverse medical and health care practices and products that are not presently considered to be part of conventional medicine. These therapies can be defined as alternative when are used in place of conventional treatments and complementary when used together with conventional treatments.