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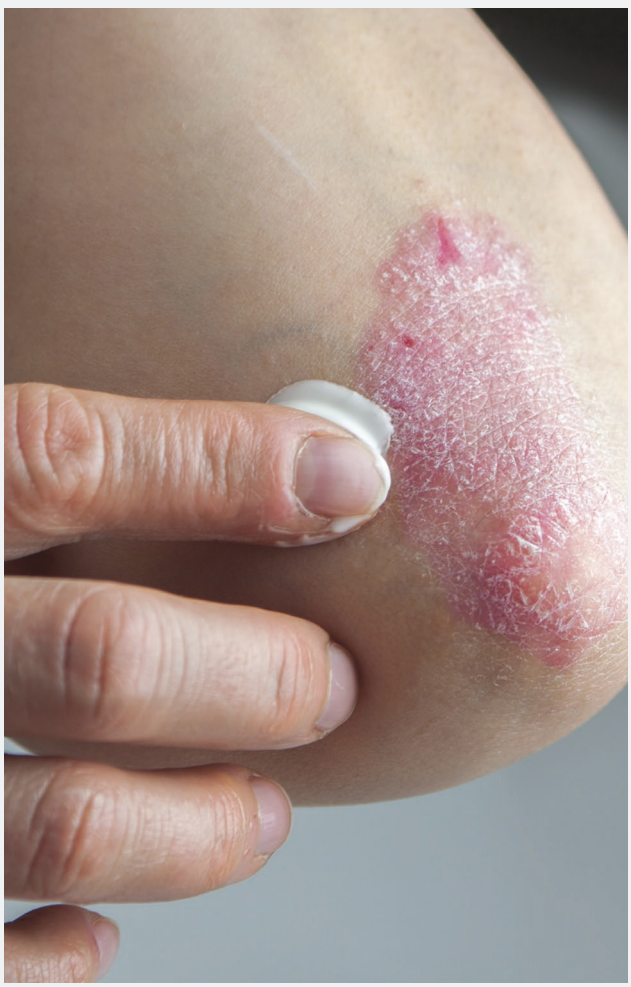

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Continuing Nursing Education: The maximum number of hours awarded for this Continuing Nursing Education activity is 1.5 contact hours. Designated for 0.7 contact hours of pharmacotherapy credit for Advanced Practice Registered Nurses.

Target Audience

This journal supplement is intended for dermatologists, family practitioners, internists, registered nurses, nurse practitioners, physician assistants, and other clinicians who treat patients and practice medical dermatology.

Educational Needs

Most patients with psoriasis will require treatment with topical medications, but patient adherence to topical treatments is low. Adherence may be improved by using more efficacious treatments, considering patient preferences in treatment selection when possible, and simplifying treatment regimens. New formulations using different vehicles to deliver the same active ingredients have been introduced in recent years, with the goal of enhancing penetration, efficacy, and patient acceptance. Commonly used topical agents include corticosteroids, vitamin D analogs, and tazarotene, a retinoid, all of which are available in several vehicles. These medications can be used as monotherapy, but combining topical agents can increase efficacy and sometimes allow for use of lower doses with fewer adverse events. The need to apply multiple medications may complicate adherence, however. Fixed-dose combination treatments, combining 2 active agents in a single vehicle, simplifies the treatment regimen and improves patient acceptance and adherence. Physicians would benefit from education on combination treatment, as well as strategies for improving patient adherence to treatment regimens.

Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Describe the assessment and treatment of patients with psoriasis based on current clinical guidelines and recommendations
- Review the efficacy, safety, and clinical use of current and emerging topical treatments for psoriasis
- Explain strategies to improve clinician-patient communication and the understanding of patient preferences

Disclosure Declarations

Individuals in a position to control the content of this educational activity are required to disclose: 1) the existence of any relevant financial relationship with any entity producing, marketing, reselling, or distributing health care goods or services consumed by, or used on, patients with the exemption of non-profit or government organizations and non-health-care-related companies, within the past 12 months; and 2) the identification of a commercial product/device that is unlabeled for use or an investigational use of a product/device not yet approved.

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Treating Psoriasis: Patient Assessment, Treatment Goals, and Treatment Options

David M. Pariser, MD; Leon H. Kircik, MD; Linda F. Stein Gold, MD

PRACTICE **POINTS**

- The National Psoriasis Foundation (NPF) recommends classifying psoriasis severity by lesion location and effect on quality of life as well as on the percentage of body surface area (BSA) affected. Patients rate itch as the most important factor contributing to severity. Classifying patients as to whether they are candidates for treatment with topical therapy only or require systemic therapy is a useful framework for clinical practice.
- The NPF defines an acceptable treatment response as attaining BSA of no more than 3% or at least 75% improvement from baseline at 3 months, with a target response of BSA less than 1% at 3 months. In clinical practice, treatment goals also depend on patient preferences.
- Many therapies are available to help patients reach the NPF targets and their personal goals. All but one of the newest agents approved by the US Food and Drug Administration for psoriasis yielded Psoriatic Area and Severity Index 75 rates of 80% or more at 12 or 16 weeks in phase 3 clinical trials.

New treatments have revolutionized the care of psoriasis in recent years, enabling patients and clinicians to set aggressive goals for disease clearance. This article reviews the National Psoriasis Foundation recommendations for assessing disease severity, targets for therapy, and follow-up intervals.

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The availability of new and increasingly efficacious topicals and biologics has changed the landscape of psoriasis therapy in recent years.Yet evidence suggests that many patients do not receive adequate care. Nearly 60% of insured patients in the United States with moderate-to-severe psoriasis received no treatment for their condition in the prior year, according a claims data analysis.[1] Nearly one-third (31%) of psoriasis patients (n=735) in a US population-based survey indicated that their current treatment did not meet their primary goals (eg, reducing symptoms, itching, and flaking).[2]

The National Psoriasis Foundation (NPF) has established treatment targets and follow-up intervals to benchmark treatment standards and expectations for patients and providers.[3] Assessment of a patient's disease severity, symptoms, and issues of greatest concern remain the most important factors influencing the choice of treatment goals and therapy.

Assessing Disease Severity

The NPF recommends classifying disease severity by the percentage of body surface area (BSA) affected as well as by lesion location and the disease's effect on the patient's quality of life. BSA less than 3% is defined as mild disease, BSA 3% to 10% is considered moderate disease, and BSA of more than 10% is categorized as severe.[4] US dermatologists responding to a survey (n=150) reported using BSA (95%) and lesions in especially sensitive locations (59%; eg, palms, feet, genital area, face, scalp, and nails) to determine disease severity. About 41% of dermatologists also consider the patient's self-assessment of his or her disease.[5] Dermatologists rated roughly 20% of patients as having severe psoriasis in 1 survey (n=391).[6]

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Patients may think differently about how to define severe disease. In a population-based survey, more than one-third (36%) listed itching as the most important factor contributing to severity, followed by lesion location and size (22%). In a survey of dermatologists, only 12% placed itching in the top 5; 76% listed lesion location and size.[2]

A useful framework for evaluating patients in clinical practice is to ask whether a patient is a candidate for topical therapy only or requires a systemic approach. The latter regimen often will combine oral or injectable medications along with topicals. Indications for systemic therapy include high BSA involvement, psoriatic arthritis, or the presence of lesions in sensitive areas. Dermatologists should ask all patients with psoriasis about the presence of joint pain, regardless of the extent of psoriasis lesions, to identify psoriatic arthritis and prescribe systemic treatment. Missing this diagnosis may result in inappropriate treatment with topical therapy only.

Patients who can apply medication to localized disease and who do not have psoriatic arthritis are candidates for topical therapy only. Patients with lesions in sensitive areas may be treated with topical therapy only or may require a systemic approach. Most patients who need systemic therapy will also receive topical treatment for resistant lesions, as systemic options often do not clear disease completely. Analysis of a US managed care database (2006-2014) to identify treatment of adults with newly diagnosed psoriasis (N=128,308) indicated that 86% received topical therapy. Of those who received any therapy (n=111,962), 83% were given topicals only. Topicals were first-line treatment in almost all (95%) patients who received therapy.[7]

A survey of dermatologists from 26 countries found that most used topicals as first-line monotherapy for patients with BSA less than 3% or BSA 3% to 10% (100% and 88%, respectively). For those with severe disease, topicals were combined with systemic therapy.[8] About three-quarters of patients with moderate-to-severe psoriasis were receiving topical therapy, with 20% given systemic therapy and 20% managed with biologics, according to a survey of North American and European dermatologists (n=391).[6]

Patient assessment can extend to screening for comorbidities associated with psoriasis or referral for such evaluations. Patients with psoriasis have an elevated risk of hypertension, metabolic syndrome, and type 2 diabetes as well as depression, anxiety, and suicidal ideation.[9] By measuring vital signs, dermatologists and other clinicians managing psoriasis may be the first to detect indicators of these comorbidities. Educating patients that psoriasis affects the body beyond the skin and urging them to see a primary care physician (PCP) to monitor those risks is an important part of care. Yet, screening for comorbid disorders is often neglected. Less than half of PCPs and cardiologists responding to a survey (N=251) reported conducting cardiovascular risk factor screening in patients with psoriasis: 43% screened for hypertension, 30% for obesity, 27% for type 2 diabetes, and 11% for dyslipidemia.[10]

Treat to Target: Individualizing the Target

What constitutes a sufficient response to a newly initiated psoriasis therapy? The NPF recommends seeing patients 3 months after starting a new therapy. It defines an acceptable response at that time as attaining BSA of no more than 3% or at least 75% improvement from baseline, with a target response of BSA less than 1%. Patients should be followed thereafter every 6 months, with a target of BSA less than 1%. Not reaching these milestones should prompt a conversation with the patient about re-evaluating the choice of therapy.[3]

In clinical practice, not reaching 1 of the NPF targets at 3 months may not require an immediate change of therapy. As the NPF acknowledges, a single focus on BSA does not consider lesion location, symptoms, health-related quality of life, risk of toxicity, or cost.[3] Patients who do not meet the NPF goals at 3 months may prefer not to increase the dose, add medication, or change therapy immediately because of concerns about adverse events (AEs), cost, or inconvenience. Some patients may need more time to achieve full benefit from a medication. Switching reflexively at 3 months if the patient is near but has not reached the NPF targets may lead to rapid exhaustion of therapeutic options. At some point, however, it is appropriate to discuss a change in therapy with patients who do not meet the treatment target. If the patient is satisfied with the response to treatment and does not want to change or add to it, the current treatment may be continued.

CHANGING TREATMENT AFTER 3 MONTHS

"If the patient is happy at the 3-month mark, I let them go for another 3 months and see where they are. If somebody came in with 60% BSA and now they have 50% BSA at 3 months, I am going to plant the seed that this probably is not our drug."

—Linda F. Stein Gold, MD

Targets may be customized in clinical practice. Patient goals may be personal and specific: eg, to wear sleeveless clothing in the summer or to look good for an important event. Asking the patient about his or her goals is the best way to identify what matters to that individual.

INDIVIDUALIZING TREATMENT TARGETS IN CLINICAL PRACTICE

"When I see a patient with psoriasis for the first time, I always ask them the question, what would you do today, how would your life be different today, if you did not have psoriasis? . . . I write this target on the chart and when they come back the next time . . . I ask about it."

—David M. Pariser, MD

"I do BSA, but I measure success by asking the patient, how are you doing? Are you happy or not? But even if they say I am happy, if they are 10% covered, I will tell them that we have other treatment available. Some will say okay, let's do it, and some will say no, I am happy . . . . The most important measure is how the patient feels."

—Leon H. Kircik, MD

Another set of treatment targets comes from the Medicare Merit-based Incentive Payment System (MIPS). Applied only to patients receiving systemic therapy for psoriasis for 6 consecutive months with a gap of no more than 4 weeks, the MIPS performance guidelines require meeting at least 1 of the following benchmarks: Physician Global Assessment (PGA) score of 2 (mild) or less, (2) BSA involvement of less than 3%, (3) Psoriatic Area and Severity Index (PASI) score less than 3, or (4) Dermatology Life Quality Index score of 5 or less.[11] Most of these measures are used in clinical trials; BSA and PGA are the easiest to record in clinical practice.

Treatment Landscape: Systemic Options

A separate article in this supplement focuses on topical therapies. Following is a summary of systemic options for managing plaque psoriasis.

Phototherapy. Ultraviolet B (UVB) phototherapy is effective. Roughly 75% of 1749 patients achieved clear or minimal disease status and reduced the use of topical therapies in the 12 months after narrow-band UVB therapy, according to an analysis of medical records.[12] The frequency of in-office phototherapy (2-5×/week)[13,14] makes the treatment inconvenient for many patients, but it can be a good choice for those willing to adhere to the schedule. Some patients without a pharmacy benefit may be able to obtain coverage for phototherapy.

Acitretin, Cyclosporine, and Methotrexate. These agents are effective, but their use has decreased substantially since the advent of the biologics for psoriasis. Each is associated with an unfavorable AE profile. Acitretin is teratogenic and associated with bone changes, headache, elevated liver enzymes, hyperlipidemia, hair loss, skin fragility, and dry eye.[4] Cyclosporine is associated with hypertension and interactions with commonly used medications (eg, antibiotics, diuretics, and selective serotonin reuptake inhibitors). Its nephrotoxicity limits its recommended duration of use to 1 year.[13] The toxicity profile of methotrexate includes hematologic toxicity, hepatoxicity, teratogenicity, immunosuppression, and multiple drug interactions (eg, with nonsteroidal anti-inflammatory drugs).[4] These drugs do have limited usefulness in special situations.

Apremilast. This oral, small-molecule phosphodiesterase 4 inhibitor received US Food and Drug Administration (FDA) approval in 2014, for both psoriasis and psoriatic arthritis.[15] About 40% of patients demonstrated a 75% improvement (PASI 75) after 16 weeks of therapy in a phase 3b clinical trial. Efficacy was maintained at 52 weeks.[16] A real-world study reported that roughly 40% of 48 patients attained PASI 50 after a median of 12.5 weeks (range, 1-87 weeks), with diarrhea, headache, and joint pain as the most common AEs.[17] The package insert warns of depression and suicidal thoughts. No laboratory monitoring or tuberculosis testing is required.[15] In practice, apremilast may be considered for biologic-naïve patients concerned about medication safety. Dermatologists without experience managing patients on biologics may be comfortable with prescribing apremilast.

Biologics. The ever-growing list of biologics that are FDA approved for plaque psoriasis include tumor necrosis factor (TNF)-α inhibitors (adalimumab, certolizumab pegol, etanercept, and infliximab), an interleukin (IL)-12 and IL-23 inhibitor (ustekinumab), IL-23 inhibitors (guselkumab, tildrakizumab), an IL-17 receptor A inhibitor (brodalumab), and IL-17A inhibitors (ixekizumab, secukinumab).[4] As the oldest biologics on the market, the TNF-α inhibitors often are used first-line among the biologics due to payer requirements. Etanercept carries an indication for psoriasis in pediatric patients ages 4 years and older.[18] Ustekinumab is indicated for psoriasis in adolescents ages 12 years and older. It also offers quarterly (every 3 months) dosing after the start-up phase, which is beneficial for patients who wish to minimize dosing frequency.[19]

The IL-17 receptor A, IL-17A, and IL-23 inhibitors are the newest classes of biologics. All but 1 of these agents demonstrated PASI 75 rates of 80% or more at 12 or 16 weeks in phase 3 clinical trials (**Table**).[20-24] Two (ixekizumab, secukinumab) are also indicated for psoriatic arthritis.[25,26]

TABLE. Efficacy Rates of Recently Approved Biologics in Plaque Psoriasis, Phase 3 Trials

	n	PASI 75	PASI 90
Anti-IL-17 receptor A			
Brodalumab (210 mg)[20]	612, 624	86%, 85%[a]	70%, 69%[a]
Anti-IL-17A			
Ixekizumab (q4w)[21]	432	83%[a]	67%[a]
Secukinumab (300 mg)[22]	245	82%[a]	59%[a]
Anti-IL-23			
Guselkumab (100 mg)[23]	329	91%[b]	73%[b]
Tildrakizumab (100 mg)[24]	309, 307	64%, 61%[a]	35%, 39%[a]

IL=interleukin; PASI=Psoriatic Area and Severity Index; q4w=every 4 weeks.
[a]Week 12.
[b]Week 16.

Summary

Undertreatment and treatment dissatisfaction are common in the management of psoriasis, despite the availability of highly efficacious therapies. In an effort to set benchmarks for appropriate care, the NPF has established treatment targets and recommended follow-up intervals while recognizing that patient priorities must be considered in clinical practice.

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Understanding Topical Therapies for Psoriasis

Linda F. Stein Gold, MD; Leon H. Kircik, MD; David M. Pariser, MD

PRACTICE **POINTS**

- Most patients receive topical therapy for psoriasis, either alone or with systemic agents.
- Fixed-dose combinations of the most commonly used active ingredients in topical psoriasis therapy are becoming available. Compared with using the same ingredients as separate agents, fixed-dose combination formulations are easier to apply, can increase efficacy, and sometimes allow for use of lower doses with fewer adverse events. They may also facilitate patient adherence.
- Starting topical therapy with biologic therapy can lead to faster response compared with biologic therapy alone.
- New vehicles have been introduced to enhance penetration, efficacy, and patient acceptance. Topical therapies with novel mechanisms of action are under study.

Although the active ingredients of the most frequently used topical therapy for psoriasis have remained the same for many years, the introduction of new vehicles and fixed-dose combination products has increased ease of patient use as well as, in some cases, efficacy and safety. Topical therapies with novel mechanisms of action are under study.

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Topical medications are the treatment of choice for most of the roughly 80% of patients with psoriasis who have mild to moderate disease.[1,2] Patients receiving systemic therapy often are treated with topicals as well, in order to manage resistant lesions.[2] The most commonly used topical therapies contain 1 or more of the following active agents: a corticosteroid, a vitamin D analog, or the retinoid tazarotene. Calcineurin inhibitors (tacrolimus, pimecrolimus) may be used off-label for facial or intertriginous psoriasis.[1,3]

Obstacles to effective management with topical therapy include skin penetration, patient acceptance, and adherence. New formulations using different vehicles to deliver the same active ingredients have been introduced in recent years, with the goals of enhancing penetration, efficacy, and patient acceptance (**Table**).[4-10]

Compared with monotherapy, combining topical agents can increase efficacy and sometimes allow for use of lower doses with fewer adverse events (AEs).[11-13] The need to apply multiple medications may complicate adherence, however. A fixed-dose combination corticosteroid and vitamin D analog became available as a foam within the last few years,[5] adding to the topical solution and ointment formulations already on the US market.[14,15] A corticosteroid-tazarotene combination has been resubmitted for US Food and Drug Administration (FDA) approval.[4] Topical agents reflecting novel mechanisms of action (eg, an aryl hydrocarbon receptor agonist and a Janus kinase inhibitor) are in development,[16,17] and the topical phosphodiesterase 4 inhibitor crisaborole has been studied (ClinicalTrials.gov identifiers NCT00755196, NCT00759161, NCT01029405, and NCT01300052) and used off-label in psoriasis.[3]

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INITIAL TREATMENT

"For somebody with plaque psoriasis and without psoriatic arthritis, I start with a high-potency topical steroid, mostly clobetasol ointment . . . . If I start somebody on clobetasol for 2 weeks, then when they come back, I start them on vitamin D or on a fixed combination of betamethasone and vitamin D." *—Leon H. Kircik, MD*

"It is important to know where on the body you are treating and the potency of the steroids you are using. Obviously, clobetasol works very well on the trunk and extremities, but not so much in the intertriginous areas or on the face where you might want to use a topical vitamin D analog; either a combination vitamin D analog/steroid or separately or even a calcineurin inhibitor." *—David M. Pariser, MD*

"I tend to use a combination topical straightaway, and I would prefer a fixed combination if I can get insurance to cover it . . . . Patients see better efficacy and ease of use." *—Linda F. Stein Gold, MD*

Corticosteroids

Topical corticosteroids used alone or with other agents are the mainstay of psoriasis treatment. They are available in a variety of strengths, potencies (https://www.psoriasis.org/about-psoriasis/treatments/topicals/steroids/potency-chart),[18] and vehicles. Lower rather than higher potency agents are recommended for use on the face or intertriginous areas, and only for a limited time. The use of higher potency preparations is recommended for thick, longstanding plaques. The American Academy of Dermatology guidelines caution that using class 1 corticosteroids (ie, the most potent agents) for more than 2 to 4 weeks raises the risk of AEs. Long-term use may be associated with cutaneous atrophy, telangiectasia, striae distensae, acne, folliculitis, purpura, and tachyphylaxis.[1]

A 0.01% lotion form of halobetasol propionate was developed recently to address the 2- to 4-week restriction recommended for high-potency steroids such as halobetasol propionate 0.05% cream. In two 8-week-long phase 3 trials, the rate of AEs was similar to that of placebo (21.5% and 23.9%, respectively), and the rate of AEs deemed treatment-related was low (1.8%).[19]

Vitamin D Analogs

Calcipotriene (calcipotriol) is indicated for moderately severe scalp psoriasis and for plaque psoriasis.[20,21] A quantitative systematic review of randomized trials (6038 patients with plaque psoriasis, 37 trials) concluded that topical calcipotriene was at least as effective as potent topical steroids.[22] Efficacy and safety depend on the formulation. Calcipotriene ointment has greater skin penetration and efficacy than the cream formulation; both formulations are associated with irritant contact dermatitis, especially when applied to the face or genitals. The calcipotriene solution, used for the scalp, has modest efficacy but causes less irritation.[23] Combination therapy with a topical corticosteroid may alleviate the irritation. Topical vitamin D analogs are not linked to the skin atrophy observed with corticosteroids.[20]

Calcitriol is the naturally occurring active form of vitamin D_3. It inhibits keratinocyte proliferation and induces keratinocyte differentiation, restoring healthy skin structure and function.[24,25] An ointment formulation (calcitriol 3 µg/g) was approved by the FDA in 2009.[10] This agent is not associated with the irritation seen with calcipotriene.[25] More than half (51% and 55%) of patients randomized to calcitriol ointment 3 µg/g reported no itch at the end of two 8-week-long studies, compared with 35% and 34% of those receiving vehicle ($P<0.001$, both comparisons). The rate of treatment-related AEs with active therapy was comparable to that of vehicle.[24] A 12-week study comparing ointment formulations of calcitriol 3 µg/g and calcipotriene 50 µg/g demonstrated similar efficacy. Fewer AEs were reported with calcitriol.[26]

Tazarotene

The topical retinoid tazarotene is effective in treating psoriasis in clinical trials and is FDA approved to treat psoriasis.[27] Tazarotene is not associated with corticosteroid-like AEs, but does cause photosensitivity as well as skin irritation.[1,20] Techniques to reduce the risk of irritation include using a lower concentration or the cream formulation, combining tazarotene with moisturizers or topical corticosteroids, or applying tazarotene on alternate days rather than every day. Tazarotene also is teratogenic; use during pregnancy must be avoided.[1]

TABLE. Topical Psoriasis Therapies: The Last 10 Years

Agent	FDA approval
Combination therapies	
Halobetasol propionate and tazarotene lotion	Resubmitted to FDA August 2018[4]
Calcipotriene and betamethasone dipropionate foam, 0.005%/0.064%	October 2015[5]
Monotherapies	
Halobetasol propionate lotion, 0.01%	November 2018[6]
Betamethasone dipropionate spray, 0.05%	February 2016[7]
Halobetasol propionate lotion, 0.05%	November 2015[8]
Desoximetasone topical spray, 0.25%	April 2013[9]
Calcitriol ointment, 3 µg/g	January 2009[10]

Fixed-Dose Combination Therapy

Corticosteroid and Vitamin D Analog. Fixed-dose combinations of the vitamin D analog calcipotriene and the corticosteroid betamethasone dipropionate (Cal/BD) are available as an ointment, gel, foam, and scalp solution. Using both active agents has produced greater efficacy than either alone,[28,29] with a similar[29] or lower rate of AEs.[30]

The combination of these agents most recently introduced in the United States is an aerosol, alcohol-free foam formulation (Cal/BD 0.005%/0.064%).[5] A foam containing Cal 50 µg/g and BD 0.5 mg/g demonstrated greater skin penetration and bioavailability in vitro than an ointment formulation of these ingredients in vitro.[31,32] The foam formulation demonstrated significantly greater efficacy compared with the ointment product at 4 weeks in 2 phase 2 studies, with similar AEs for both agents.[33,34]

In a phase 3 study, rates of treatment success (ie, Physician Global Assessment [PGA] clear/almost clear with a ≥2-grade improvement) with Cal 50 µg/g and BD 0.5 mg/g were significantly higher with the foam at 4 weeks than with the gel at 8 weeks (**Figure 1**).[35] The rate of AEs was similar with both therapies.[35] Patients receiving the foam demonstrated significantly higher health-related quality of life than those treated with the gel, as measured by the proportion with Dermatology Life Quality Index scores of 0 or 1 at weeks 4 and 12 (week 4: 46% vs 32%, *P*=0.013; week 12: 61% vs 44%, *P*=0.003; respectively).[36]

More than half (53%) of patients achieved clear/almost clear on the PGA in another phase 3 study after 4 weeks of therapy with the Cal/BD foam formulation (n=323, active therapy; n=103, vehicle). Most (84%) of patients receiving the active agent achieved a 70% reduction in itch by week 4; a significant difference in rates of patients reporting itch reduction was observed by day 3.[37] A real-world evaluation of 410 patients receiving the Cal/BD foam in clinical practice reported a similar efficacy rate, with 49% of patients achieving clear/almost clear on the Investigator Global Assessment (IGA). Few AEs were reported, the most common being insufficient response (6%). Onset of benefit was rapid. At 1 week, two-thirds (68%) of patients reported visible improvement, and 60% had experienced 24 hours without itching.[38]

To compare the efficacy of Cal/BD foam with that of systemic therapy in the absence of head-to-head trials, Bewley and coauthors performed a matching-adjusted indirect comparison of data from 4 Cal/BD trials of 749 patients with 1 study each of apremilast, methotrexate, and acitretin. Efficacy (percent of patients achieving PGA 0/1) with Cal/BD foam was higher at 4 weeks than with apremilast at 16 weeks (53% vs 30%, respectively; *P*<0.001). Higher proportions of patients demonstrated 75% improvement from baseline (Psoriasis Area and Severity Index [PASI 75]) with Cal/BD foam at 4 weeks than with apremilast, methotrexate, or acitretin at 12 weeks (51% vs 27% [apremilast], *P*<0.001; 51% vs 34% [methotrexate], *P*<0.001; and 51% vs 32% [acitretin], *P*=0.003).[39]

Corticosteroid and Tazarotene. Long-term use of high-potency topical corticosteroids is limited by the risk of AEs such as skin atrophy and tachyphylaxis; the use of topical tazarotene is limited by irritation. Combining a mid- or high-potency topical corticosteroid with topical tazarotene 0.1% gel led to greater efficacy (ie, reduced scaling, erythema, and lesion severity) and lower rates of burning compared with tazarotene plus placebo after 12 weeks of therapy in an early study using 2 separate agents.[11]

A lotion containing a fixed combination of halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) demonstrated efficacy superior to that of its individual components in a phase 2 study of patients with moderate-to-severe psoriasis (body surface area [BSA] 3%-12%; N=212).[13]

As early as 2 weeks, a significantly higher proportion of patients receiving the combination achieved the primary endpoint compared with TAZ.[40] Higher proportions of patients maintained benefit after treatment cessation with HP/TAZ than with the individual components.[41] Treatment-emergent adverse events (TEAEs) and AEs leading to discontinuation occurred most frequently in the TAZ group.[13]

In 2 phase 3, vehicle-controlled studies, more than one-third (36%) and nearly one-half (45%) of patients receiving HP/TAZ lotion achieved the primary endpoint (clear/almost clear and ≥2-grade improvement [IGA]) at 8 weeks).[42] **Figure 2** displays the primary efficacy results of a pooled analysis of these trials, along with the proportion of patients who maintained efficacy 4 weeks after treatment cessation.[43]

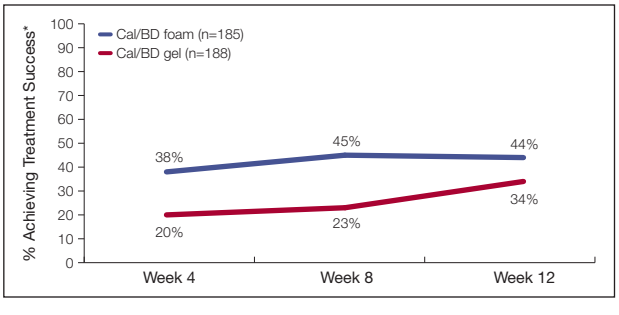

FIGURE 1. Efficacy of Cal/BD Foam and Gel in Psoriasis: Phase 3 Trial

*Clear/almost clear and ≥2-grade improvement, Physician Global Assessment. *P*<0.001 for treatment success rates of Cal/BD foam at week 4 vs gel at week 8 (primary endpoint).

BD=betamethasone 0.5 mg/g; Cal=calcipotriol 50 µg/g.

Data from Paul C, et al. *J Eur Acad Dermatol Venereol*. 2017;31:119-126.[35]

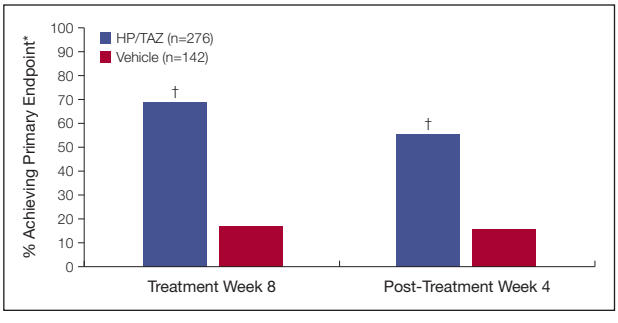

FIGURE 2. Efficacy of HP/TAZ in Psoriasis: Pooled Phase 3 Trials

*Clear/almost clear and ≥2-grade improvement, Physician Global Assessment

†*P*<0.001 vs vehicle.

HP=halobetasol propionate 0.01%; TAZ=tazarotene 0.045%.

Data from Sugarman JL, et al. J *Drugs Dermatol*. 2018;17:855-861.[43]

Patients in the phase 3 trials (N=418) had moderate-to-severe psoriasis, although no patient had BSA >12% affected.[42] Itching (rated 0-3, where 3 is severe) improved by 54% from baseline at 2 weeks, with the benefit maintained at 8 weeks. Dryness and burning/stinging (also rated 0-3) had improved by 44% and 46% at 8 weeks, respectively, compared with baseline. The most frequently seen AEs deemed related to active therapy were contact dermatitis (6.3%), application site pain (2.6%), and pruritus (2.2%).[42]

Combining Topicals and Biologics

Topical therapies are used adjunctively in patients receiving biologic therapy, as many patients do not experience full disease clearance with biologics alone.[44] A few studies have evaluated the effect of adding a topical to a biologic.

USING A TOPICAL AGENT WITH BIOLOGIC THERAPY

"A potent topical can kick in very rapidly, usually faster than any systemic."

—Linda F. Stein Gold, MD

"[In patients treated with a biologic] I always start a topical because when patients are coming to see you, they want something to be done. If you start them on a biologic, you don't know if they are going to get it for at least a couple of weeks. Therefore, no matter what the systemic treatment is, topical treatment is always part of the regimen."

—Leon H. Kircik, MD

Starting patients on Cal/BD as well as adalimumab (ADA) led to higher early responses than initiating therapy with ADA alone. By week 16, response rates were similar for both groups. Participants in whom at least 2 systemic therapies had failed were randomized to receive ADA with either vehicle (n=364) or topical Cal/BD (n=366). Initially, higher proportions of patients achieved PASI 75 with the combination therapy (15% vs 6% at week 2, $P<0.001$; and 41% vs 32% at week 4, $P=0.021$). By week 16, rates of PASI 75 response did not differ significantly between the groups (65% and 71%, ADA + Cal/BD and ADA + vehicle, respectively; $P=0.086$).[45]

Adding clobetasol propionate foam to etanercept for 2 courses of up to 2 weeks each during weeks 11-12 and 23-24 (n=295) led to higher rates of efficacy (PASI 75) than etanercept alone at 12 weeks (n=297) (65% and 48%, respectively, $P<0.001$). By 24 weeks, rates of PASI 75 did not differ significantly between the treatment arms. Both treatment groups received etanercept 50 mg twice weekly for 12 weeks, followed by 50 mg once weekly for 12 weeks.[46]

Adding a topical corticosteroid-containing agent as needed to etanercept 50 mg weekly resulted in efficacy similar to that of patients who received twice the dose of etanercept without the topical steroid, in a randomized study.[47] All patients received etanercept 50 mg twice weekly for 12 weeks. For the next 12 weeks, patients were randomized to continue etanercept 50 mg twice weekly (n=144) or to receive half the etanercept dose (50 mg once weekly) plus a topical corticosteroid-containing agent as needed (n=143). The change in the PASI score from week 12 to 24 did not differ significantly between the groups. Proportions of patients reaching PASI 50, 75, and 90 at week 24 also did not differ between the groups. Rate of AEs and treatment-related AEs was similar in both arms.[47]

Adding Cal/BD 0.005%/0.064% foam to biologic therapy in 25 patients whose psoriasis had an inadequate response to biologic therapy led to increased efficacy. Patients were instructed to use the foam once daily for 4 weeks, then twice weekly for 12 weeks. Patients had a median BSA involvement of 3%, median PGA of 3, and median PGA×BSA of 8 at baseline. Median PGA was 1 (almost clear) at weeks 4 and 16. More than a quarter (28%) achieved total clearance (no BSA involvement, PGA 0) by week 4. Most patients achieved treat-to-target goals (BSA ≤1% and PGA ≤1 at week 4 [76%] and 16 [68%]). No treatment-related AEs were observed.[48]

Choosing a Topical Therapy

Factors to consider when selecting any therapy for psoriasis include efficacy and safety in view of the disease severity, locations, symptoms (eg, itch), and comorbidities. Patient preferences and concerns also are important; failing to elicit and consider these factors may result in partial adherence or nonadherence. Studies have demonstrated that patient preferences about topical products vary widely and are not predictable by patient demographics.[49,50] Consider asking patients about their preferences regarding characteristics such as frequency of application, texture of formulation (eg, not greasy), odor, visibility on skin after application, and speed of application.

Summary

The introduction of fixed-dose combination products and new vehicles has increased the quality of options available for psoriasis. Fixed-combination topical agents for psoriasis can increase efficacy and reduce AEs compared with the individual components of the combination.[11-13] The aerosol foam vehicle used in Cal/BD increased skin penetration and efficacy compared with the ointment formulation.[31,33,34]

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Improving Adherence to Topical Therapies Through Improved Clinician–Patient Communication and Shared Decision Making

Leon H. Kircik, MD; Linda F. Stein Gold, MD; David M. Pariser, MD

PRACTICE **POINTS**

- Many patients do not adhere to topical therapy for psoriasis. Possible reasons may include dissatisfaction with therapy, failure of treatment to relieve signs and symptoms important to the patients, a mistaken belief that therapy can be applied only when symptoms are severe, and products that are messy and inconvenient to apply.
- Minimizing the number of agents and application frequency, soliciting the patient's preferences about treatment characteristics, and early follow-up after starting a new therapy may promote adherence.
- A structured clinician–patient communication program led to improved efficacy.
- Resources are available for patient education and to support patient adherence.

Nonadherence to topical therapies for psoriasis is common. Reasons include miscommunication or inadequate communication between patients and clinicians, a mismatch between physician and patient treatment priorities, the complexity of treatment regimens, and a lack of information conveyed to the patient about realistic expectations from therapy. Interventions to facilitate communication and education are available to support clinicians and patients.

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Reported rates of nonadherence to topical therapies for psoriasis are high, ranging from 40% to 65%.[1-3] Physicians may overestimate patient adherence. Use of topical therapies among patients with moderate-to-severe psoriasis was estimated at 79% in a survey of dermatologists (n=101) and 40% by patients (n=1005) in a population-based survey.[4]

Reasons for Nonadherence

Dissatisfaction With Therapy. Nearly one-fifth (18%) of 633 US patients with psoriasis have reported dissatisfaction with their psoriasis therapy in a survey.[5] More than 80% of patients whose treatment had not changed after at least 2 recent clinical visits said they were not satisfied with their level of disease control and would consider trying new a therapy, according to a small survey (n=33).[6]

Treatment Does Not Alleviate Signs and Symptoms Important to Patients. Compared with patients who were satisfied with their psoriasis control, dissatisfied patients were more likely to have more severe pain, itching, and scaling.[5] When asked to rank attributes of the ideal psoriasis therapy, patients (n=196) rated alleviation of signs (redness, thickness, scaling) and symptoms, and improved quality of life at a higher level of importance than did dermatologists (n=200). Dermatologists, in turn, prioritized reduction in body surface area (BSA) involvement over improved signs, symptoms, and quality of life.[7]

Misconceptions About Therapy. Nearly half (47%) of 799 patients with psoriasis reporting treatment nonadherence said they used topicals only when needed.[2] Patients

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who refused to take physician-recommended therapy (n=50) were more likely than those who accepted treatment (n=205) to believe that psoriasis is not manageable (80% vs 61%), that psoriasis treatments never work (58% vs 28%), and that all creams have the same effect (54% vs 32%).[8]

Promoting Adherence

Ask Patients What Is Important to Them. Topical therapies for psoriasis vary widely on characteristics other than safety and efficacy. Frequency, speed, and ease of application; how the product feels on the skin; whether it dries rapidly or is visible after application; whether it sticks to or stains clothing; and whether it can be used on all affected body areas are among many attributes that may be tailored to patient preferences.

Patient preferences vary and are not always predictable. It is best to ask individuals what will be acceptable to them. One focus group found that patients tend to prefer products that are not oily, thick, or greasy.[9] In clinical practice, however, some patients prefer ointments. A survey of patient preferences for the gel or foam formulation of fixed-dose combination calcipotriene 50 µg/g (Cal) and betamethasone dipropionate 0.5 mg/g (BD) found that about half of the patients preferred the gel and half favored the foam.[10] Recommending a treatment consistent with patient preferences improved treatment satisfaction over time in 1 study.[11]

> "We have to be cognizant of what the patient is really going to do. They are not going to use a greasy ointment in their scalp in the morning before they go to work or school." —*David M. Pariser, MD*

Prescribe as Simple a Regimen as Possible. A treatment plan that minimizes the number of prescriptions and the number of applications is likely to promote adherence, preferably one application, once a day. A fixed-combination therapy is easier to use than 2 topicals that must be applied individually.

Set Expectations regarding how much response to expect and how long it will take to see a benefit. Patients anticipating complete or near-complete disease control in a short time are likely to be disappointed and may discontinue treatment.

Educate the Patient about why the medication must be used as prescribed rather than only when symptoms become intolerable. Patients need to understand that psoriasis is a chronic illness requiring ongoing therapy with maintenance treatment between flares. Patient concerns about safety should also be addressed. Physician assistants or nurses may be able to provide patient education in some practices.

Offer Patients Time to Decide Which Treatment Is Preferable. Patients may be overwhelmed by the information about their disease and recommended therapies. Letting patients know that they can notify the office of their treatment preference after the visit can reduce stress. Other patients may prefer to decide immediately to avoid an additional office visit and copay. When possible, allowing the patient to try a sample of a recommended topical medication in the office can be helpful. First-hand experience with the texture, ease of application, odor, and feel on the skin may aid the patient's decision.

> "It is important to advise the patient that even if we get you completely clear, we did not cure you. If you stop your medication, then the disease will come back." —*Linda F. Stein Gold, MD*

Consider Seeing the Patient 1 Month After Initiating a New Therapy. Early follow-up facilitates discussion of any adverse events or implementation issues and offers an opportunity to adjust therapy if needed. Prescribing only 1 month's worth of medication allows for early evaluation of adherence. A patient who denies the need for a refill at the follow-up visit may not be using the therapy as prescribed. Discussing the reasons for nonadherence may promote appropriate use or reveal a need to change medication.

Ask Patients to Take Photos of Their Worst Lesions Between Visits. Evaluating photographs of patient lesions taken once a week between office visits enables the clinician to see how the disease has responded in more detail. Asking patients to bring photographs to the next visit engages the patients and may improve adherence. Medicare offers codes to pay for clinicians to evaluate a photograph submitted by a patient between office visits (remote evaluation of recorded video and/or images submitted by an established patient, HCPCS code G2010).[12]

Tools to Support Communication and Adherence

Clinician–Patient Communication. Giving patients information on many possible treatments can be bewildering, but offering information about 2 or 3 medically appropriate agents allows the patient to take part in the treatment selection. Helpful information might include efficacy, safety, convenience, time to see results, adverse events, and insurance coverage.

A program offering structured guidance for one-to-one conversations between a dermatologist or nurse and a patient, as well as patient information materials, telephone/e-mail helpdesks, and treatment reminders, led to improved efficacy after 8 weeks of therapy in a phase 4 trial.[13] All patients received Cal/BD gel; half were randomized to the intervention (Topical Treatment Optimization Programme [TTOP], n=893) and half (n=897) received usual care. A significantly higher proportion of patients randomized to TTOP achieved the primary efficacy endpoint (clear or almost clear, Physician Global Assessment [PGA]) at 8 weeks: 36.3% and 31.3%, TTOP and non-TTOP patients, respectively (P=0.0267). Efficacy was higher in the TTOP group despite a lower mean use of study medication per percentage of BSA involved. Patients randomized to TTOP rated the structured one-to-one conversations with their dermatologist or nurse as the most important element of the program.[13]

Smartphone App. A smartphone app that provided once-daily reminders to apply psoriasis treatment was associated with increased adherence to Cal/BD foam in the short term (4 weeks), compared with those who did not receive the app: 65% of 68 patients vs 38% of 66 patients; P=0.004. The app also included information on the number of treatment applications and the amount of Cal/BD foam applied—

information obtained as the app was synced to a monitor on the foam canister. The app also enabled but did not require patients to record their symptoms. Patients using the app also showed greater improvement in treatment efficacy at week 4, as measured by the change from baseline on the 8-point Lattice System Physician's Global Assessment (LS-PGA; mean change 1.86 and 1.46, intervention and nonintervention group, respectively; P=0.047). The difference in treatment efficacy between groups was not significant at weeks 8 and 26.[14]

National Psoriasis Foundation Patient Navigation Center. Trained navigators can help patients prepare for medical appointments and obtain insurance coverage or other access to treatments (https://www.psoriasis.org/navigationcenter/resources).

Patient Decision Aids developed by health care professionals provide disease state and medication information in patient-friendly language. A printable resource was developed by Tan and Wolfe based on focus groups of dermatologists and patients with psoriasis (http://www.wcri.ca/wp-content/uploads/2016/03/DECISION_AID-psx-v-Oct2012.pdf).[15] An internet-based, interactive patient decision aid developed based on focus groups of patients with psoriasis asks patients to rate what is important in a treatment (values) and to weigh trade-offs of their values against the available options (**Figure**; https://www.informed-decisions.org/psoriasispda.php).[16]

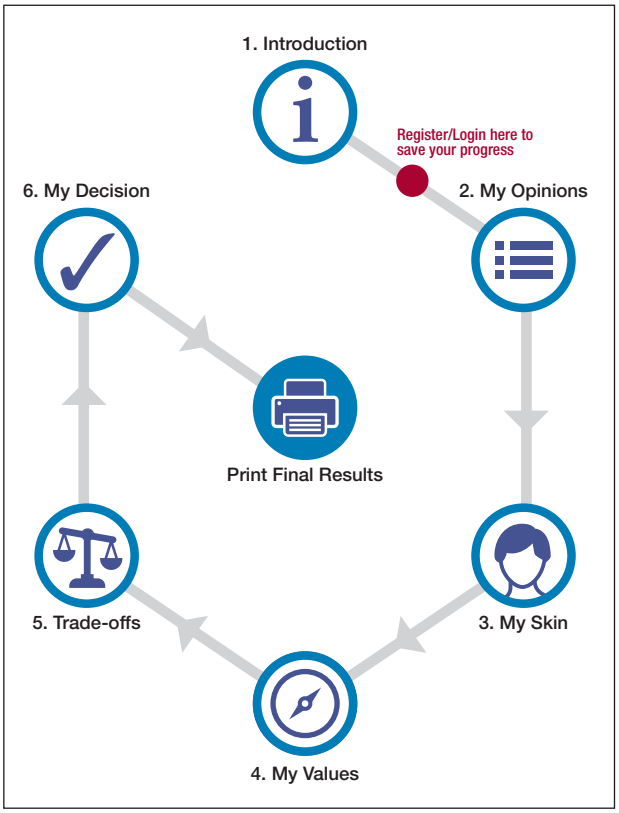

FIGURE. Patient Decision Aid

Source: Reprinted from InforMed. https://www.informed-decisions.org/psoriasis-pda.php. Last Updated: May 2017. Accessed February 25, 2019.

Summary

Many factors contribute to the low rate of adherence to topical therapies for psoriasis. Educating patients about the chronic nature of psoriasis and the need for ongoing therapy, as well as setting realistic expectations for when and what type of response might occur, are key elements of clinician–patient conversations about therapeutic choices. Asking patients which disease signs and symptoms are most important to address, and soliciting patient preferences about topical vehicle, frequency of application, and other parameters, can build clinician–patient rapport and may increase the likelihood of adherence. Decision aids and support services from the National Psoriasis Foundation and other sources can provide additional information for patients.

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