Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy

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Psoriasis is a chronic inflammatory disease involving multiple organ systems and affecting approximately 3.2% of the world's population. In this section of the guidelines of care for psoriasis, we will focus the discussion on ultraviolet (UV) light–based therapies, which include narrowband and broadband UVB, UVA in conjunction with photosensitizing agents, targeted UVB treatments such as with an excimer laser, and several other modalities and variations of these core phototherapies, including newer applications of pulsed dye lasers, intense pulse light, and light-emitting electrodes. We will provide an in-depth, evidence-based discussion of efficacy and safety for each treatment modality and provide recommendations and guidance for the use of these therapies alone or in conjunction with other topical and/or systemic psoriasis treatments. (J Am Acad Dermatol 2019;81:775-804.)

Key words: climatotherapy; Goeckerman; grenz ray; intense pulsed dye laser; narrowband ultraviolet light A (NB-UVA); narrowband ultraviolet light B (NB-UVB); photochemotherapy; photodynamic therapy; phototherapy; psoralen ultraviolet light A; psoriasis; pulsed dye laser; PUVA (topical; bath; oral); visible light.

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

DISCLAIMER

Adherence to these guidelines will not ensure successful treatment in every situation. Furthermore, these guidelines should not be interpreted as setting a standard of care, nor should they be deemed either inclusive of all proper methods of care or exclusive of other methods of care reasonably directed toward obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient and the known variability and biologic 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 will likely require revisions to the recommendations in this guideline to reflect new data.

BACKGROUND

Although many patients with psoriasis may be capable of adequately controlling their disease with the use of topical treatments alone, often these interventions are insufficient and disease severity dictates the need for alternative options. While systemic and biologic treatments are heavily relied on for severe and widespread skin disease, these medications do come with risks of systemic side effects and immunosuppression that many patients may not be willing or able to assume. Phototherapy serves as a reasonable and effective treatment option for patients requiring more than topical medications and/or those wishing to avoid systemic medications or simply seeking an adjunct to a failing regimen.

DEFINITION OF PSORIASIS

See Appendix 1 for definitions.

SCOPE

This section covers the use of phototherapy in the treatment of psoriasis in adults; psoriasis treatment in the pediatric population is addressed in the Joint American Academy of Dermatology–National Psoriasis Foundation Guidelines of Care for the Management and Treatment of Psoriasis in Pediatric Population (in preparation).

METHOD

An evidence-based model was used, and evidence was obtained by using a search of the PubMed and MEDLINE databases from January 1, 2008, to December 31, 2017, for all newly identified clinical questions (Table I). Searches were limited to publications in the English language. Medical Subject Heading (MeSH) terms used alone or in various combinations in the search included *psoriasis* (*plaque*, *vulgaris*, *guttate*, *erythrodermic*, *inverse*, *pustular*), *phototherapy*, *ultraviolet* (*short-wave*, *long-wave*), *targeted phototherapy* (*excimer laser*), *narrowband ultraviolet B* (*NB-UVB*), *photochemotherapy*, *psolaren ultraviolet A*, *broadband*

Abbreviations used:

ALA:	5-aminolevulinic acid
BB:	broadband
BSA:	body surface area
FAE:	fumaric acid ester
IPL:	intense pulsed light
MAL:	methyl aminolevulinic acid
MED:	minimal erythema dose
8-MOP:	methoxypsoralen
MTX:	methotrexate
NAPSI:	Nail Psoriasis Severity Index
NB:	narrowband
PASI:	Psoriasis Area and Severity Index
PASI 75:	75% improvement in Psoriasis Area and Severity Index score
PASI 90:	90% improvement in Psoriasis Area and Severity Index score
PDL:	pulsed dye laser
PDT:	photodynamic therapy
PpIX:	protoporphyrin IX
PUVA:	psoralen plus ultraviolet A
QoL:	quality of life
RCT:	randomized controlled trial
SAPASI:	Self-Administered Psoriasis Area Severity Index
TMP:	trimethylpsoralen
UV:	ultraviolet
UVA:	ultraviolet A
UVB:	ultraviolet B

ultraviolet B (*BB-UVB*), *grenz ray*, *climatotherapy*, *photodynamic therapy*, *visible light* (*red/blue*), *TURBO-UVB*, *intense pulsed light*, and *Goeckerman therapy*.

For detailed methodology, see Appendix I.

Table I. Clinical question

What are the efficacy, effectiveness, and adverse effects of the following phototherapy/photochemotherapy modalities used as monotherapy or in combination with other psoriasis therapies to treat psoriasis in adults?

1) Narrowband ultraviolet B (NB-UVB)
2) Broadband ultraviolet B (BB-UVB)
3) Targeted phototherapy (excimer laser and excimer lamp)
4) Psoralen plus ultraviolet A (PUVA) therapy
   a. Topical
   b. Bath
   c. Oral
5) Photodynamic therapy
6) Grenz ray therapy
7) Climatotherapy
8) Visible light therapy
9) Goeckerman therapy
10) Pulsed dye laser and Intense pulsed light

NB-UVB

NB-UVB refers to wavelengths ranging from 311 to 313 nm, which are widely used for the treatment of generalized plaque psoriasis.[1-4] As outlined in Table II,[5-9] the starting dose for NB-UVB therapy can be based on skin phototype or minimal erythema dose (MED).[2,9-11] A frequency of twice or thrice weekly is effective and is therefore recommended.[1,12,13] A frequency greater than thrice weekly results in little added benefit, while at the same time exposing the patient to a higher total dose of UVB radiation and greater risk of ultraviolet (UV)-induced erythema.[13] Although both twice-weekly treatment and thrice-weekly treatment eventually achieve clearance in equal proportions, twice-weekly treatments appear to take about 1.5 times longer to achieve skin disease clearance as compared with thrice-weekly treatments.[12] More specifically, patients receiving twice-weekly NB-UVB treatments achieve clearance in a mean of 88 days compared with 58 days for those receiving 3 treatments per week.[12] Maintenance treatment sessions after improvement or skin clearance may be spaced farther apart, usually once weekly.[8]

Application of a thin layer of emollient, such as petrolatum, is recommended before NB-UVB treatment sessions, as this increases treatment effectiveness in psoriasis and also reduces UV-induced erythema.[14-16] Thickly applied emollient may, however, decrease UVB transmission and potentially diminish efficacy.[17]

In a recent systematic review and meta-analysis of 41 randomized controlled trials (RCTs) involving 2416 patients with psoriasis treated with phototherapy, there were 9 trials, with a total of 293 patients with plaque psoriasis that utilized a 75% improvement in Psoriasis Area Severity Index score (PASI 75) as the primary end point in assessing the efficacy and safety of NB-UVB monotherapy. Across these 9 studies, 62% of patients achieved PASI 75.[1] With clearance rate as the primary end point, the authors also analyzed another 10 trials with 379 patients with plaque psoriasis treated with NB-UVB. An average clearance rate of 68% was observed.[1] In a systematic review and meta-analysis of 8 trials, 70% of patients achieved PASI 75 with NB-UVB phototherapy.[2]

Comparative studies have been conducted to determine the efficacy of NB-UVB as compared with that of psoralen plus UVA (PUVA). A recent randomized prospective trial of the 60 patients with generalized plaque psoriasis (defined as >25% body surface area [BSA] involvement) compared NB-UVB monotherapy (n = 30) with oral PUVA (n = 30); all patients (those treated with

Table II. Determination of MED, subsequent visits, maintenance therapy, and maximum dose for NB-UVB phototherapy

Dose category			Reference
Estimation of initial NB-UVB dose by skin type will be performed by skin type, as assessed by the prescribing physician and/or the phototherapist, as follows: • Skin types I and II: 300 mJ/cm^2 • Skin types III and IV: 500 mJ/cm^2 • Skin types V and VI: 800 mJ/cm^2			5
Skin type	**Skin color**	**Characteristics**	
I	White, very fair, red or blond hair, blue eyes, freckles	Always burns, never tans	6
II	White; fair; red or blond hair; blue, hazel, or green eyes	Usually burns, tans with difficulty	
III	Cream-white, fair with any eye or hair color	Sometimes mild burn, gradually tans	
IV	Brown, typical Mediterranean white skin	Rarely burns, tans with ease	
V	Dark brown, Middle Eastern skin types	Very rarely burns, tans very easily	
VI	Black	Never burns, tans very easily	
Determination of MED*			
• MED should be tested in a sun-protected region on the hip or buttock. All other areas of the skin should be covered. The patient should wear eye protection during delivery of the UV doses • The tested areas should be uniform in size, approximately 2 × 2 cm, and marked with a skin pen to identify the tested area • The following dosage schedule should be used depending on skin type:			7
Skin types I-II (mJ/cm^2)	**Skin types III-IV* (mJ/cm^2)**		7
250	350		
400	500		
550	650		
700	800		
850	950		
1000	1100		
1150	1250		
1300	1400		
• Start the delivery with all testing areas open and cover after the specific dose of light has been delivered • Instruct the patients to keep this area covered for the next 24 h, avoiding exposure to natural or artificial UV light • The patient should return 24 h later. The MED is the lowest dose with any identifiable erythema within the tested area			7
*Note: MED testing should not be performed in patients with skin types V and VI. These patients should be started at an initial dose of 800 mJ/cm^2 and increased as tolerated according to the protocol below.			
Subsequent visits			
In subsequent visits, patient response to phototherapy is assessed by the degree and duration of skin erythema and possible subjective symptoms of burning (stinging, pain, or itch)			7
The effect of skin erythema on UVB dosing will be as follows: • Minimal erythema lasting <24 h following treatment: increase dose by 20% • Erythema persistent for >24 h but <48 h: dose held at previous level until erythema lasting <24 h • Erythema lasting >48 h: No treatment on that day followed by return of dose to the last lower dose that did not cause persistent erythema			5

Continued

Table II. Cont'd

If the patient missed a treatment, the following schedule should be used:		[7]
Days missed		
• 1 wk	• Hold the previous dose constant	
• 1-2 wk	• Decrease the previous dose by 25%	
• 2-4 wk	• Decrease the previous dose by 50%	
• >4 wk	• Return to starting dose	
Maintenance therapy		
• Once the patient's psoriasis has cleared, the patient may choose to continue maintenance therapy as a taper or indefinitely		
• The maintenance dose should be the last dose given prior to clearing		
• The maintenance therapy taper protocol is treatment twice weekly for 4 wk and then once weekly for 4 wk. The dose should be held constant		[8]
• For prolonged maintenance therapy, the patient should receive a treatment every 1-2 wk. The final dose should be decreased by 25% and held constant for all maintenance treatments		[7,9]
Maximum dose		
Upon reaching the dose, contact the prescriber for guidance. Dosing may be increased, typically at 5%-10% at each treatment, as tolerated if skin is not clear. The recommended maximum dose of phototherapy is as follows:		
Note: Regardless of Fitzpatrick skin type, the maximum dose for treatment of facial areas should not exceed 1 J/cm^2. Higher doses should be prescribed by a physician's order based on individual patient conditions.		
Skin type	Dose (mJ/cm^2)	[7]
• I and II	• 2000	
• III and VI	• 3000	
• V and VI	• 5000	

MED, Minimal erythema dose; *NB*, narrowband; *UV*, ultraviolet; *UVB*, ultraviolet B.

NB-UVB and those treated with PUVA) achieved a PASI 75 by 3 months, and there was no statistically significant difference.[3] Though the end result was ultimately the same, PUVA resulted in faster clearance with less treatment than with NB-UVB (12.7 treatments, and 49.2 days for PUVA compared with 16.4 treatments and 65.6 days for NB-UVB). In a retrospective cohort study of 293 patients with psoriasis treated with various types of phototherapy at a single center, 55 of 69 patients treated with NB-UVB (79.7%) achieved a good (60%-80% skin clearance) or excellent (80%-100% skin clearance) response.[4]

Though more effective, oral PUVA causes a higher rate of adverse effects, with symptomatic erythema and blistering observed in 17% of patients versus in 7.8% with NB-UVB.[1] Additionally, 5% of patients receiving PUVA treatment withdrew from their respective studies on account of adverse effects, compared with only 2% of those treated with NB-UVB. In a meta-analysis, which included 3 trials comparing NB-UVB with PUVA, the clearance rate for PUVA was 80% compared with 70% for NB-UVB. Fewer treatments were required to reach clearance with PUVA than with NB-UVB (17 vs 25), and there was a higher likelihood of remission 6 months following PUVA treatment than following NB-UVB treatment (odds ratio, 2.73; 95% confidence interval, 1.19-6.27).[2]

Several other studies have corroborated the greater efficacy of PUVA compared with that of NB-UVB in plaque psoriasis.[18,19] Some trials, however, did not find a statistically significant difference in overall clearance rates between PUVA and NB-UVB, although many found faster skin clearance and more adverse effects with PUVA.[3,20-22] A Cochrane review and meta-analysis of NB-UVB and PUVA studies found heterogeneity that precluded a pooled analysis.[21] One pooled analysis of 3 studies of 231 patients indicated, however, that withdrawal rates due to adverse effects did not differ significantly between PUVA and NB-UVB groups.[18,19,21,22]

Studies are conflicting on the effectiveness of bath PUVA versus NB-UVB. One study found a 45% mean

improvement in PASI score with bath PUVA versus a 77% mean improvement in PASI score with NB-UVB, and another showed skin clearance rates of 54% versus 75%, respectively.[23,24] On the other hand, in another study of 34 patients, bath PUVA was more effective, with patients experiencing an 85% reduction in PASI score versus a 59% reduction with NB-UVB.[25]

Although PUVA monotherapy was more effective than NB-UVB in many studies, superior short-term and long-term safety, simplicity, and lower cost favor NB-UVB as the preferred treatment for plaque psoriasis.[1-4,20,21,26] NB-UVB is also preferred over BB-UVB (vide infra), given increased efficacy, quicker treatment response, and lower rates of adverse effects.[1,4,27-30] NB-UVB has also been used for guttate psoriasis regardless of patient age.[11,31,32]

Home NB-UVB

For patients for whom travel to a phototherapy center is a limiting factor, home NB-UVB units should be considered. It has been the general impression of dermatologists that home phototherapy devices do not work as well as office units and are associated with a greater number of side effects. In a comparison of 196 patients with mild-to-severe psoriasis, half of the patients received 311-nm NB-UVB treatments at home and the other half obtained treatments at a local hospital.[32] Topical steroids and vitamin D derivatives were allowed during the study and were more common in subjects treated at local hospitals. PASI scores and other parameters of efficacy were equivalent in the 2 settings, as was the cumulative dose of UV light. Of the individuals who received hospital-based phototherapy, 41.7% achieved PASI 75 after 46 treatments compared with 40.7% of those receiving home phototherapy. Quality of life (QoL) indices were also similar in the 2 groups. Side effects were comparable, although severe erythema was more frequent among home phototherapy patients, and blistering was more likely to occur among hospital-based phototherapy subjects. The burden of treatment was significantly lower, and patients were happier with their treatments when the UV light was delivered in the home phototherapy setting.

Combination therapy with NB-UVB

Although NB-UVB monotherapy is an effective first-line treatment for generalized plaque psoriasis, additional medications are often added to enhance efficacy. The data are mixed with respect to the use of topical calcipotriol in conjunction with NB-UVB. In 1 trial, the addition of calcipotriol did not improve efficacy compared with NB-UVB alone.[33] The apparent lack of an added effect of calcipotriol might be due to the fact that vitamin D analogues are degraded by exposure to UV radiation.[34] In another study, fewer NB-UVB treatments and a lower total dose were required for clearance in patients treated with the combination therapy.[35,36]

Tazarotene is another topical medication that has been assessed in combination with NB-UVB. In 1 study, tazarotene decreased responsiveness to phototherapy, with only 10% of the patients achieving PASI 75, compared with 62% of those who underwent NB-UVB monotherapy. However, a more recent, bilateral comparison study of 40 patients with plaque psoriasis showed greater improvements in PASI score and Physician Global Assessment score following application of 3% coal tar than with petrolatum followed by NB-UVB.[37] Thus, although maintaining use of topical therapies such as vitamin D analogues, retinoids, corticosteroids, and/or coal tar preparations during treatment with NB-UVB phototherapy may be common in clinical practice, it is important that coal tar not be applied immediately before NB-UVB treatment.[1,14,33,34,36-38]

The benefit of topical psoralens in combination with UVA has led researchers to test their efficacy with NB-UVB as well. A prospective study with 30 patients compared twice-weekly NB-UVB monotherapy with twice-weekly application of 8-methoxypsoralen (8-MOP) 0.1% solution 15 minutes before NB-UVB treatment. There was a greater improvement with the psoralen after 8 weeks of therapy but not at 4 or 12 weeks.[39] Though the psoralen group required fewer treatments and a lower cumulative radiation dose, these differences did not reach statistical significance and patients experienced more adverse effects, such as erythema, pruritus, hyperpigmentation, and burning. With limited literature investigating this combination, there is insufficient evidence to recommend pretreatment with psoralens in conjunction with NB-UVB phototherapy.

The literature does support the use of methotrexate (MTX) as a systemic adjunct to NB-UVB. A recent trial of 120 patients with generalized plaque psoriasis (defined in this study as >10% BSA involvement) compared improvement in PASI between 3 different groups—patients receiving MTX monotherapy, NB-UVB monotherapy, or a combination of MTX and NB-UVB—and found no difference in clearance rate (>90% reduction in PASI) among the groups.[40] The authors did, however, determine that patients in the combination group

required fewer weeks of treatment to obtain clearance, a lower mean number of UVB exposures, lower cumulative dose of UVB, and lower cumulative dose of MTX compared with those in the monotherapy groups. Pruritus, erythema, and nausea were more common in the combination group than in the group receiving NB-UVB monotherapy. In a randomized, prospective trial of 40 adult patients with generalized chronic plaque psoriasis (defined as BSA >20%), patients receiving MTX alone (maximum dose, 30 mg/wk) were less likely to achieve clearance than were those who received NB-UVB twice weekly plus MTX.[41] The combination group also had a shorter duration of treatment, a lower cumulative dose of MTX, and lower incidence of gastrointestinal adverse effects, although about 30% developed erythema. Multiple other studies have confirmed the benefits of combination NB-UVB with MTX, which include higher rates of PASI 75 in less time, lesser number of treatments, and less total UV radiation dose.[1,42]

Oral retinoids have a beneficial effect when used in conjunction with NB-UVB. Oral retinoids decrease the number of treatments and total UVB dose required.[43-45] Because oral retinoids are relatively safe and nonimmunosuppressive and because their addition may decrease cumulative radiation exposure and, theoretically, skin cancer risk, they are particularly useful in patients at increased risk of skin cancer.

Cyclosporine is an effective systemic medication utilized in the treatment of psoriasis. A sequential regimen of low-dose cyclosporine, 3 mg/kg/d for 4 weeks, followed by a rapid taper and subsequent NB-UVB phototherapy was compared with NB-UVB monotherapy in 30 different patients; the study revealed equal PASI reduction in both groups but a decrease in the total number of exposures and cumulative UVB dose required for the group treated with cyclosporine plus NB-UVB.[46] In addition, the group pretreated with cyclosporine had a more rapid resolution of pruritus and also experienced improvement in plaque severity at sites that were completely or almost completely shielded from UV exposure. The simultaneous use of NB-UVB and cyclosporine is contraindicated because of the increased likelihood of skin cancer: a theoretical risk extrapolated (by expert opinion) from numerous studies demonstrating the increased rate of photocarcinogenesis when cyclosporine is used in conjunction with PUVA.[47,48] Although patients may appreciate the need for fewer phototherapy sessions, as demonstrated in this study, cyclosporine is not recommended for use in combination with NB-UVB given the lack of significant supporting evidence and likely increased risk of nonmelanoma skin cancer secondary to immunosuppression and UV exposure.[46]

The efficacy of combination fumaric acid esters (FAEs) with NB-UVB administered thrice weekly was assessed, anticipating that the addition of early phototherapy could counterbalance the relatively slow onset of action for FAE therapy.[49] After 6 weeks, patients with psoriasis receiving combination treatment experienced a greater reduction in PASI compared with the FAE monotherapy arm (69% vs 35%, respectively [P = .016]). Additionally, PASI 75 was achieved by 79% of patients with combined therapy versus by none of the patients who received FAE monotherapy. The combination group also had more rapid improvement in Dermatology Life Quality Index scores, suggesting that the addition of NB-UVB accelerates the therapeutic response to FAEs in moderate-to-severe psoriasis. These findings support those of a previous study that analyzed data from 363 patients with psoriasis to determine that FAE therapy in conjunction with phototherapy resulted in a faster clinical response to treatment, although there was no difference in overall efficacy noted at 12 months.[50] This study included patients treated with several different types of phototherapy, including BB-UVB, NB-UVB, UVA, and PUVA, and it found no significant differences based on phototherapy type. Overall, these data suggest that the addition of NB-UVB is particularly useful at the initiation of FAE therapy in the treatment of psoriasis.

Combination treatment with NB-UVB and certain biologics is also supported by the literature and recommended for cases in which monotherapy with either treatment modality is inadequate. One study specifically focused on patients with moderate-to-severe psoriasis who did not respond to either NB-UVB or etanercept monotherapies. Although 8 of 322 patients were unable to achieve PASI 75 with either treatment alone, all of them ultimately obtained PASI 75 with combination NB-UVB and etanercept treatment, and 3 subjects experienced complete remission after 14.6 plus or minus 3.3 NB-UVB sessions while taking etanercept.[51] Lynde et al took patients who failed to achieve a 90% improvement in PASI score (PASI 90) after 12 weeks of treatment with etanercept and randomized them into 2 groups: those who would receive another 12 weeks of etanercept monotherapy (n = 38) versus those who would continue treatment with etanercept in addition to a 4-week course of thrice-weekly NB-UVB phototherapy (n = 37).[52] Only 22% of those in the combination group were more than 80% adherent with the NB-UVB regimen, but those who were experienced a greater likelihood of PASI 90 at week

24 than did those treated with etanercept alone (43% vs 21%, respectively). In addition to greater reductions in modified PASI scores with combination treatment, biopsy specimens of psoriatic plaques taken after 6 weeks of etanercept plus NB-UVB treatment had greater histologic improvement compared with biopsy specimens of plaques that were shielded from UVB exposure.[53]

In patients treated with NB-UVB thrice weekly in conjunction with adalimumab, 40 mg every other week, 95% of patients achieved PASI 75, 75% achieved PASI 90, and 55% achieved a 100% improvement in PASI score at week 12, with 65% of patients retaining PASI 75 at week 24.[54] There were no monotherapy arms in this study for comparison. No serious adverse events were recorded, and the most frequent adverse effect was mild-to-moderate UV erythema after phototherapy sessions. In a small study with 4 patients with psoriasis who were taking adalimumab and had one-half of their body additionally treated with NB-UVB thrice weekly for 6 weeks while the other half served as a control, the end of treatment PASI for irradiated body halves was 2.0 compared with 6.9 in the nonirradiated halves, corresponding to an overall mean PASI reduction of 86% compared with 53%, respectively.[55] In a similar trial, patients were treated with ustekinumab and had half of their body treated with NB-UVB 3 times per week for 6 weeks while the other half was left as a control.[56] PASI scores were lower for the irradiated body halves at the end of 6 weeks, with a mean PASI score reduction of 82% in the irradiated half versus 54% in the half not treated with NB-UVB.

The oral phosphodiesterase-4 inhibitor apremilast has been used in conjunction with phototherapy, a combination that circumvents the need for regular injections. To investigate the efficacy and safety of this combination, 29 patients with psoriasis were treated during a 12-week period with apremilast, 30 mg twice daily, plus NB-UVB thrice weekly.[57] Of these 29 patients, 22 (76%) ultimately completed the full 12 weeks, and 16 of them (73%) achieved PASI 75. The mean scores for several other measures of psoriasis severity also improved at week 12, including the scores for the PASI (77%), visual analogue scale for pain (77%), visual analogue scale for itch (69%), Dermatology Life Quality Index (70%), and Physician's Global Assessment (67%). The authors concluded that combination treatment was effective and there were no unexpected safety signals. The most common adverse events were mild and moderate erythema reactions, which were experienced by 38% of patients. A separate retrospective study also concluded that apremilast can safely be combined with NB-UVB in patients not responding to phototherapy alone.[58]

Several studies involving small numbers of patients have investigated the potential benefits of combined therapy with NB-UVB and PUVA, finding enhanced efficacy, fewer treatment sessions, and lower cumulative UVA and UVB doses than with either treatment alone.[59-61] Despite these findings, concerns remain about the long-term risk of photocarcinogenesis with this combination, and there is insufficient evidence at this time to recommend combined therapy with NB-UVB and PUVA for the treatment of psoriasis.

Risks of NB-UVB

Overall, NB-UVB is a safe and well-tolerated intervention, as long as safeguards and cautions are implemented. On the basis of studies involving BB-UVB phototherapy, genital shielding is recommended in all patients during phototherapy sessions to reduce the risk of genital skin cancer.[62] Wavelengths ranging from 295 nm to 320 nm increase the risk of UV-induced cataracts, with 300 nm representing the most potent wavelength.[63] Though evidence is lacking for an increased risk of cataracts in patients with psoriasis treated with phototherapy of any kind, eye protection with goggles is recommended during treatment sessions to reduce the potential risk of UVB-related ocular toxicity, including keratitis and corneal burns.[64]

Another potential concern is photocarcinogenesis. Skin cancer risk in patients with psoriasis treated with UVB (both NB-UVB and BB-UVB) was correlated with the number of treatments received, although the calculated risk of malignancy was not significantly greater than that of the general population[65]; there was no significant difference in the rates of actinic keratosis or skin cancer between NB-UVB and BB-UVB. Multiple studies specifically assessing the carcinogenic potential of NB-UVB did not find an increased risk of skin cancer in treated patients.[26] Unfortunately, there are few prospective studies assessing the risk of skin cancer in patients with psoriasis treated with NB-UVB. Because of the theoretical possibility of this risk, physicians should use caution in prescribing NB-UVB for patients with a history of melanoma, multiple nonmelanoma skin cancers, arsenic intake, or exposure to ionizing radiation.

NB-UVB is considered safe in pregnancy and is recommended for the treatment of generalized plaque or chronic guttate psoriasis.[66-69] However, UVB exposure may be associated with a dose-dependent degradation of folate with cumulative exposures

higher than 40 J/cm^2, and per-treatment exposures higher than 2 J/cm^2 are associated with a 19% to 27% drop in serum folate levels.[70] This is a concern, as folate deficiency in pregnancy has been associated with fetal neural tube defects, which occur as early as 4 weeks after conception and before many women realize that they are pregnant. With this in mind, all women of childbearing potential who are being treated with phototherapy should supplement with folate, 0.8 mg daily, to decrease the risk of neural tube defects resulting from unplanned pregnancies.[71] NB-UVB should not be used in patients with photosensitive disorders, such as xeroderma pigmentosa, and it should be used with caution in patients with a history of recurrent oral herpes simplex virus infection. Although NB-UVB has historically been contraindicated in those with lupus, expert opinion dictates that it can be used with caution in patients with lupus who do not have a history of photosensitivity and are SS-A–negative. Because almost all photosensitizing medications have an action spectrum in the UVA range, and because NB-UVB lamps emit negligible UVA, it is safe to deliver NB-UVB phototherapy in patients who are taking photosensitizing medications. None of the previously mentioned studies investigated NB-UVB in pustular, scalp, inverse, or erythrodermic psoriasis, and very few studies included palmoplantar psoriasis.

Recommendations for NB-UVB

The strength and level of evidence of the recommendations for NB-UVB are summarized in Tables III and IV.*

BB-UVB

BB-UVB lamps emit a broad spectrum of wavelengths, ranging from 270 to 390 nm, with a peak emission at 313 nm. BB-UVB phototherapy represents an older form of phototherapy than NB-UVB. Because of this, many of the adverse effects and several of the innovative combination therapies have been conducted with BB-UVB light sources and extended to NB-UVB. Because BB-UVB phototherapy for psoriasis has been in use for such a long time, there are relatively few clinical trials evaluating its safety and efficacy. As with NB-UVB, the starting dose for BB-UVB treatment can be selected according to patient phototype or MED.[9] BB-UVB is an effective treatment for generalized plaque psoriasis, and it can be recommended as monotherapy.[1,4,15,81] In an analysis of 3 trials including 246 patients with plaque psoriasis treated with BB-UVB the PASI 75 rate was 73%, and in an analysis of 4 other trials including 148 patients the clearance rate was 59%.[1] Several smaller studies have also shown similar results.[4,81] Dosing schedules of both thrice weekly and 5 times weekly demonstrated impressive results in a prospective comparative study, which found 100% clearance in 18 of 20 patients receiving 3 treatments per week (average, 23.2 treatments) and in all of 26 patients receiving 5 treatments per week (average, 27 treatments).[15]

Although effective, BB-UVB is less effective than oral PUVA and NB-UVB for the treatment of plaque-type psoriasis.[1,4,27] For the treatment of palmoplantar psoriasis, BB-UVB is less effective than topical PUVA.[82]

Combination therapy with BB-UVB

Concomitant use of acitretin with BB-UVB clears lesions more rapidly than do doses UVB monotherapy, and with a lower required cumulative UVB dose.[83,84] In a large meta-analysis, the psoriasis clearance rates were 59% with BB-UVB monotherapy and 54%, 63%, and 56% when BB-UVB was combined with topical fluocinonide, coal tar, and topical calcipotriol, respectively.[1] Thus, there is insufficient evidence to recommend combined treatments of topical corticosteroids or vitamin D analogues with BB-UVB. A thin layer of topical emollient, however, is recommended before treatment because of improved efficacy.[15-17]

Risks of BB-UVB

The risks associated with BB-UVB are similar to those associated with NB-UVB, including ocular toxicity and photocarcinogenesis. The 12-year prospective cohort study that helped to determine the risk of genital skin cancers in patients treated with phototherapy utilized BB-UVB, rather than NB-UVB, as the mode of UVB exposure. Patients should wear genital and eye protection during treatment sessions, and caution should be used when prescribing BB-UVB in patients with an increased risk of skin cancer because of a personal history or prior environmental exposures, such as arsenic or ionizing radiation.[62-65,79,85]

Recommendations for BB-UVB

The strength and level of evidence of the recommendations for NBB-UVB are summarized in Tables V and VI.†

*1-4,8,10-13,18-34,36,43-46,57,58,65-67,70,73-80

†1,2,4,15,19,27,62,65,79,81-84,86-88

Table III. Strength of recommendations for NB-UVB

Recommendation No.	Recommendation	Strength of recommendation
1.1	NB-UVB phototherapy is recommended for adults with plaque psoriasis as monotherapy	A
1.2	The recommended starting dose for NB-UVB phototherapy for adults with generalized plaque psoriasis should be based on the MED or determined by using a fixed dose or skin phototype protocol	A
1.3	During the treatment phase, 3-times/wk dosing of NB-UVB phototherapy for adults with generalized plaque psoriasis is recommended	B
1.4	Short-term PUVA monotherapy is more efficacious than NB-UVB for treatment of psoriasis in adults	B
1.5	Though less effective, NB-UVB is preferred to PUVA monotherapy for the treatment of psoriasis in adults because of enhanced safety, convenience, and cost savings	A
1.6	NB-UVB is recommended over BB-UVB monotherapy for adults with generalized plaque psoriasis	A
1.7	NB-UVB monotherapy is recommended for patients with guttate psoriasis, regardless of age	A
1.8	Home NB-UVB phototherapy is recommended for appropriate patients with generalized plaque psoriasis as an alternative to in-office NB-UVB phototherapy	B
1.9	NB-UVB phototherapy is recommended for pregnant women with generalized plaque psoriasis and guttate psoriasis	C
1.10	Concomitant topical therapy with vitamin D analogues, retinoids, and corticosteroids during NB-UVB phototherapy can be used safely with a potential to improve efficacy	B
1.11	Combination therapy with oral retinoids and NB-UVB phototherapy is recommended for appropriate patients with generalized plaque psoriasis who do not respond adequately to monotherapy	B
1.12	Long-term combination therapy with cyclosporine and NB-UVB phototherapy is not recommended for adults with generalized plaque psoriasis because of increased incidence of skin cancer	C
1.13	Combination therapy with apremilast and NB-UVB phototherapy can be considered for adult patients with generalized plaque psoriasis who do not respond adequately to monotherapy	C
1.14	Genital shielding is recommended in all patients during NB-UVB phototherapy to reduce the risk of genital skin cancer	C
1.15	Eye protection with goggles is recommended during NB-UVB phototherapy to reduce the risk of UVB-related ocular toxicity	C
1.16	NB-UVB should be used with caution in patients with a history of melanoma or multiple nonmelanoma skin cancers, history of arsenic intake, and/or prior exposure to ionizing radiation due to the potential risk of photocarcinogenesis	C
1.17	Women of childbearing age receiving NB-UVB phototherapy should take folate supplementation	B
1.18	Maintenance phototherapy can be considered to maintain clinical response	B

BB, Broadband; *MED*, minimal erythema dose; *NB*, narrowband; *PUVA*, psoralen plus ultraviolet A; *UVB*, ultraviolet B.

TARGETED UVB

Targeted UVB treatments such as excimer laser (308 nm), excimer light (308 nm), and targeted NB-UVB light (311-313 nm) are well suited and recommended for treating localized psoriatic lesions.[80,90-95] An advantage of targeted phototherapy is that it spares unaffected skin, permitting higher doses, faster clearing, and less risk. Because only small areas are treated, burns are generally well tolerated when they occur. An analysis of 13 different studies calculated a pooled, weighted estimate of 61% for the proportion of patients achieving PASI 75 with targeted UVB treatments.[80] In a study of 120 patients with psoriasis treated with a 308-nm excimer laser, approximately 85% achieved at least a 90% improvement after 7 to 13 treatments.[92] In addition to

Table IV. Level of evidence for NB-UVB recommendations

Recommendation	Recommendation No.	Level of evidence	Studies
NB-UVB for adults	1.1	I-II	1-4
Dosing			
• NB-UVB dose based on skin type	1.2	I-II	10,26
• NB-UVB therapy 2-3 times/wk	1.3	I-II	1,12,13
Treatment comparison			
• NB-UVB vs short-term PUVA	1.4	I-II	1-4,18-26
• NB-UVB vs PUVA monotherapy	1.5	I-II	1-4,18-26
• NB-UVB vs BB-UVB	1.6	I-II	1,4,27-30
• NB-UVB home vs in-office	1.8	I	32
Special psoriasis cases			
• NB-UVB and guttate psoriasis	1.7	I-II	11,31,32,72
• NB-UVB and pregnancy	1.9	III	66,67,70,73
Combination therapy			
• NB-UVB + topical therapies	1.10	I-II	33,34,36,74-78
• NB-UVB + oral retinoid	1.11	I-III	43-45
• NB-UVB + cyclosporine	1.12	II	46
• NB-UVB + apremilast	1.13	II	57,58
Precautions			
• Shield genital area	1.14	II	79
• Wear eye protection	1.15	III	Expert opinion
• Screen for a history of skin cancer and previous phototherapy or photochemotherapy	1.16	I-II	26,65,80
• Women who are of childbearing age and taking a folic supplement	1.17	III	66,70
• NB-UVB maintenance dose for remission	1.18	I	8

BB, Broadband; *NB*, narrowband; *PUVA*, psoralen plus ultraviolet A; *UVB*, ultraviolet B.

efficacy, a systematic review of localized phototherapy modalities found that targeted UVB therapy requires fewer treatments and a lower cumulative dose than nontargeted phototherapy.[94] Specifically for palmoplantar plaque psoriasis and palmoplantar pustulosis, an excimer laser and excimer light were effective in multiple studies, with up to 57% of patients achieving complete clearance with a laser and more than 40% achieving substantial improvement with light.[96-100]

The ideal frequency of treatment with targeted UVB is twice to thrice weekly, and the starting dose can be determined by using a fixed dose protocol, skin phototype, or MED.[9,80,90] Further adjustment can be made on the basis of physical characteristics (size, thickness, location) of an individual lesion (see Table VII).[9,80,90] A recent study determined that a more aggressive "medium-dose" regimen of excimer laser (starting at 200% of the MED with 25% dose increments) was no more efficacious than the standard "low-dose" regimen (starting at 70% of the MED with 20% dose increments) and led to an increased incidence of adverse effects such as pain and blistering.[101] Painful erythema and blistering are common adverse effects from targeted UVB phototherapy, with the incidence ranging from 0% to 92% depending on the particular protocol used and a pooled weighted estimate of 16% incidence.[80] Other common adverse effects include pruritus, burning, hyperpigmentation, and transient perilesional edema.

Excimer lasers have been used with great efficacy in the management of scalp psoriasis, and this treatment may represent a viable intermediate treatment option before starting systemic medication for severe or recalcitrant scalp psoriasis not responding to topical therapies.[102] For the treatment of localized plaque psoriasis, including scalp and palmoplantar psoriasis, a recent systematic review and meta-analysis of 13 studies concluded that the excimer laser is the most effective of the 3 targeted UVB therapies (70% of patients achieved PASI 75), followed by the excimer light (59% rate of achievement of PASI 75) and then targeted NB-UVB light (49% rate of achievement of PASI 75).[80] The same meta-analysis analyzed data from 3 RCTs comparing the efficacy of targeted UVB phototherapy with that of topical PUVA and determined that topical PUVA is comparable to excimer light in efficacy and superior to targeted NB-UVB light.[80,103-105] Multiple authors, however, have noted that targeted NB-UVB may present a lower risk of adverse effects and results in better

Table V. Strength of recommendations for BB-UVB

Recommendation No.	Recommendation	Strength of recommendation
2.1	In cases where NB-UVB is unavailable, BB-UVB phototherapy is recommended for use as monotherapy in adults with generalized plaque psoriasis	A
2.2	BB-UVB monotherapy should be considered inferior in efficacy to NB-UVB and oral PUVA monotherapy for use in adults with generalized plaque psoriasis	A
2.3	BB-UVB monotherapy may be offered for use in adults but is considered inferior in efficacy to topical PUVA monotherapy	B
2.4	BB-UVB monotherapy may be considered for use in adults with guttate psoriasis	C
2.5	Genital shielding is recommended in all patients during BB-UVB phototherapy to reduce the risk of genital skin cancer	B
2.6	Eye protection with goggles is recommended during BB-UVB phototherapy to reduce the risk of UVB-related ocular toxicity	C
2.7	Due to the potential risk of photocarcinogenesis, BB-UVB should be used with caution in patients with a history of melanoma or multiple nonmelanoma skin cancers, history of arsenic intake, or prior exposure to ionizing radiation	B
2.8	Acitretin can be considered in combination with BB-UVB for adults with generalized plaque psoriasis	B

BB, Broadband; *NB*, narrowband; *PUVA*, psoralen plus ultraviolet A; *UVB*, ultraviolet B.

Table VI. Level of evidence for BB-UVB recommendations

Recommendation	Recommendation No.	Level of evidence	Studies
BB-UVB for adults	2.1	I-III	1,4,15,81
Comparison			
• BB-UVB vs PUVA	2.2	I-II	1,2,4,19,27
Special psoriasis cases			
• Palmoplantar psoriasis	2.3	I-II	2,19,82
• Guttate psoriasis	2.4	II-III	79,86
Combination therapy			
• BB-UVB + acitretin	2.8	I-II	83,84
Precautions			
• Shield genital area	2.5	II	62,79
• Wear eye protection	2.6	III	Expert opinion
• Screen for a history of skin cancer and previous phototherapy	2.7	II	62,65,87-89

BB, Broadband; *NB*, narrowband; *PUVA*, psoralen plus ultraviolet A; *UVB*, ultraviolet B.

compliance compared with PUVA, given that there is no need for prior application of topical psoralen. Targeted NB-UVB may thus be preferred over topical PUVA because of its larger margin of safety.[104,105] For palmoplantar pustular psoriasis, however, 1 study of 64 patients revealed that ultraviolet A1 phototherapy is superior to targeted NB-UVB (a mean improvement in Palmoplantar Pustular Psoriasis Area and Severity Index score of 6.0 ± 2.4 vs 4.4 ± 1.4 [$P < .05$] after 30 treatments) and may thus be preferred in the treatment of this specific entity.[106]

Although the aforementioned analyses would suggest that the excimer laser is more effective than topical PUVA, there are no RCTs directly comparing the 2 modalities. As such, there is insufficient evidence to recommend the excimer laser rather than topical PUVA for treatment of localized plaque psoriasis. Studies do support the combination of the excimer laser with oral or bath PUVA for the treatment of plaque psoriasis, a pairing that decreases number of treatment sessions and cumulative UVA dose by up to half but it is not more effective than PUVA monotherapy.[107] Excimer lasers may also

Table VII. Dosing guidelines for targeted therapy

Initial dose for psoriasis				
Plaque thickness	**Induration score**	**Fitzpatrick skin type I-III (dose in mJ/cm^2)**		**Fitzpatrick skin type IV-VI (dose in mJ/cm^2)**
None	0	0		0
Mild	1	300		400
Moderate	2	500		600
Severe	3	700		900
Dose for subsequent treatments				
No effect	**Minimal effect**	**Good effect**	**Considerable improvement**	**Moderate/severe erythema (with or without blistering)**
No erythema at 12-24 h and no plaque improvement	Slight erythema at 12-24 h but no significant improvement	Mild-to-moderate erythema response 12-24 h	Significant improvement with plaque thinning or reduced scaliness or pigmentation occurred	
Typical dosing change from prior treatment dose				
Increase dose by 25%	Increase dose by 15%	Maintain dose	Maintain dose or reduce by 15%	Reduce dose by 25% (treat around blistered area, do not treat blistered area until it heals, or crust disappears)

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be used in conjunction with topical steroids for plaque psoriasis combination therapy; this combination has greater efficacy (PASI improvement of 83% after 10 treatments versus 72% with excimer monotherapy).[108]

Administration of high-dose excimer laser therapy at 6 to 10 times a patient's MED has been termed *TURBO-UVB*, and it was effective in a preliminary study of 18 patients with psoriasis to whom investigators administered a single treatment of TURBO-UVB at 10 times the MED with subsequent 8-week follow-up.[109] Plaque-type psoriasis on the body was the only type of psoriasis treated in the study, and patients with a history of skin cancer, photosensitivity, or current use of immunomodulatory or anti-inflammatory drugs were excluded. After the single TURBO-UVB treatment, patients experienced an average improvement of PASI score of 42%. Skin thickness and lesional T-cell counts were still improved at 8 weeks after treatment. Only 5 of 18 patients developed mild (grade 0) erythema, edema, and clear exudate at the treatment site within the 24 to 48 hours following TURBO-UVB treatment, and these effects resolved within the ensuing 2 to 3 days. Although the initial assessment of this treatment method shows promise, there is currently little evidence about TURBO-UVB, and therefore a recommendation cannot be made regarding its use in the treatment of psoriasis.

Recommendations for targeted UVB

The strength and level of evidence of the recommendations for targeted UVB are summarized in Tables VIII and IX.‡

PUVA (TOPICAL, ORAL, BATH)

The term *PUVA* refers to the use of photosensitizing agents, called psoralens, to sensitize target cells to the effects of UVA light for the treatment of psoriasis and other skin conditions. Some psoralens are synthetic whereas others are naturally occurring tricyclic furocoumarins found in plants. They can be administered topically as a cream or mixed with the bath water, or they may be ingested orally (see Tables X and XI for oral PUVA dosing).[9] Psoralens exert their effects by intercalating between DNA base pairs and forming DNA cross-links upon exposure to UVA, effectively preventing DNA replication. They also facilitate the production of reactive oxygen species, which damage cell membranes and result in cell death, and they deplete lymphoid cells in the skin.[111] In the United States, 8-MOP is the only commercially available oral psoralen; in Europe, 5-methoxypsoralen is used because of its lower tendency to cause phototoxicity, and trimethylpsoralen (TMP) is often utilized for bath PUVA.

‡80,90-100,108,110

Table VIII. Strength of recommendations for targeted UVB

Recommendation No.	Recommendation	Strength of recommendation
3.1	Targeted UVB phototherapy, including excimer laser (308 nm), excimer light (308 nm), and targeted NB-UVB light (311-313 nm), is recommended for use in adults with localized plaque psoriasis (<10% BSA), for individual lesions, or in patients with more extensive disease	A
3.2	To achieve maximal efficacy, treatment with targeted UVB phototherapy for adults with localized plaque psoriasis should be carried out 2-3 times/wk rather than once every 1-2 wk	A
3.3	The starting dose for targeted UVB phototherapy for adults with localized plaque psoriasis can be determined on the basis of the MED or by a fixed dose or skin phototype protocol	A
3.4	An excimer laser (308 nm) is more efficacious than an excimer light (308 nm), which is more efficacious than localized NB-UVB light (311-312 nm) for the treatment of localized plaque psoriasis in adults	B
3.5	Targeted UVB phototherapy, including excimer laser (308 nm) and excimer light (308 nm), is recommended for use in adults with plaque psoriasis, including palmoplantar psoriasis	A
3.6	Excimer laser (308 nm) may be combined with topical corticosteroids in the treatment of plaque psoriasis in adults	B
3.7	Excimer laser (308 nm) is recommended in the treatment of scalp psoriasis in adults	B

BSA, Body surface area; *MED*, minimal erythema dose; *NB*, narrowband; *UVB*, ultraviolet B.

Topical PUVA

Topical PUVA is best suited for the treatment of localized psoriasis and is recommended in particular for palmoplantar disease. There are 2 options for administering topical PUVA: either as 0.1% 8-MOP solution compounded with an emollient and applied 20 minutes before UVA exposure or as 1 mL of 1% 8-MOP solution mixed with 2 L of water and soaked into hands and feet for 30 minutes before UVA exposure. In a meta-analysis of 7 studies looking at the efficacy of topical PUVA, 77% of subjects achieved PASI 75 compared with 61% for targeted UVB phototherapy.[80] Although topical PUVA shares with targeted UVB the benefit of sparing unaffected skin, there is a comparatively narrow therapeutic window owing to the risk of phototoxicity with topical PUVA. Additionally, the accessibility of this treatment option is an important practical consideration, as targeted UVB phototherapy is becoming more widely used, and fewer centers are offering topical PUVA.

Bath PUVA

Bath PUVA involves mixing a psoralen with the bathwater and soaking affected areas before treatment with UVA light. Bath PUVA is commonly administered as 0.5 to 1 mg/L of 8-MOP in water or 0.33 mg/L of TMP in water.[112] Bath PUVA is as effective as oral PUVA in the treatment of psoriasis.[113-115] A recent systematic review, however, concluded that bath PUVA is less effective than oral PUVA, with only 47% of patients obtaining PASI 75 compared with 73% of patients receiving oral PUVA.[1] Bath PUVA tends to cause fewer adverse effects, such as erythema and nausea, there are fewer drug interactions, and it offers the added benefit of requiring a lower cumulative dose of UVA than of oral PUVA to obtain clearance.[114,115] Bath PUVA is effective in the treatment of psoriasis, and it may be considered preferable to oral PUVA for some patients. In 1 survey of 99 patients, 55% of patients chose bath PUVA over oral PUVA.[116]

Risks of bath PUVA. No long-term studies on photocarcinogenesis with bath PUVA have been reported. Unlike with use of oral PUVA, however, systemic psoralen absorption is minimal. Phototoxicity can occur with bath PUVA, and without studies confirming its safety, the same restrictions apply as with oral PUVA with respect to the types of patients in whom treatment should be avoided or used with caution. Although bath PUVA is effective and used in Europe for the treatment of psoriasis, its use in the United States is limited for several reasons. TMP, which is frequently used for bath PUVA in Europe, is not approved by the US Food and Drug Administration and thus cannot be utilized in the United States. Additionally, practitioners have experienced difficulty in obtaining insurance reimbursement for this treatment. Further, maintenance and operation of a bath PUVA unit require substantial resources, including

Table IX. Level of evidence for targeted UVB phototherapy recommendations

Recommendation	Recommendation No.	Level of evidence	Studies
Targeted UVB for adult psoriasis	3.1	I-II	80,90,92-95,110
Dose			
• 2-3 times/wk vs 1-2 times/wk	3.2	I	80
• Initial dose based on minimal erythema dose	3.3	I	80
Comparison			
• Excimer laser vs excimer light vs NB-UVB	3.4	I	80
Special psoriasis type			
• Excimer laser and light for palmoplantar psoriasis	3.5	I-II	80,96-100
• Excimer laser and scalp psoriasis	3.7	II-III	91,93
Combination			
• Excimer laser + topical therapy	3.6	II	108

NB, Narrowband; *UVB*, ultraviolet B.

Table X. Dosing of 8-methoxypsoralen for oral psoralen plus ultraviolet A

Patient weight		
lb	kg	Drug dose, mg
<66	<30	10
66-143	30-65	20
144-200	66-91	30
>200	>91	40

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Table XI. Dosing of ultraviolet A radiation for oral psoralen plus ultraviolet A

Skin type	Initial dose, J/cm^2	Increments, J/cm^2	Maximum dose, J/cm^2
I	0.5	0.5	8
II	1.0	0.5	8
III	1.5	1.0	12
IV	2.0	1.0	12
V	2.5	1.5	20
VI	3.0	1.5	20

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nursing staff, space, regular cleaning of the bathtub, and immediate availability of the PUVA therapy booth after the bath.

Oral PUVA

In a study of more than 1300 patients with psoriasis, 88% of subjects cleared with oral 8-MOP followed by UVA light treatment. Following remission, maintenance therapy regimens with once-weekly, twice-weekly, or thrice-weekly PUVA were all sufficient and equal in maintaining skin clearance at a higher rate than the rate in those not undergoing maintenance treatments.[117] In 2009, a large systematic review including analysis of more than 122 studies reaffirmed that maintenance therapy with PUVA is effective at maintaining skin clearance.[118] There was "high-quality evidence" that, among 1005 patients with psoriasis who cleared completely with PUVA, the rate of relapse within 18 months among those undergoing maintenance therapy (27%-34% depending on treatment frequency) was lower than the rate among patients who did not undergo maintenance therapy (62%).[118] In patients with severe psoriasis, 88.8% of 3175 subjects experienced at least "marked" improvement in their disease with PUVA.[119] In this study the probability of a patient remaining in remission for a period of 80 weeks was the same regardless of whether maintenance treatments were administered.

Combining oral PUVA with an oral retinoid, such as acitretin, is more effective than either treatment alone. In a large systematic review analyzing combination treatments in psoriasis, 7 trials with a total of 265 patients analyzed the use of oral vitamin A derivatives with PUVA. These trials suggested that combination treatment was associated with a 22% greater likelihood of skin clearance than was PUVA monotherapy and a 47% greater likelihood than was vitamin A derivative monotherapy.[120] Another trial involving 60 patients with severe psoriasis compared PUVA plus acitretin with PUVA monotherapy; 96% of the patients cleared with combination therapy whereas only 80% of those receiving PUVA alone cleared, and additionally, the cumulative UVA dose was 43% lower in the combination group.[121]

Risks of oral PUVA. Although strong evidence exists for the efficacy of oral PUVA in the treatment of psoriasis, this treatment modality has been used much less often owing to the wide availability of NB-UVB phototherapy and the greater risk of

adverse effects with PUVA. Acute and subacute adverse effects include phototoxicity, nausea, pruritus, photo-onycholysis, and melanonychia. Lentigines and photocarcinogenesis (primarily squamous cell carcinoma) are adverse effects of long-term oral PUVA exposure.[122] The risk of basal cell carcinoma is not greatly increased, even with high-dose PUVA exposure. The risk of squamous cell carcinoma is increased primarily in patients who have received more than 350 treatments; patients who have received fewer than 150 treatments have, at most, only a mild increase in risk.[122]

Nonmelanoma skin cancer with oral PUVA, however, appears to be a problem chiefly for whites and other fair-skinned individuals, as those with skin of color do not have an increased risk.[123] Melanoma risk with oral PUVA is uncertain, as American studies have demonstrated an increased incidence whereas European studies have not.[26,124-127] Given the associated risks, oral PUVA is contraindicated in those younger than 10 years; pregnant patients; nursing mothers; and those with a personal history of melanoma, lupus erythematosus, or xeroderma pigmentosum. Oral PUVA should be used with caution in those 10 to 18 years of age and those with a personal history of dysplastic nevi, nonmelanoma skin cancer, photosensitivity, exposure to carcinogenic agents (eg, ionizing radiation, arsenic) or immunosuppressive medications (eg, methotrexate, cyclosporine).[112] As nearly all drug-induced phototoxicity has an action spectrum in the UVA range, it is important to be cautious in patients who are taking photosensitizing medications as well.[128] There are numerous photosensitizing medications, including diuretics such as thiazides, antibiotics such as tetracyclines, and many other commonly used agents.[129] Given the widespread availability and ease of administration of NB-UVB, along with the expense of 8-MOP and the relative scarcity of UVA units, currently, oral PUVA is not as widely used as other treatments are.

Recommendation for PUVA

The strength and level of evidence of the recommendations for PUVA are summarized in Tables XII and XIII.[§]

PDT

Photodynamic therapy (PDT) uses photosensitizing chemicals to destroy premalignant or malignant cells. The principal topical sensitizing agents used in practice are 5-aminolevulinic acid (ALA) and methyl aminolevulinic acid (MAL) (the related but more lipophilic methyl ester of ALA that can penetrate more deeply into the targeted skin). Both are precursors of protoporphyrin IX (PpIX) in the heme biosynthetic pathway. Major absorption peaks for both agents fall within the range of blue (410-420 nm) and red (630 nm) light. Treatment protocols for ALA typically use blue light, whereas MAL treatment protocols use red light to activate the compound.

PpIX accumulates preferentially in psoriatic plaques; PDT-induced apoptosis of T lymphocytes could lead to reductions in inflammatory cytokines and, in turn, to improvement of psoriasis.[131,132] Despite the theory, clinical studies have failed to find significant benefit from treatment of psoriasis with ALA-PDT or MAL-PDT. In an analysis of 3 studies investigating the effect of ALA-PDT in the treatment of plaque psoriasis, the estimate of efficacy was calculated to be 22%.[80] There was also a relatively high rate of adverse effects. Another systematic review, of 14 studies corroborated the conclusion that ALA-PDT is minimally effective with significant adverse effects.[133]

PDT has also been investigated as a treatment for nail psoriasis. In an open, intrapatient, left-to-right comparison study with 14 subjects, 61 psoriatic nails were treated with MAL-PDT using a pulse dye laser (PDL) as the light source, whereas 60 psoriatic nails were treated with PDL alone.[134] Patients underwent monthly treatments with evaluation of Nail Psoriasis Severity Index (NAPSI) scores at baseline, 3 months, and 6 months. Although NAPSI scores improved with both treatments, there was no significant difference in psoriatic nails treated with topical MAL plus PDL versus with PDL alone. On the basis of the available evidence, the use of MAL-PDT with PDL for the treatment of nail psoriasis cannot be recommended.

Recommendations for PDT

The strength and level of evidence of the recommendations for PDT are summarized in Tables XIV and XV.[80,133,134]

GRENZ RAY

Grenz ray therapy involves the use of long-wavelength ionizing radiation for the treatment of a variety of dermatoses. The radiation in grenz ray therapy has a low penetrance, with 75% absorbed by the first 1 mm of skin and 95% within the first 3 mm, allowing very little residual radiation to pass into deeper tissues. Grenz ray therapy has been used for psoriasis for decades but is rarely used in modern-day dermatology owing to the growing number of effective alternatives. Even so, grenz ray therapy can

[§]1,26,80,103,105,113-117,119,121-123,130

Table XII. PUVA therapy strength of recommendation

Recommendation No.	Recommendation	Strength of recommendation
4.1	Topical PUVA phototherapy is superior to localized NB-UVB light (311 to 313 nm) in the treatment of localized plaque psoriasis, particularly for palmoplantar psoriasis and palmoplantar pustular psoriasis, in adults	B
4.2	Oral PUVA is recommended for the treatment of psoriasis in adults	A
4.3	Bath PUVA is recommended for the treatment of moderate to severe plaque psoriasis in adults	B

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

Table XIII. Level of evidence of PUVA recommendations

Recommendation	Recommendation No.	Level of evidence	Studies
Type of PUVA therapy administration for adult psoriasis			
• Topical	4.1	I-III	80,103,105
• Oral	4.2	I-II	26,117,119,121-123,130
• Bath	4.3	I-III	1,113-116

PUVA, Psoralen plus ultraviolet A.

Table XIV. Strength of recommendations for PDT

Recommendation No.	Recommendation	Strength of recommendation
5.1	For localized psoriasis, including palmoplantar psoriasis and nail psoriasis, in adults, topical ALA-PDT and MAL-PDT are not recommended	A

ALA, 5-Aminolevulinic acid; *MAL*, methyl aminolevulinic acid; *PDT*, photodynamic therapy.

Table XV. Level of evidence for PDT

Recommendation	Recommendation No.	Level of evidence	Studies
• Topical ALA-PDT and MAL-PDT are not recommended for localized psoriasis, nail psoriasis and palmoplantar psoriasis	5.1	I-II	80,133,134

ALA, 5-Aminolevulinic acid; *MAL*, methyl aminolevulinic acid; *PDT*, photodynamic therapy.

be an alternative to UV therapy for resistant localized psoriasis, including palmoplantar psoriasis, in cases in which patients have not responded to numerous other treatments, or when UV therapy cannot be used. The typical treatment regimen involves administration of 200 rad per session at weekly intervals up to a total of 800 to 1000 rad. After a 6-month rest, treatments can be resumed up to a total cumulative dose of 5000 rad.[135] Radiation dermatitis is a risk of grenz ray therapy, if not properly administered.

In a single-center questionnaire study of 351 patients treated with grenz ray therapy from 1990 to 2001, 98 patients (28%) responded to the survey.[136] Only 65% of those responders had psoriasis, and 62% of this psoriasis subgroup noted improvement or resolution of psoriasis. Of the patients with psoriasis treated with grenz ray therapy, only 48% thought that the treatment was worthwhile and 45% indicated that they would use the treatment again, whereas the remaining responders were either unsure or disagreed with these statements. Overall, there is limited literature evaluating grenz ray therapy in the treatment of plaque psoriasis and consequently not enough evidence to recommend its routine use for psoriasis. Furthermore, the accessibility of this modality is extremely restricted, as only a few centers in the United States still offer grenz ray therapy. It is typically reserved for patients with recalcitrant disease who have failed several topical and systemic alternatives.

CLIMATOTHERAPY

Climatotherapy is a treatment for psoriasis that involves temporary or, in some cases, permanent relocation to areas of the world that provide a favorable climate and natural resources that can be

utilized for disease control. The most notable of these locations is the Dead Sea, although treatment centers exist at several other sites in the world, including the Black Sea coast, Blue Lagoon in Iceland, and the Canary Islands, to name a few. The exact treatment protocol varies from center to center, but in general, climatotherapy involves consultation with medical professionals, psoriasis education, group discussions, daily physical training, individualized sun exposure schedules, psychosocial support, and other location-specific novel components. The Dead Sea has been studied for its unique geographic attributes. At 419 meters below sea level, it is the lowest inhabited place on the earth. Compared with sea level, this unparalleled low altitude results in a higher percentage of longer-wavelength UVA, as a result of which a lower percentage of shorter-wavelength UVB reaches the surface, thus allowing for increased duration of natural sun exposure with less risk of UV-induced erythema. The sea may contribute to the environment's natural UV protection by creating an ever-present miasma of salt and mineral-infused moisture that is thought to diffuse and mitigate the sun's rays. Bathing in the mineral-rich Dead Sea may also produce antiproliferative effects on keratinocytes, and the relaxing nature of a climatotherapy getaway, in general, can decrease psychosocial stress and allow for a soothing and healing effect, which may result in decreased inflammation and disease improvement.

In several studies on climatotherapy, psoriasis improved both objectively and subjectively. In a retrospective study, Harari et al analyzed the records of 605 patients with psoriasis that were taken from the database of the Research Institute at the Dead Sea. Most of the patients received climatotherapy at the Dead Sea for a period of 4 weeks (mean, 4.1 weeks), and by the end of treatment, 94% had achieved PASI 75 and 73% had achieved a 95% improvement in PASI score.[137] In a prospective observational study of 119 patients with psoriasis, 45% and 20% had improvement in QoL by the end of the treatment that persisted for 3 months after treatment (45% and 20%, respectively).[138]

Although Dead Sea climatotherapy is effective in improving psoriasis severity and patient QoL, other locations for climatotherapy exist and have been tested. Treatment on Gran Canaria in the Canary Islands, Spain, consists of a 3-week program of medical consultations, group education sessions, sun exposure, and physical training. In a prospective study of 254 adults with psoriasis who completed this program, patients were asked to complete the Health Education Impact Questionnaire, as well as the Self-Administered PASI (SAPASI), at baseline, 3 weeks, and 3 months.[139] By the end of treatment, there was a statistically significant improvement seen in all Health Education Impact Questionnaire scales, with the largest change seen in health-directed activity, followed by in emotional distress and skill and technique acquisition. SAPASI score had also improved from a mean of 8.6 to 1.6. Three months after completion of therapy, the emotional distress scale was the only scale score that was still better than at baseline. The SAPASI score had increased to 6.4, although this was still significantly better than at baseline.

These studies reveal the potential benefit of climatotherapy but also expose 1 of its limitations, which is the apparent transient nature of its beneficial effects. The improvement in psoriasis severity and psychologic health seems to wane after a few months, although there have been no formal studies on the remission duration associated with climatotherapy.

VISIBLE LIGHT

Visible light has been explored as a potential treatment for psoriasis. Blue and red light have been the focus of investigation, as stand-alone treatments. Psoriatic plaques have higher levels of endogenous PpIX than normal-appearing skin or skin affected by other dermatologic diseases do.[140] With this knowledge, researchers posited that naturally occurring PpIX could serve as a viable target for visible light therapy in psoriasis, without the need for prior application of exogenous photosensitizing agents. Most studies have been small, though promising.

Kleinpenning et al treated 20 patients with psoriasis with either blue or red light 3 times a week for 4 consecutive weeks.[141] A compound of 10% salicylic acid in petrolatum was used as a pretreatment for 1 week before and then daily throughout the study to decrease the plaque scale, which could serve as a barrier to light penetration. The pretreatment was so effective at decreasing plaque scale that the final scores of desquamation and induration were not appreciably different between the 2 light groups and the control group, which received only the pretreatment. However, improvements in erythema were better among the groups receiving light treatments (43% with blue light, 36% with red light, and 10% with salicylic acid monotherapy). The blue light was most effective, as the improvement in erythema with blue light was not only more pronounced but continued throughout the study period, whereas no significant improvement in erythema was seen over the final 6 treatments with red light. Visible light treatment was safe with minimal side effects, as no patients developed erythema surrounding treated lesions. Hyperpigmentation was the most common side effect; it was seen in nearly all patients undergoing blue light

treatment and directly related to the number of treatments received.

Another study tested blue light treatment at 420 nm and 453 nm, each of which was administered daily for a period of 4 weeks. Both groups experienced statistically significant improvements in Local Psoriasis Severity Index scores by the end of the treatment course.[142] Non-UV blue light treatment was safe and effective in improving Local Psoriasis Severity Index scores, whether delivered as a high-intensity regimen of 453 nm at 200 mW/cm^2 or a low-intensity regimen at 100 mW/cm^2 (though high-intensity treatment was more effective).[143]

Intense pulsed light (IPL) administered every 2 weeks for 6 months can be successful in treating nail psoriasis, with 71.2% improvement in the nail bed, 32.2% improvement in the matrix, and 82.4% improvement in total NAPSI score.[144] The effects of IPL therapy were enduring, with only 3 of the 22 patients relapsing within the 6 months following treatment. Although these few, small studies suggest the potential of IPL, there is insufficient evidence currently available to recommend its use for the treatment of psoriasis.

GOECKERMAN THERAPY

Goeckerman therapy is a psoriasis treatment that was developed in 1921 and involves the use of coal tar in combination with UVB phototherapy. It is a safe and effective option for patients with severe or recalcitrant psoriasis.[145] Coal tar and UVB are thought to work in concert to inhibit angiogenesis and keratinocyte proliferation, as well as to decrease T-lymphocyte numbers in the skin and alter inflammatory cytokine expression.[146] When it was first developed at the Mayo Clinic, Goeckerman therapy was an inpatient treatment requiring significant resources for both the patient and the care providers. The original regimen called for the application of 1% to 5% crude coal tar to affected skin sites, allowing 30 minutes to 2 hours before wiping or washing it off and subsequently exposing the treated site to UVB light. Treatments were carried out 5 days per week. In the 1960s, outpatient Goeckerman treatment centers were established, which made treatment more widely accessible but still required a day-long regimen of tar application followed by UVB exposure.

A case-control study with 48 subjects compared a modified Goeckerman regimen with "conventional" treatments (including phototherapy in combination with topical steroids, oral immunosuppressants, and/or biologics); the 2 groups experienced similar reductions in PASI score and comparable improvements in QoL and psychosocial distress scores.[147] The duration of remission following a 30-day treatment period was longer for patients treated using the Goeckerman regimen than for patients who received conventional treatments (mean, 22.3 months vs 4.6 months, respectively) and the cost was less.[147] In a retrospective study analyzing data from 51 patients with psoriasis who had achieved skin clearance from a 3-week outpatient Goeckerman regimen, 51% of patients maintained remission for up to a year or longer (some up to 2 years), with those continuing maintenance home NB-UVB treatments achieving the longest duration of remission.[148]

Risks of Goeckerman therapy

Because the Goeckerman regimen is an old treatment, there are no RCTs or systematic reviews evaluating its effectiveness and long-term risks.[118] Photocarcinogenesis is a theoretical risk but has not been demonstrated despite long-term follow-up.[145] The most common reported adverse effects have been local burning as a result of tar sensitivity ("tar smarts").[148] The necessary time investment on the part of the patient is a disadvantage of Goeckerman therapy, and outpatient treatment requires close proximity to a capable medical facility. The relatively rapid and robust clinical response seen with the Goeckerman regimen, the long duration of remission, and the low adverse effect profile render Goeckerman therapy an attractive option for the treatment of psoriasis, particularly for those with resistant disease. Difficulty obtaining appropriate reimbursement from insurance companies has contributed to the decline of Goeckerman therapy in the United States. Because of the messy and cumbersome nature of tar application and the wide availability of highly effective NB-UVB, the Goeckerman regimen is no longer commonly used. Despite this, there is ample evidence to recommend this treatment for psoriasis.

PDL

The pulsed dye laser (PDL) is effective for treatment of nail psoriasis.[134,149-151] In a study of 60 psoriatic nails with PDL alone and another group with a combination of PDL and methylaminolaevulinic acid,[134] treatments were administered monthly, and NAPSI scores were calculated at baseline, 3 months, and 6 months. NAPSI scores decreased in both the nail matrix and nail bed. In a bilateral comparison controlled trial, 19 patients completed a 6-month course of topical tazarotene 0.1% cream applied to all 10 nails, with the nails of 1 hand also receiving monthly 595-nm PDL treatments.[150] At the end of 6 months, the nails that received PDL in addition to tazarotene had a greater decrease in NAPSI scores, higher scores on the patient's global assessment of

Table XVI. Strength of recommendations for grenz ray, climatotherapy, visible light, Goeckerman, PDL, and IPL therapies

Recommendation No.	Recommendation	Strength of recommendation
6.1	There is insufficient evidence to recommend grenz ray for the treatment of psoriasis	C
7.1	There is sufficient evidence to recommend the use of climatotherapy for the treatment of psoriasis	B
8.1	There is insufficient evidence to recommend the use of visible light to be more effective for the treatment of psoriasis, except in the case of nail psoriasis	C
9.1	There is sufficient evidence to recommend the use of Goeckerman for the treatment of psoriasis	B
10.1	PDL may be considered for nail psoriasis	B

IPL, Intense pulsed light; *PDL*, pulsed dye laser.

Table XVII. Level of evidence for grenz ray, climatotherapy, visual light, Goeckerman, PDL, and IPL therapy recommendations

Recommendation	Recommendation No.	Level of evidence	Studies
Grenz ray	6.1	III	136
Climatotherapy	7.1	II-III	137-139
Visible light therapy	8.1	II-III	141-144
Goeckerman therapy	9.1	II-III	147,148
PDL for nail psoriasis	10.1	II	152

IPL, Intense pulsed light; *PDL*, pulsed dye laser.

improvement, and higher rate of achieving a 75% improvement in physician's global assessment scores (31.6% versus 5.3%, respectively). A study of 20 patients with nail psoriasis compared 96 psoriatic nails treated using monthly PDL with 96 untreated nails[152]; there was greater improvement in NAPSI scores with the PDL treatment (scores at baseline, month 3, and month 7 of 25.45 ± 5.38, 15.40 ± 5.78, and 4.95 ± 4.03, respectively, in PDL-treated nails compared with scores of 24.95 ± 5.35, 26.95 ± 4.45, and 28.75 ± 4.69 for the control nails [$P < .001$]).

Another study confirmed the benefit of PDL and further demonstrated that pulse duration does not significantly alter efficacy in treating psoriatic nails, as 6-months of treatment using a pulse duration of 6 milliseconds resulted in a decrease in NAPSI score similar to that with treatment using a 0.45-millisecond pulse duration.[151] Monthly PDL was more effective than was twice-weekly excimer laser in the treatment of nail psoriasis.[149] In a bilateral comparison study with 42 patients, a PDL decreased NAPSI score by 26.3 compared with by 13.5 for an excimer laser (measured 3 months after the end of a 3-month treatment course), and the rates of 50%, 75%, and 100% improvements in NAPSI score were 81%, 55%, and 14%, respectively, for PDL-treated nails versus 16%, 0%, and 0% with the excimer laser.[149] Onycholysis and subungual hyperkeratosis were the most responsive nail psoriasis characteristics, and nail pitting was the least responsive. Adverse effects from the aforementioned studies were mild, including hyperpigmentation of the cuticles, transient petechiae, and slight pain during treatment sessions. PDL can therefore be recommended as a viable treatment for nail psoriasis.

Recommendations for grenz ray, climatotherapy, visible light, Goeckerman, and IPL therapies

The strength and level of evidence of the recommendations for grenz ray, climatotherapy, visible light, Goeckerman, and IPL therapies are summarized in Tables XVI and XVII.[¶]

ROLE OF PATIENT PREFERENCES

Efficacy and safety data should be discussed with patients to make an informed treatment decision regarding initiation of phototherapy or when considering switching between phototherapy modalities or adding adjunctive topical or systemic agents.

In addition to disease severity, QoL assessment should be considered and discussed with patients before starting phototherapy or switching to an alternate modality.

Other factors that can affect patient preference and should be discussed with patients include dosing frequency, cost, and immediate availability of/proximity to the respective phototherapy unit.

For the sake of convenience, less frequent phototherapy dosing (twice weekly) may be preferred by

[¶] 136-139,141-144,147,148,152

some patients despite the need to extend treatment duration to obtain the desired effect.

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APPENDIX 1

Method

A multidisciplinary workgroup (WG) of recognized psoriasis experts, consisting of dermatologists (including private practitioners), a rheumatologist, a cardiologist, and representatives from a patient advocacy organization, was convened to update and expand on the previously published 2010 American Academy of Dermatology (AAD) psoriasis guideline.[7] The WG determined the scope of the guideline and identified important clinical questions with regard to psoriasis photochemotherapy and phototherapy treatment (Table I). WG members completed a disclosure of interests that was periodically updated and reviewed for potential relevant conflicts of interests throughout the guideline development.

An evidence-based model was used, and evidence was obtained by using a search of the PubMed and MEDLINE databases from January 1, 2008, to December 31, 2017, for all newly identified clinical questions. Searches were limited to publications in the English language. Medical Subject Heading (MeSH) terms used in various combinations in the literature search included *psoriasis* (*plaque, vulgaris, guttate, erythrodermic, inverse, pustular*), phototherapy, *ultraviolet* (*short-wave, long-wave*), *targeted phototherapy* (*excimer laser*), narrowband *ultraviolet B* (*NB-UVB*), *photochemotherapy*, *psoralen ultraviolet long-wave*, *broad-band ultraviolet B* (*BB-UVB*), *grenz ray*, *climatotherapy*, *photodynamic therapy*, *visible light* (*red/blue*), *broadband ultraviolet A* (*BB-UVA*), *ultraviolet B light-emitting diode* (*LED*) (*UVB-LED*), *TURBO-UVB*, *intense pulsed light*, and *Goeckerman therapy*.

After removal of duplicate data, 56 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 utilized by the WG in developing recommendations. The Academy's prior published guidelines on psoriasis were evaluated, as were other current published guidelines on psoriasis.

The available evidence was evaluated by using a unified system called the Strength of Recommendation Taxonomy (SORT), which was developed by editors of the US family medicine and primary care journals (ie, *American Family Physician*, *Family Medicine*, *Journal of Family Practice*, and *BMJ USA*). Evidence was graded by using a 3-point scale based on the quality of methodology (eg, randomized control 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 basis of the best available evidence. These are ranked as follows:

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

In those situations in which documented evidence-based data are not available, we have utilized expert opinion to generate our clinical recommendations or opted not to generate a recommendation.

This guideline has been developed in accordance with the AAD/AAD Association Administrative Regulations for Evidence-Based Clinical Practice Guidelines (May 2014),[153] which includes the opportunity for review and comment by the entire AAD membership and final review and comment by the AAD Board of Directors. Additionally, this guideline has been developed in collaboration with the National Psoriasis Foundation, and as part of the review process, the National Psoriasis Foundation medical board members provided their feedback. This guideline will be considered current for a period of 5 years from the date of publication unless reaffirmed, updated, or retired before that time.

Definitions

Psoriasis vulgaris is a chronic inflammatory skin disease that classically presents with well-demarcated, pink plaques with silvery scale, commonly involving the scalp, elbows, knees, and presacral region, though any area of skin may be involved, including the palms and soles. The severity of psoriasis is generally defined by the total body surface area (BSA) involved, with less than 3% BSA involvement considered mild, 3% to 10% BSA

involvement considered moderate, and more than 10% BSA involvement considered severe disease. The Psoriasis Area Severity Index is a more specific means of quantifying the extent and severity of psoriasis, as it takes into account not only BSA but also intensity of redness, scaling, and plaque thickness, ultimately producing a score from 0 (no disease) to 72 (maximal disease severity). The Psoriasis Area Severity Index is frequently used in research for monitoring response to treatments, and it is also utilized by dermatologists in general practice and specialized psoriasis clinics.

Psoriasis is an autoimmune condition stemming from inappropriate activation of cutaneous T cells and dendritic cells, with subsequent release of inflammatory cytokines such as interleukin 1 (IL-1), IL-6, IL-12, IL-17, IL-23, and tumor necrosis factor-α. These chemical signals are responsible for keratinocyte hyperproliferation manifesting as characteristic scaly plaques, and they also contribute to the rampant inflammation underlying a number of systemic disease associations, including metabolic syndrome, heart disease, and arthritis. To combat the inflammation at the root of this condition, a number of topical and systemic medications have been created and utilized with varying success.

In addition to medication, treatment with light waves has proven to be an effective and largely safe intervention that can lead to significant improvement in—or even complete clearance of—associated psoriatic skin lesions. Phototherapy refers to the treatment of medical conditions via controlled exposure to certain types of electromagnetic radiation, in particular, ultraviolet radiation, which includes wavelengths ranging from 200 nm to 400 nm on the electromagnetic spectrum. Although the use of light in medicine is truly an ancient concept extending thousands of years into the past—to the ancient Greeks, Egyptians, and Chinese—focus in modern times began in the late 19th century. Since its rediscovery, advancements in science have enabled more measured application of light, allowing practitioners to choose the specific wavelengths of radiation that they wish to apply, and offering various topical or systemic means of modifying or amplifying the patient's response to these treatments.

Psoralens are naturally occurring photosensitizing agents that, in combination with UVA radiation (PUVA), have demonstrated significant benefit in the treatment of psoriasis and other inflammatory skin conditions. With wavelengths ranging from 320 to 400 nm, UVA radiation is capable of penetrating deeper into the skin than UVB light and can thus assert effects on a wider variety of cell types, including dermal mast cells, granulocytes, dendritic cells, T lymphocytes, fibroblasts, and endothelial cells, in addition to the more superficial dendritic cells and keratinocytes of the epidermis.[154] UVB comprises a range of shorter wavelengths from 280 to 320 nm and is less capable of penetrating the epidermis than UVA is. Thus, its effects are typically restricted to epidermal keratinocytes and dendritic cells. Although the entire UVB spectrum was used in initial UVB-based phototherapy (broadband UVB; BB-UVB), action spectrum studies have since determined that wavelengths between 304 and 313 nm produce the most therapeutic effect in clearing psoriatic plaques, whereas wavelengths from 290 to 300 nm, in fact, have very little benefit and mostly contribute to the development of sunburn.[155] This revelation led to the development of a more precise treatment termed *NB-UVB*, which has now been used for many years with great efficacy. Further variations of UVB administration have been developed over the years and are being utilized and further investigated today, including various lasers, light-emitting diode lights, and combinations with other medications/preparations. Even visible light (400-700 nm) has been explored as a treatment for psoriasis and will be discussed alongside other noted therapies in the subsequent text.