Phototherapy and photochemotherapy for skin conditions

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Coverage policy

Ultraviolet A phototherapy, ultraviolet B therapy, and photochemotherapy using psoralen ultraviolet A are clinically proven and, therefore, may be medically necessary for the following skin conditions after conventional therapies have failed (Davis, 2023; Elmets, 2019; Ling, 2016; Menter, 2020; Olsen, 2016):

- Atopic dermatitis (eczema).
- Cutaneous T-cell lymphoma, including mycosis fungoides and Sézary syndrome.
- Dermatoses (other).
- Lichen planus.
- Psoriasis.
- Vitiligo.

Psoralen ultraviolet A home therapy is investigational/not clinically proven and, therefore, not medically necessary.

Ultraviolet B home phototherapy is clinically proven and, therefore, may be medically necessary when all of the following conditions are met (Davis, 2023; Elmets, 2019):

- The member is diagnosed with any of the conditions listed above.
- The member is unable to travel for office-based therapy.
- The condition is considered severe and extensive.
- Disease is refractory to conventional treatments for at least four months.
- The member requires treatment at least three times per week.

Ultraviolet B home phototherapy is investigational/not clinically proven and, therefore, not medically necessary for any of the following (Hum, 2019):

- When treatment is conducted at home for member convenience.
- When ultraviolet B therapy is used as first-line therapy.
- When ultraviolet B therapy is used for cosmetic purposes.
- For any treatment beyond a single course.
- For any condition other than those listed above.

Limitations

All other uses of psoralen ultraviolet A and narrowband ultraviolet B are investigational/not clinically proven, and therefore, not medically necessary.

Alternative covered services

Standard-of-care first-line treatments for skin conditions.

Background

Ultraviolet light — a cause of sunburns, wrinkles, and skin cancer — can be used in a medical setting as therapy for certain hard-to-treat skin problems and other medical conditions. Phototherapy is the controlled administration of non-ionizing radiation to the skin involving ultraviolet light. The main forms of phototherapy apply ultraviolet A (with or without a photosensitizing agent) and ultraviolet B (Rathod, 2023).

Psoralen ultraviolet A uses psoralens to sensitize target cells to the effects of ultraviolet A light at 320 to 400 nanometers in wavelength. Psoralen ultraviolet A treatment typically involves administration of an oral drug (e.g., methoxypsoralen) followed by exposure to ultraviolet A 45 to 60 minutes. Topical administration of psoralen ultraviolet A treatment include (Rathod, 2023):

- Bath psoralen ultraviolet A, in which the affected area is immersed in a basin of water containing 8-methoxypsoralen; it is rarely used in the United States.
- Application of 8-methoxypsoralen ointment or lotion directly to lesions on palms and plantar surfaces of the feet, followed by ultraviolet A exposure.

The original intent of psoralen ultraviolet A was treatment of psoriasis, a relatively common skin disorder. Other uses include conditions such as vitiligo and mycosis fungoides (the most common type of T-cell lymphoma).

While topical medications often control mild psoriasis, severe cases often require treatments involving ultraviolet A light exposure (Cole, 2023).

There is the potential for psoralen ultraviolet A to increase the risk of skin cancer, especially when treating psoriasis. Persons at elevated risk for skin cancer from psoralen ultraviolet A include children and persons with a genetic predisposition, a history of skin cancer, or a history of at least 150 prior psoralen ultraviolet A treatments. Types of toxicity to psoralen ultraviolet A include erythema, pruritus, xerosis, irregular pigmentation, and gastrointestinal symptoms. Altering or dividing the dose can avoid most toxicity (Cole, 2023).

Oral psoralen ultraviolet A is contraindicated in patients younger than 10 years, pregnant patients, nursing mothers, and patients with a personal history of melanoma, lupus erythematosus, or xeroderma pigmentosa (Elmets, 2019). Caution should be exercised for: patients age 10 to 18 years; patients with skin types 1 and 2 who tend to burn easily; those with a history of dysplastic nevi, photosensitivity, melanoma or nonmelanoma skin cancer; or those with exposure to carcinogenic agents (e.g., arsenic intake or ionizing radiation) or immunosuppressive agents.

Available forms of ultraviolet B treatment are broadband, narrowband, and targeted applications. Broadband emits wavelengths ranging from 270 to 390 nanometers. Narrowband emits wavelengths ranging from 311 to 313 nanometers. Targeted ultraviolet B treatments may employ narrowband, excimer laser (308 nanometers), or excimer light (308 nanometers) (Elmets, 2019).

Findings

Guidelines

In general, phototherapy serves as a reasonable and effective treatment option for patients requiring more than topical medications, wishing to avoid systemic medications, or needing an adjunct to a failing regimen. Psoralen ultraviolet A or ultraviolet B therapy-related guidelines are often specific to a patient's condition.

The American Academy of Dermatology conditionally recommends phototherapy (primarily narrowband ultraviolet B), for adults with atopic dermatitis based on low certainty evidence of safety and efficacy; psoralen ultraviolet A is not recommended (Davis, 2023) .

For mycosis fungoides and Sézary syndrome, for which ultraviolet light is often used, the United States Cutaneous Lymphoma Consortium suggests a more refined guideline based on patient stage and centers, and in combination with other agents in practice and clinical trials (Olsen, 2016).

According to the American Academy of Dermatology, narrowband ultraviolet B administered two to three times weekly has largely replaced broadband ultraviolet B as the technique of choice for treating psoriasis in adults, although a small portion of persons with skin conditions who do not respond well to narrowband do respond to broadband. Narrowband ultraviolet B may be administered as monotherapy or in combination with oral or topical medications to increase efficacy. Targeted ultraviolet treatment options may be appropriate for localized lesions. Home narrowband ultraviolet B may offer a treatment alternative for patients with limited access to outpatient treatment (Elmets, 2019).

Narrowband ultraviolet B is contraindicated in patients with photosensitive disorders (e.g., xeroderma pigmentosa). It should be used cautiously in patients with a history of melanoma, multiple nonmelanoma skin cancers, arsenic intake, or exposure to ionizing radiation. Narrowband ultraviolet B is considered safe to use in pregnant patients and may be used cautiously in patients with lupus erythematosus who have no history of

photosensitivity and are Ro(SSA)-negative (Elmets, 2019). Other specific recommendations include (Elmets, 2019):

- Narrowband ultraviolet B phototherapy or oral psoralens ultraviolet A over broadband ultraviolet B as monotherapy, but broadband ultraviolet B therapy may be used when narrowband ultraviolet B therapy is unavailable.
- Narrowband ultraviolet B monotherapy for patients with guttate psoriasis, regardless of age, consider broadband ultraviolet B monotherapy for adults with guttate psoriasis.
- Narrowband ultraviolet B phototherapy for pregnant women with generalized plaque psoriasis and guttate psoriasis.
- Topical psoralen ultraviolet A phototherapy over narrowband ultraviolet B phototherapy for localized plaque psoriasis, particularly for palmoplantar psoriasis and palmoplantar pustular psoriasis.
- Bath psoralen ultraviolet A for treatment of moderate to severe plaque psoriasis.
- Combination therapy for patients with generalized plaque psoriasis who do not respond adequately to monotherapy.
- Home narrowband ultraviolet B phototherapy for whom travel to an outpatient facility is a limiting factor.
- Guideline-directed maintenance phototherapy to maintain clinical response.

For treating psoriasis in pediatric populations, the American Academy of Dermatology recommends narrowband ultraviolet B phototherapy for moderate to severe pediatric plaque and guttate psoriasis (Menter, 2020). Excimer laser or psoralen ultraviolet A therapy may be efficacious and well-tolerated, but the supportive evidence for these options is limited.

A 2016 guideline from the British Association of Dermatologists and British Photodermatology Group states as follows, based on evidence in the professional literature (Ling, 2016):

- For psoriasis, narrowband ultraviolet B is the preferred treatment. Ultraviolet A is indicated for chronic plaque psoriasis and atopic eczema if ultraviolet B treatment is ineffective.
- For some indications, ultraviolet A is the first-line phototherapy — mycosis fungoides beyond patch stage, pustular psoriasis, pompholyx, hand and foot eczema, and adult generalized pityriasis rubra pilaris.
- For eczema, narrowband ultraviolet B is the first-line phototherapy.
- For cutaneous T-cell lymphoma, ultraviolet A is the first-line treatment. Ultraviolet B can be used in early stages of the disease.
- For vitiligo, narrowband ultraviolet B is at least as effective as psoralen ultraviolet A.
- For photodermatoses, ultraviolet A and B are equally effective, with safety concerns.
- For hand and foot dermatoses, ultraviolet A and B are equally effective.

<u>Evidence reviews – phototherapy efficacy and safety</u>

Psoriasis

Psoriasis is the condition most studied for phototherapy outcomes. While the optimal protocol has not established, phototherapy used as monotherapy or in combination offers a safe and effective treatment for psoriasis (Damiani, 2022; Li, 2022).

A systematic review of 10 trials of pediatric psoriasis cases showed narrowband ultraviolet B to be 80% effective (Kim, 2020). A systematic review of 35 studies found systemic treatment for psoriasis, including ultraviolet B phototherapy, reduced pruritus but did not reduce prevalence of lesions (Therene, 2018).

A systematic review of 29 articles (n = 675) of persons with palmoplantar pustular psoriasis found that phototherapy, cyclosporine, and topical corticosteroids each controlled palmoplantar pustular psoriasis, with psoralen ultraviolet A having greater efficacy than ultraviolet B therapy (Sevrain, 2014). Another meta-analysis of psoriasis (23 studies, n = 765) also found psoralen ultraviolet A to be more efficacious than non-larger targeted ultraviolet B phototherapy, although both treatments had positive outcomes (Almutawa, 2015).

Carcinogenic risk is a concern for patients undergoing ultraviolet light treatment for psoriasis. Lighter skin phototypes are well-studied, as numerous studies have been conducted on Caucasian patients, while darker phototypes have increased morbidity and mortality for skin cancer due to atypical lesions or advanced stage at presentation. Earlier research compared the carcinogenic risk of phototherapy on Caucasians versus non-Caucasians. A systematic review of eight studies analyzed skin cancer risk with different types of phototherapy according to Fitzpatrick skin phototype, which uses human skin pigmentation and reaction to ultraviolet light to rank skin phototypes (from I to VI) to determine initial dosing. While cutaneous oncogenic risk was reported in some studies, contradictory evidence and limited reporting of Fitzpatrick skin phototype prevented drawing strong conclusions about the oncogenic risk in psoriasis patients based on skin phototypes (Thatiparthi, 2022).

Atopic dermatitis

A Cochrane review of phototherapy for atopic dermatitis (eczema) included 32 trials of 1,219 participants from secondary care dermatology clinics with a range severities who underwent any form of phototherapy (Musters, 2021). Low-certainty evidence supported all reported outcomes. The strongest evidence suggests that, compared to placebo or no treatment, narrowband ultraviolet B (13 trials) may improve physician-rated signs, patient-reported symptoms, and Investigator Global Assessment after 12 weeks, without a difference in withdrawal due to adverse events. Comparisons to other forms of phototherapy were inconclusive.

An analysis of 28 systematic reviews found reasonable evidence that ultraviolet B treatment is effective for atopic eczema (Solman, 2019). A systematic review of 22 studies with low risk of bias concluded that various treatments, including ultraviolet radiation, were effective treatments for eczema (Nankervis, 2017).

A systematic review of 21 randomized controlled trials including 961 participants determined that narrowband ultraviolet B and ultraviolet A1 phototherapy in moderate to severe atopic dermatitis were helpful, but data on psoralen ultraviolet A use and phototherapy in children are scarce (Perez-Ferriols, 2015). Another systematic review of 19 studies (n = 905) found that ultraviolet A1 and narrowband ultraviolet B were the most effective treatments for reducing signs and symptoms of atopic dermatitis (Garritsen, 2014).

Vitiligo

Ultraviolet phototherapy is a safe treatment for vitiligo and poses no significant risk of skin cancer (Wu, 2022). A meta-analysis of 38 studies of persons with vitiligo compared narrowband ultraviolet B phototherapy (n = 1,201) to psoralen ultraviolet A phototherapy (n = 227). The ultraviolet B group had more “at least mild” responses at six and 12 months after therapy (74.2% and 75.0%) than did the psoralen ultraviolet A group (51.4% and 61.6%). Marked responses were more common in the face and neck (44.2%) than in the trunk (26.1%) and the extremities (17.3%) after six months of ultraviolet B phototherapy (Bae, 2017).

A systematic review determined narrowband ultraviolet B had fewer side effects and was marginally better than psoralen ultraviolet A for vitiligo, and that (along with topical corticosteroids) it offered the greatest benefits of any vitiligo treatment (Whitton, 2016). A systematic review of seven studies (n = 232) comparing vitiligo treatment by psoralen ultraviolet A and narrowband ultraviolet B revealed no statistically significant difference between the two on the rate of participants who achieved more than 50% or more than 75% repigmentation (Xiao, 2015).

Four new systematic reviews and meta-analyses examined the efficacy of phototherapy as monotherapy or combination therapy for repigmentation of vitiligo. The results suggest combination therapy using either narrowband-ultraviolet B phototherapy or excimer laser with tacrolimus (Chang, 2021), or narrowband ultraviolet B, psoralen ultraviolet A, or excimer laser with calciprotriol (Hu, 2021) may provide greater clinical improvement than phototherapy alone. The results supporting the superiority of narrowband ultraviolet B with or without fractional CO_2 laser are mixed, likely the result of heterogeneous selection criteria and treatment protocols (Chang, 2020; Kim, 2021).

For patients with vitiligo, a systematic review and network meta-analysis of 22 randomized controlled trials (n = 1,194) concluded that hospital-based narrowband ultraviolet B combined with carboxytherapy, Er: YAG laser plus topical 5% 5-fluorouracil, needling/micro-needling, betamethasone intramuscular injection, or topical tacrolimus was more efficacious than monotherapy in inducing a successful repigmentation response rate ≥ 75% and avoiding failed treatment. Narrowband ultraviolet B combined with either Er: YAG laser plus topical 5% 5-fluorouracil or needling/microneedling would be the preferred therapeutic approaches, as they were less likely to result in an ineffective repigmentation response (≤ 25%). Data limitations prevented a quantitative analysis of adverse effects. Commonly reported phototoxic effects were erythema, edema, pruritus, pain, and burning sensation; two studies reported serious adverse effects of Koebner's phenomenon and scarring (Zhu, 2023).

Mycosis fungoides/cutaneous T-cell lymphoma

Mycosis fungoides is the most common cutaneous T-cell lymphoma, and conventional therapy is not always effective in treating it. A review of 20 papers documented photodynamic therapy as a promising and well-tolerated option for treating localized lesions, with excellent cosmetic outcomes (Xue, 2017). Psoralen ultraviolet A and narrowband ultraviolet B monotherapy were effective first-line interventions for mycosis fungoides; the effectiveness of psoralen ultraviolet A either as maintenance therapy or combined with drugs as first-line therapy is uncertain, but may be beneficial for relapse and late-stage disease (Dogra, 2015).

A systematic review/meta-analysis of seven studies (n = 778 participants with mycosis fungoides) compared 527 treated with psoralen ultraviolet A and 251 with narrowband ultraviolet B. The ultraviolet A group had superior outcomes in percent with any response (P = .20) and complete response (P = .04). The ultraviolet A group was superior in the percent with partial response (P = .07). Rates of adverse effects were similar (Phan, 2019).

A Cochrane review of 20 randomized controlled trials (n = 1,369) included five studies addressing psoralen ultraviolet and found no evidence challenging the general consensus that it be used as first-line treatment for mycosis fungoides (Valipour, 2020).

Lichen planus

In a Cochrane review of 16 studies, 11 of which were randomized controlled trials, psoralen ultraviolet A treatment for cutaneous lichen planus had comparable outcomes to a psoralen ultraviolet A bath and narrowband ultraviolet B (Atzmony, 2016).

A review of 14 studies (n = 64) of pediatric participants with pityriasis lichenoides determined that broadband ultraviolet B, narrowband ultraviolet B, and psoralen ultraviolet A had initial clearance rates of 90%, 73%, and 83%, respectively, with recurrence rates of 23.1%, 0%, and 60%, respectively (Maranda, 2016).

An analysis of two systematic reviews and nine randomized controlled trials upheld the efficacy of narrowband ultraviolet B treatment for lichen planus (Fazel, 2015).

Reviews - home phototherapy efficacy and safety

Phototherapy is usually administered in an outpatient setting, but this treatment is also available for home use.

A multicenter randomized controlled trial (n = 196) concluded that home narrowband ultraviolet B delivered at practitioner-determined dosing schedules was as safe, effective, and cost-effective as outpatient treatment for mild to severe psoriasis, was more convenient, and generated higher satisfaction compared to outpatient treatment; data on patient adherence and adverse events were not reported (Koek, 2009; PLUTO study; ClinicalTrials.gov identifier NCT00150930).

A recent systematic review found no other randomized trials of narrowband ultraviolet B phototherapy home treatment and reached similar conclusions (Ontario Health [Quality], 2020). Other observational studies were heterogeneous with respect to types of ultraviolet light used, making comparisons across studies difficult, and double-blind or placebo-controlled trials were not available. The authors were uncertain about any potential differences in risk of adverse events between the two settings.

Several reviews identified criteria for selecting patients for home treatment who are candidates for office-based narrowband ultraviolet B phototherapy. Home phototherapy is feasible for many patients for whom office-based phototherapy is not accessible (e.g., patients who live far from a phototherapy center, are unable to travel because of extensive disease, or incur prohibitive travel) (Ashraf, 2022; Cohen, 2022).

Treatment schedules generally vary based on skin condition, but Hum (2019) recommended narrowband ultraviolet B (311 nanometers), administered on alternating days, as a safe and effective treatment mode for home phototherapy. Systematic reviews of randomized controlled trials confirmed that home-based phototherapy and phototherapy for psoriasis (Damiani, 2022; Li, 2022), vitiligo (Wu, 2022), and atopic dermatitis (Xiao, 2022) are safe and effective treatment options, although the optimal treatment administration has not been determined.

In 2022, we removed four older reviews and added two updated guidelines from the American Academy of Dermatology and six new systematic reviews. The results are consistent with previous findings, and no policy changes are warranted. As a potential new indication, a Cochrane review of 37 randomized controlled trials (n = 1,663) found insufficient evidence supporting the effectiveness of various interventions for chronic palmoplantar pustulosis, including ultraviolet A phototherapy (Obeid, 2020).

In 2023, we added several systematic reviews to the policy. The new information warrants no changes to the policy. New indications for phototherapy and photochemotherapy are emerging. Currently, the evidence from research is insufficient, and no guidelines support routine clinical use for the following indications:

- In patients with systemic sclerosis, limited low-quality evidence from small observational studies and individual case reports suggests ultraviolet A (340-400 nm) and psoralen ultraviolet A reduced skin thickening and increase skin elasticity with no serious side effects (Miziołek, 2022).
- A systematic review of 31 case series examined the safety and effectiveness of light- and laser-based treatments for granuloma annulare. The clearance rates for the phototherapies were psoralen ultraviolet A (59%; n = 131), ultraviolet A (31%, n = 86), and ultraviolet light B or narrowband ultraviolet light B (40%; n = 47). Although psoralen ultraviolet A had higher complete response rate, concerns for carcinogenesis may limit its use and, instead, favor ultraviolet B modalities for their moderate effectiveness and safety profile (Mukovozov, 2022).

In 2024, we added new literature to the policy with no policy changes warranted. For port wine stains, a systematic review and meta-analysis found low-quality evidence from three randomized clinical trials and 23 cohort studies supporting the safety and effectiveness of photodynamic therapy. Collectively, 51.5% of

participants achieved at least a 60% improvement in port wine stain appearance across different administrations of treatment, age groups, lesion locations, and subtypes. Adverse effects were documented infrequently, but most experienced moderate pain and edema. Other adverse effects such as photosensitive dermatitis, hyperpigmentation, blister, and scar were infrequently reported (Wang, 2023).

In 2025, we reorganized the findings section, updated the references, and added no newly published, relevant literature to add to the policy. No policy changes are warranted.

References

On January 6, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “phototherapy," "photochemotherapy," “PUVA therapy,” “UVA,” “UVB,” “psoriasis,” “vitiligo,” “eczema,” “mycosis,” and “fungoides.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

5/2015: initial review date and clinical policy effective date: 10/2015

5/2016: Policy references updated.

4/2017: Policy references updated.

3/2018: Policy references updated.

5/2019: Policy references updated. The policy ID changed to CCP.1169.

3/2020: Policy references updated.

2/2021: Policy references updated.

2/2022: Policy references updated.

2/2023: Policy references updated.

2/2024: Policy references updated.

2/2025: Policy references updated.