Policy Number	**THE801.033**
Policy Effective Date	**01/01/2025**

Phototherapy for Dermatologic Conditions

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Disclaimer

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Coverage

Office-based phototherapy **OR** photochemotherapy (see **NOTE 1**) **may be considered medically necessary** when there has been a failure, intolerance, or contraindication to treatment with topical or systemic drug therapy for **ANY ONE** of the following dermatological conditions:

1. Atopic dermatitis/eczema (refractory),
2. Cutaneous T-cell lymphoma, including mycosis fungoides and Sézary's syndrome,
3. Lichen planus,
4. Morphea and localized skin lesions associated with scleroderma,
5. Parapsoriasis,
6. Photodermatoses,
7. Pityriasis lichenoides,
8. Pruritic eruptions in human immunodeficiency virus infection,
9. Psoriasis (moderate to severe),
10. Urticaria pigmentosa, **and**
11. Vitiligo (leukoderma).

NOTE 1: Office-based phototherapy includes actinotherapy (type A ultraviolet [UVA] or type B ultraviolet [UVB]) and combination UVA/UVB. Photochemotherapy includes psoralens and UVA, known as PUVA, and combinations of psoralens and UVA/UVB.

Office-based Goeckerman regimen (UVB treatment in conjunction with topically applied chemicals, e.g., tars) **may be considered medically necessary** for the following:

1. Atopic dermatitis, **or**
2. Psoriasis.

Targeted phototherapy (e.g., laser UVB) **may be considered medically necessary** for the treatment of:

1. Mild to moderate localized psoriasis that is unresponsive to conservative treatment; **or**
2. Moderate to severe localized psoriasis comprising less than 20% body area for which narrowband (NB)-UVB or PUVA are indicated.

Targeted phototherapy (e.g., laser UVB) **is considered experimental, investigational and/or unproven** for the following:

1. First-line treatment of mild psoriasis, atopic dermatitis, atopic eczema;
2. Treatment of generalized psoriasis or psoriatic arthritis; **and**
3. All other dermatologic conditions and diagnoses, including but not limited to:
    a. Acne vulgaris,
    b. Alopecia areata,
    c. Granuloma annulare,
    d. Hypertrichosis,
    e. Keloids,
    f. Vitiligo, **or**
    g. Warts.

Home setting phototherapy (see **NOTE 2**) using UVB **may be considered medically necessary** when the above criterion for office-based phototherapy is met **AND ALL** of the following are met:

1. Improvement has been demonstrated with the use of UV treatments in the physician's office or clinic; **and**
2. Patient is capable of operating the home phototherapy unit, staying within prescribed periods of exposure, and the unit is expected to be used frequently (e.g., 3 times/week) on a long-term basis.

NOTE 2: Refer to DME101.000, DME Introduction, for coverage regarding DME use in residence/home setting.

Home setting phototherapy using UVA or PUVA is **considered not medically necessary.**

Tanning beds for home phototherapy **are considered not medically necessary.**

Combination bathing in Dead Sea water and phototherapy (e.g., Balneo-Phototherapy) **is considered experimental, investigational and/or unproven.**

NOTE 3: This medical policy does not address photodynamic therapy to treat dermatological conditions, such as actinic keratoses, squamous cell carcinoma, or basal cell carcinoma. Refer to THE801.027, Dermatological Applications of Photodynamic Therapy.

NOTE 4: This medical policy does not address treatment of rosacea. Refer to THE801.030, Nonpharmacologic Treatment of Rosacea.

Policy Guidelines

None

Description

The skin is the largest organ in the body and roughly 15% of body weight (20 pounds in an adult). The skin shields the body from the elements, while tough, it is not impenetrable. Allergens, environmental irritants, infection, hereditary factors, and stress are just a few of the forces that can trigger or exacerbate dermatological conditions.

Background
As a method of dermatological treatment, the majority of patients undergoing ultraviolet (UV) treatments are treated in the office or clinic with:

- Type A ultraviolet (UVA),
- Type B ultraviolet (UVB),
- Psoralens and UVA (PUVA),
- Goeckerman regime, or
- Laser treatment.

Disease Severity
The National Psoriasis Foundation Medical Board has described criteria to assist medical professionals in distinguishing between mild, moderate, and severe psoriatic disease based on body surface area (BSA) and impact on quality of life. BSA might be used for other dermatological conditions (e.g., pruritic conditions, vitiligo). Affected BSA has been frequently used to assess disease severity. One percent of BSA is approximately equal to the patients open hand with fingers tucked together and thumb tucked to the side. In clinical trials, severe disease often is commonly defined as more than 10% affected BSA, and the U.S. Food and Drug Administration (FDA) has used 20% BSA to indicate severe disease. In 2010, the American Academy of Dermatology published a consensus statement on psoriasis therapies that also used the mild, moderate, and severe criteria to guide treatment plans. (1) In this system, patients with mild disease have limited BSA involvement and may be treated with topical therapies. Although moderate and severe disease categories may overlap, patients with

moderate to severe disease generally have greater than 5% affected BSA, and appropriate therapies include phototherapy or systemic therapy.

Skin Disorders

Atopic Dermatitis (AD)

AD is the most common of many types of eczema, which is a skin disease characterized by areas of severe itching, redness, scaling, and loss of the surface of the skin. When the eruption has been present for a prolonged time, chronic changes occur due to the constant scratching and rubbing. There are periods of remissions and exacerbations. The etiology is unknown. Skin care, avoidance of substances that might irritate the skin, and ointments and creams (e.g., immunomodulators and corticosteroids) may be indicated. If these are ineffective, a physician might prescribe an oral or topical corticosteroids, antihistamines, or phototherapy (i.e., UVA, UVB, and/or PUVA). (2)

Cutaneous T-Cell Lymphomas (CTCL)

CTCLs are any of a group of T-cell non-Hodgkin lymphomas (NHL) that begins in the skin as an itchy, red rash that can thicken or form a tumor. The most common types are mycosis fungoides (MF) and Sézary syndrome (SS). SS is an advanced form of MF. MF affects only the skin while SS, cancerous T-cell lymphocytes affect the skin and the peripheral blood. MF has 3 phases: patch, plaque, and tumor. Patch phase is flat, red, and scaly, while plaque phase is thicker raised lesions or hardened lesions on the skin, and tumor phase has larger lesions that can be shaped like a mushroom. (3, 4)

In CTCL, skin all over the body is reddened, itchy, peeling, and painful. There may also be patches, plaques, or tumors on the skin. Cancerous T-cells are found in the blood. Treatments include creams and ointments to skin (e.g., cortisone, nitrogen mustard, and retinoids), oral medications (e.g., corticosteroids, retinoids, and methotrexate), phototherapy (UVB, NB-UVB, and PUVA), interferon, chemotherapy, and radiation. The treatments including but not limited to PUVA and UVB are noted by the National Cancer Institute, which are hard to cure. Treatment is usually palliative, to relieve symptoms and improve the quality of life. (3, 4)

Lichen Planus (LP)

LP is a common inflammatory disease that affects the skin, the mouth, or even the genital area with small, uncomfortable, pink or purple spots that occur mainly on the wrists, shins, lower back and genitalia. The cause of LP is unknown; however, most dermatologists believe it can be classified as an autoimmune disease. It can present as reddish-purple, flat-topped bumps or white lacy appearance that may be very itchy.

The AAD states there is no cure for LP and treatment is aimed at relieving itching and in improving the appearance of the rash until it goes away. (5) Mild cases may be treated with topical corticosteroid (TCS) creams, ointments, or other anti-inflammatory drugs. Severe cases of LP may require stronger medications such as cortisone taken internally or phototherapy.

Morphea (Localized Scleroderma)

Morphea is a disorder characterized by excessive collagen deposition leading to thickening of the dermis, subcutaneous tissues, or both. (6)

Parapsoriasis
Parapsoriasis is a group of cutaneous diseases that can be characterized by scaly patches or slightly elevated papules and/or plaques that have a resemblance to psoriasis but are unrelated with respect to pathogenesis, histopathology, and response to treatment. Parapsoriasis may precede CTCL. Treatment is possible when limited to the skin, otherwise palliative. Topical treatments include steroids, nitrogen mustard, and phototherapy. For advanced stages, chemotherapy and radiation is the most effective. Excimer laser may be used for parapsoriasis due to shorter period required for treatment and targeting individual lesions without affecting surrounding healthy skin. (7)

Photodermatoses
Photodermatoses refers to skin disorders induced or exacerbated by light. The most common type is polymorphic light eruption, with a high prevalence of up to 10-20% in the U.S. The skin might appear as spots, blisters, plaques, or eczema. The exact mechanism of the diverse skin reactions to light radiation remains unclear. Treatment options include avoiding the sun, using high skin protection factor (SPF) sunscreens, TCS or OCS. Appropriate therapy for severe cases includes phototherapy. (8)

Pityriasis Lichenoides (PL)
PL is an uncommon skin condition that is difficult to diagnose and treat. It has potential to progress to cutaneous lymphoma or an ulceronecrotic presentation, which carry a risk of mortality. PL presents as:

- PL et varioliformis acuta (PLEVA) presents as multiple, small, red papules on the skin that develops into polymorphic lesions, with periods of remissions and periods of hyper/hypopigmentation and varicella-like scars;
- PL chronica (PLC) presents as small red to brown flat maculopapules with mica-like scale with long periods of remission; and
- Febrile ulceronecrotic Mucha-Habermann disease (FUMHD) presents as generalized eruption of purpuric and ulceronecrotic plaques with systemic involvement and a mortality rate of up to 25%.

The treatments for PLEVA and PLC are phototherapy, systemic antibacterials, and TCS. The treatment for FUMHD is immunosuppressant and/or immunomodulating agents, narrow-band UVB (NB-UVB) and intensive supportive care. (9, 10)

Pruritic Eruptions in Human Immunodeficiency Virus (HIV) Infection
Pruritic papular eruption of HIV is the most common rash associated with HIV infection and is often the presenting sign in an otherwise asymptomatic HIV-positive person. HIV infected patients present with a chronic, itchy rash with small, red, firm papules which evolve into hyperpigmented macules and nodules. The rash is commonly located on the exposed skin,

primarily the extremities. Treatment options include antihistamines, corticosteroids, and phototherapy. (11)

Psoriasis

Psoriasis is a common chronic immune-mediated disease characterized by skin lesions ranging from minor localized patches to complete body coverage. There are several types of psoriasis; most common is plaque psoriasis, which is associated with red and white scaly patches on the skin, most frequently found on the elbows, knees, scalp, and trunk. The skin involvement can range from localized areas to generalized body involvement. The disease is lifelong and characterized by periods of remissions and exacerbations. Psoriasis can negatively impact many organ systems and is associated with an increased risk of cardiovascular disease, some types of cancer, and autoimmune diseases (e.g., celiac disease, Crohn disease). Although disease severity is minimally defined by body surface area (BSA; mild psoriasis affects <3% of BSA, moderate psoriasis affects 3%-10%, and severe disease affects >10% of BSA), lesion characteristics (e.g., location and severity of erythema, scaling, induration, pruritus) and impact on quality of life are also taken into account. The Psoriasis Area Severity Index (PASI) is a more specific means of quantifying the extent and severity of psoriasis and is utilized by both clinicians in practice and in clinical trials to monitor disease severity. The PASI takes into account the affected BSA along with the intensity of redness, scaling, and plaque thickness. Severity scores generated using PASI range from 0 (no disease) to 72 (maximal disease severity); a score >10 generally indicates moderate-to-severe disease. In clinical trials of patients with moderate-to-severe psoriasis, a 75% reduction in PASI (i.e., PASI 75) is a common endpoint.

PUVA uses a psoralen derivative in conjunction with long wavelength UVA light (sunlight or artificial) for photochemotherapy of skin conditions. Psoralens are tricyclic furocoumarins that occur in certain plants and can also be synthesized. They are available in oral and topical forms. Oral PUVA is generally given 1.5 hours before exposure to UVA radiation. Topical PUVA therapy refers to directly applying the psoralen to the skin with subsequent exposure to UVA light. Bath PUVA is used in some European countries for generalized psoriasis, but the agent used, trimethylpsoralen, is not approved by the FDA. Paint PUVA and soak PUVA are other forms of topical application of psoralen and are often used for psoriasis localized to the palms and soles. In paint PUVA, 8-methoxypsoralen (8-MOP) in an ointment or lotion form is put directly on the lesions. With soak PUVA, the affected areas of the body are placed in a basin of water containing psoralen. With topical PUVA, UVA exposure is generally administered within 30 minutes of psoralen application.

PUVA has most commonly been used to treat severe psoriasis, for which there is no generally accepted first-line treatment. Each treatment option (e.g., systemic therapies such as methotrexate, phototherapy, biologic therapies, etc.) has associated benefits and risks. Common minor toxicities associated with PUVA include erythema, pruritus, irregular pigmentation, and gastrointestinal tract symptoms; these generally can be managed by altering the dose of psoralen or UV light. Potential long-term effects include photoaging and skin cancer, particularly squamous cell carcinoma (SCC) and possibly malignant melanoma (MM).

PUVA is generally considered more effective than targeted phototherapy for the treatment of psoriasis. However, the requirement of systemic exposure and the higher risk of adverse reactions (including a higher carcinogenic risk) have generally limited PUVA therapy to patients with more severe disease. (12-15)

Urticaria Pigmentosa (UP)
Urticaria Pigmentosa is the name of a type of pale, itchy, brownish-pink patches on the skin that are common and are part of an allergic reaction. It can be helpful to eliminate possible foods, drugs, infections, insect bites and extreme temperatures that could be the cause. A physician might prescribe oral antihistamines, topical steroids, and for systemic urticaria that persists, PUVA or other forms of treatment. (16)

Vitiligo
Vitiligo is an idiopathic skin disorder that causes depigmentation of sections of skin, most commonly on the extremities. Depigmentation occurs because melanocytes are no longer able to function properly. The cause of vitiligo is unknown; it is sometimes considered an autoimmune disease. The most common form of the disorder is non-segmental vitiligo (NSV) in which depigmentation is generalized, bilateral, symmetrical, and increases in size over time. In contrast, segmental vitiligo (SV), also called asymmetric or focal vitiligo, covers a limited area of skin. The typical natural history of vitiligo involves stepwise progression with long periods in which the disease is static and relatively inactive, and relatively shorter periods in which areas of pigment loss increase.

<u>Treatment</u>
There are numerous medical and surgical treatments aimed at decreasing disease progression and/or attaining repigmentation. Topical corticosteroids (TCS), alone or in combination with topical vitamin D_3 analogues, are common first-line treatments for vitiligo. Alternative first-line therapies include topical calcineurin inhibitors, systemic steroids, and topical antioxidants. Treatment options for vitiligo recalcitrant to first-line therapy include, among others, light-box therapy with narrow-band ultraviolet B (NB-UVB) and psoralen plus ultraviolet A (PUVA).

Topical Treatments
Topical agent therapy (e.g., corticosteroids, coal tar, vitamin D analogues [including calcipotriol and calcitriol], tazarotene, and anthralin) is generally considered first-line treatment(s) of psoriasis, especially for mild disease.

Phototherapy/Photochemotherapy
Phototherapy and systemic therapy are treatment options for patients with more extensive and/or severe disease and those who fail conservative treatment with topical agents. Phototherapy is available in various forms including exposure to natural sunlight, use of broadband ultraviolet B (BB-UVB) or NB-UVB devices, targeted phototherapy, and PUVA. NB-UVB is an established treatment for psoriasis, based on efficacy and safety.

Established treatments for psoriasis include use of topical ointments and UV light ("light-lamp") treatments. Lasers and targeted UVB lamps are considered equivalent devices; targeted UV devices are comparable to UV light panels for treatment purposes. First-line treatment of UV-sensitive lesions may involve around 6- to 10-office visits; treatment of recalcitrant lesions may involve around 24- to 30-office visits. Maintenance therapy or repeat courses of treatment may be required.

Targeted Phototherapy
Targeted phototherapy with handheld lamps or lasers is also being evaluated. Potential advantages of targeted phototherapy include the ability to use higher treatment doses and to limit exposure to surrounding tissue. Original ultraviolet B (UVB) devices consisted of a Phillips TL-01 fluorescent bulb with a maximum wavelength (lambda max) of 311 nm. Subsequently, xenon chloride (XeCl) lasers and lamps were developed as targeted ultraviolet B treatment devices; these devices generate monochromatic or very narrowband radiation with a lambda max of 308 nm. Targeted phototherapy devices are directed at specific lesions or affected areas, thus limiting exposure to the surrounding normal tissues. They may, therefore, allow higher dosages compared with a light box, which could result in fewer treatments.

Psoralen plus ultraviolet A uses a psoralen derivative in conjunction with long-wavelength ultraviolet A (UVA) light (sunlight or artificial) for photochemotherapy of skin conditions. Psoralens are tricyclic furocoumarins that occur in certain plants and can also be synthesized. They are available in oral and topical forms. Oral PUVA is generally given 1.5 hours before exposure to UVA radiation. Topical PUVA therapy refers to the direct application of psoralen to the skin with subsequent exposure to UVA light. With topical PUVA, UVA exposure is generally administered within 30 minutes of psoralen application.

Balneo-Phototherapy
Balneo-phototherapy is a combination of bathing in thermal mineral water with prolonged exposure to ultraviolet light. The water temperature (typically 30–40C) and the mineral and chemical composition vary based on each center. In addition, there is no standard duration or frequency of immersion, and variable treatment cycles of days, weeks, or months. It is believed that Balneo-phototherapy have both anti-inflammatory and anti-proliferative actions. (17)

<u>Treatment Locations</u>
Home Phototherapy
A home phototherapy unit can be used to treat various dermatologic conditions. These devices are designed solely for the medical treatment of skin diseases, and usually contain multiple fluorescent lights, which emit high intensity, long-wave UV on specific wavelengths.

Some patients require frequent treatments or live in remote locations such that office or clinic visits are not feasible. Home therapy with UVB light is an alternative. Concerns regarding over-exposure to unsafe levels of UV radiation in the home setting have been addressed with the evolution of integrated security features such as keys, pass codes, etc. Nonetheless, routine

clinical evaluation should be conducted to ensure that exposure is kept to the minimum level compatible with adequate control of disease and the prevention of complications.

During the course of therapy, the patient will need to be assessed on a regular basis to determine the effectiveness of therapy and the development of side effects. These evaluations are essential to ensure that the exposure dose of radiation is kept to the minimum compatible with adequate control of disease. Therefore, PUVA is generally not recommended for home therapy.

Non-therapeutic or cosmetic use of UV is the use of a tanning bed. This device emits UV radiation (typically 95% UVA and 5% UVB) from fluorescent bulbs in the range of 12- to 28-100-watt lamps for home use or 24 to 60 100- to 200-watt lamps for salon use, used to produce a cosmetic tan.

Regulatory Status
In 2001, XTRAC™ (PhotoMedex), a xenon chloride (XeCl) excimer laser, was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for the treatment of skin conditions, such as mild-to-moderate psoriasis and vitiligo. The 510(k) clearance was subsequently obtained for a number of targeted UVB lamps and lasers, including newer versions of the XTRAC™ system, including XTRAC Ultra™, the VTRAC™ lamp (PhotoMedex), the BClear™ lamp (Lumenis), the 308 excimer lamp phototherapy system (Quantel Medical), MultiClear Multiwavelength Targeted Phototherapy System, Psoria-Light™, and the Excilite™ and Excilite µ™ XeCl lamps. The intended use of all of these devices includes vitiligo among other dermatologic indications. FDA product code: GEX.

In 2010, the Levia Personal Targeted Phototherapy® UVB device (Daavlin; previously manufactured by Lerner Medical Devices) was cleared for marketing by the FDA through the 510(k) process for home treatment of psoriasis.

Some light-emitting devices are handheld. FDA product code: GEX.

The oral psoralen product Oxsoralen-Ultra® (methoxsalen soft gelatin capsules), has been approved by the FDA and is made by Bausch Health. A generic product is also available from various manufacturers. Topical psoralen products (Oxsoralen®, Valeant Pharmaceuticals) and methoxsalen hard gelatin capsules have been discontinued. Injectable methoxsalen is available but is not used for psoriasis. (18, 19)

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function - including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition.

Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Atopic Dermatitis (AD)

The American Academy of Dermatology (AAD) noted in the *Atopic Dermatitis: Recommendations for the Use of Phototherapy* the following:

"Numerous studies document the efficacy of phototherapy for atopic dermatitis. Multiple forms of light therapy are beneficial for disease and symptom control, including natural sunlight, narrow-band (NB) ultraviolet (UV) light B (NB-UVB), broad-band (BB) ultraviolet light B (BB-UVB), ultraviolet light A (UVA), topical and systemic PUVA, ultraviolet light A and B (UVAB), and Goeckerman therapy. While it would be helpful to denote one or more forms of phototherapy as superior to all others, this is not possible given limited head-to-head trials and a lack of comprehensive comparative studies." The AAD stated that home phototherapy may be considered for a subset of patients who are unable to go to an office setting, although they note that there are no available studies that document the safety and efficacy of home phototherapy for AD. (20)

A 2007 systematic review of peer-reviewed scientific literature in the Cochrane Central Register of Controlled Trials, performed by Meduri et al. (21) found:

- Three studies demonstrated that UVA1 is both faster and more efficacious than combined UVAB for treating acute AD;
- Two trials disclosed the advantages of medium dose [50 J/cm^2] UVA1 for treating acute AD; 2 trials revealed the superiority of combined UVAB in the management of chronic AD;
- Two additional studies demonstrated that NB-UVB is more effective than either BB-UVA or UVA1 for managing chronic AD.

Meduri felt phototherapy with medium dose [50 J (joules)/cm (centimeter)^2] UVA1, if available, should be used to control acute flares of AD while ultraviolet light B (UVB) modalities, specifically NB-UVB, should be used for the management of chronic AD. (21)

Cutaneous T-Cell Lymphomas (CTCL)

Gathers et al. (2002) performed a study on 24 patients (12 stage IA, 12 stage IB) with patch stage mycosis fungoides (MF) to determine the effect of NB-UVB in the treatment of early stage MF and determined that NB-UVB is a viable, comparably safe, and easily administered alternative in the management of early stage MF. (22) Outcomes from clinical trials state that NB-UVB is beneficial for the patch stage MF stating that time to complete remissions range from 6 weeks to 66 months. After complete response mean time to relapse was 12.5 weeks.

Lichen Planus (LP)

Chan et al. (1999) performed a Cochrane Review and found 9 RCTs that assessed the effectiveness and safety of cyclosporines, retinoids, steroids and phototherapy. (23) The report concluded there is lack of strong evidence to support palliative treatment of LP due to small trial size, but enough evidence to justify larger trials. All treatment was reported as effective, but how effective compared to placebo was unknown. Wackernagel et al. (2007) performed a small retrospective study in 2007, which suggests phototherapy is effective in treating LP (24).

Oberti et al. (2019) assessed each intervention used in the management of oral LP and the efficacy of each type of treatment. (25) The PubMed database was searched for articles on oral LP management. RCTs comparing an active treatment with placebo, or between different active treatments, were reviewed. Only patients with symptomatic oral LP were included and all intervention types were considered (i.e., topical treatment, systemic drugs, non-pharmacological intervention). Twenty-five RCTs were examined in this systematic review. Steroids are the most frequently employed drug in the treatment of oral LP and their efficacy and safety are demonstrated. In addition, calcineurin inhibitors and photodynamic therapy are used in different studies for OLP management, with positive results. The authors concluded that topical steroids remain the first-line treatment for symptomatic oral LP, however, many different pharmacological and non-pharmacological therapies would represent a valid alternative for its management but will require additional investigation.

Morphea (Localized Scleroderma)

A search of Medline database revealed the following 2 articles. In 2008, Zulian discussed the mechanism of phototherapy, methotrexate and possible future treatments. (26) A 2006 RCT of 64 patients by Kreuter et al., demonstrated the effectiveness of UVA treatment in localized scleroderma. (27) Available literature including systematic reviews and RCTs support the efficacy of UVA and PUVA for the treatment of localized scleroderma. (27–30)

Parapsoriasis

A study from Sweden by Eklund et al. (2016) followed 44 patients from 1996 to 2010. (31) The mean follow-up was 5.6 years. The overall response rate was 81% following treatment with PUVA. The overall mortality rate was 25%, but only 11% could be verified as caused by mycosis fungoides (MF), which is a primary CTLC, with slow disease progression and preceded by parapsoriasis.

Photodermatoses

Gambichler et al., (2006) conducted a prospective RCT comparing the effects of bath PUVA, UVA, and NB-UVB in patients with subacute prurigo. (32) This trial revealed PUVA, UVA1 and NB-UVB appeared to be an effective and safe treatment option for patients, and UVA1 and PUVA seemed superior to NB-UVB in management of subacute prurigo.

Pityriasis Lichenoides (PL)

Maranda et al. (2016) reported a systematic review of 14 articles, which included 64 patients diagnosed with PL treated with phototherapy. (33) Three different modalities were utilized: 5 studies using BB-UVB, 9 studies using NB-UVB, and 2 studies with PUVA. Overall, the use of BB-UVB had an initial clearance rate of 89.6% with 23.1% recurrence, whereas NB-UVB cleared 73% with no recurrence. PUVA initially cleared 83% of the lesions with 60% recurrence. The authors concluded that phototherapy was safe and a valued treatment.

In a systematic review, Bellinato et al. (2019) examined the treatments of patients with PL. (34) Investigators carried out a systematic review according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for studies examining PL treatment including 3 or more subjects and published between January 1970 and April 2019. A total of 441 studies were screened, and 37 original manuscripts meeting the inclusion/exclusion criteria were identified, including 12 case-series studies, 18 reviews, 4 prospective studies, 2 comparative studies and 1 RCT. In most studies, UV phototherapy (NB-UVB, broadband UVB, UVA1 or PUVA) was employed. Clearance rates with the different modalities were hardly comparable between different studies, ranging approximately between 70 % and 100 %. NB-UVB showed an effectiveness similar to PUVA as such as the combination of UVA and UVB versus PUVA. Oral erythromycin showed clearance rates ranging between 66 % and 83 %, whereas methotrexate up to 100 % but in small and dated studies. Evidence for other treatments was scarce. There was a lack of high level of evidence studies on PL treatment. The interpretation of the results was biased by the possible auto-resolution of the disease, the sample heterogeneity between children and adults and the short follow-up period of the studies. Only some studies examined how results were durable following cessation of therapy; QOL and the impact of treatment were never assessed. The authors suggested that NB-UVB phototherapy as 1st-line treatment. Oral erythromycin with or without topical corticosteroids and low-dose methotrexate as 2nd-line therapies.

A 2022 UpToDate review on “Pityriasis lichenoides chronica” (35) states that “Narrowband ultraviolet B (NBUVB), broadband ultraviolet B (UVB), and psoralen plus ultraviolet A (PUVA) are the primary phototherapeutic modalities used to treat these diseases. We favor use of UVB phototherapy based upon the more favorable safety profile compared with PUVA photochemotherapy.”

Pruritic Eruptions in Human Immunodeficiency Virus (HIV) Infection

Itching as part of HIV has been well documented for several decades. Gelfand and Rudikoff (2001) described the numerous skin and associated skin condition complaints they studied following a HIV diagnosis in patients. (36) Once the dermatoses had been evaluated and accounted for, the cause of the dermatitis, idiopathic HIV-pruritus in nature, was diagnosed. In

this review by the authors, phototherapy is a common modality used to treat pruritic eruptions safely and therapeutically.

An earlier study in 1999 from Akaraphanth and Kim reported there were no adverse effects to HIV-infected patients treated for pruritic eruptions using UV radiation as in phototherapy and photochemotherapy. (37) As a result of concern that there are immunosuppression effects from UV radiation, this issue was studied. The study assessed human as well as animal models.

In 2023 UpToDate (38) reviewed pruritus in palliative care. UpToDate states for refractory pruritus, phototherapy using UVB light is most useful in pruritus associated with uremia although it may also benefit pruritus associated with cholestasis and malignant skin infiltrations. The treatment sessions are usually 3 times per week although this may not be practical in terminally ill patients, depending on the clinical circumstances and goals of care.

Psoriasis

Targeted Phototherapy

Mild Localized Psoriasis

The original indication of the excimer laser was mild-to-moderate psoriasis, defined as involvement of less than 10% of the skin. Typically, this patient population has not been considered for light-box therapy, because the risks of exposing the entire skin to the carcinogenic effects of UVB light may outweigh the benefits of treating a small number of lesions. The AAD does not recommend phototherapy for patients with mild localized psoriasis whose disease can be controlled with topical medications, including steroids, coal tar, vitamin D analogues (e.g., calcipotriol, calcitriol), tazarotene, and anthralin. (12)

Section Summary: Mild Localized Psoriasis

There is no evidence and no clinical recommendation for targeted phototherapy to treat patients with mild localized psoriasis whose disease can be controlled with topical medications.

Treatment-Resistant Mild Psoriasis

Several small studies have suggested that targeted phototherapy can be effective for treatment-resistant lesions. One 2003 patch comparison from Taneja et al., reported effective clearing (pre-Psoriasis Area and Severity Index [PASI] score, 6.2; post-PASI score, 1.0) of treatment-resistant psoriatic lesions; 6 of the patients had previously received topical treatment, 5 had received conventional phototherapy, and 3 had received combined treatments including phototherapy. (39) In 2004, the same investigator group, Taylor et al., reported that 12 of 13 patients with “extensive and stubborn” scalp psoriasis (i.e., unresponsive to class I topical steroids used in conjunction with tar and/or zinc pyrithione shampoos for at least 1 month) showed clearing following treatment with the 308-nm laser. (40) In a 2006 open trial from Europe, 44 (81%) of 54 patients with palmoplantar psoriasis resistant to combined phototherapy and systemic treatments were cleared of lesions with a single NB-UVB lamp treatment weekly for 8 weeks. (41)

Section Summary: Treatment-Resistant Mild Psoriasis

For individuals who have mild psoriasis that is resistant to topical medications who receive targeted phototherapy, the evidence includes small (N<60) within-subject studies. Studies have shown that targeted phototherapy can improve mild localized psoriasis that has not responded to topical treatment. Targeted phototherapy is presumed to be safer or at least no riskier than whole body phototherapy, due to risks of exposing the entire skin to the carcinogenic effects of UVB light. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Moderate-to-Severe Localized Psoriasis

There are several systematic reviews of the literature on targeted phototherapy. Reviews differed in the type of study selected and the comparison interventions. A 2015 systematic review by Almutawa et al. considered only RCTs; PUVA was the comparison intervention. (42) The reviewers identified 3 RCTs comparing the efficacy of targeted UVB phototherapy with PUVA for treatment of plaque psoriasis. Two of the 3 trials used an excimer laser (308 nm) as the source of targeted phototherapy, and the third used localized NB-UVB light. There was no statistically significant difference between the techniques in the proportion of patients with at least a 75% reduction in psoriasis. The pooled odds ratio (OR) was 3.48 (95% confidence interval [CI], 0.56 to 22.84).

Mudigonda et al. (2012) published a systematic review of controlled studies (RCTs and non-RCTs) on targeted versus nontargeted phototherapy for patients with localized psoriasis. (43) The reviewers identified 3 prospective nonrandomized studies comparing the 308-nm excimer laser with NB-UVB. Among these studies was a 2006 study by Goldinger et al. that compared the excimer laser with full-body NB-UVB in 16 patients. (44) At the end of 20 treatments, PASI scores were equally reduced on both sides of the body, from a baseline of 11.8 to 6.3 for laser and from 11.8 to 6.9 for nontargeted NB-UVB treatment. A study by Kollner et al. (2005) included 15 patients with stable plaque psoriasis. (45) The study compared the 308-nm laser, the 308-nm excimer lamp, and standard TL-01 lamps. One psoriatic lesion per patient was treated with each therapy (i.e., each patient received all 3 treatments). Investigators found no significant differences in the efficacy of the 3 treatments after 10 weeks. The mean number of treatments to achieve clearance of lesions was 24.

Section Summary: Moderate-to-Severe Localized Psoriasis

For individuals who have moderate-to-severe localized psoriasis who receive targeted phototherapy, the evidence includes systematic reviews of small (N≤25) controlled trials (RCTs and non-RCTs). Systematic reviews of small, controlled trials in patients with moderate-to-severe psoriasis have found that targeted phototherapy has efficacy similar to whole-body phototherapy. Targeted phototherapy is presumed to be safer or at least no riskier than whole body phototherapy, due to risks of exposing the entire skin to the carcinogenic effects of UVB light. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Psoralens Plus Ultraviolet A (PUVA) for Generalized Psoriasis

A number of RCTs and systematic reviews of RCTs have compared PUVA with other light therapies or with placebo. A 2013 Cochrane review by Chen et al. assessed light therapy for psoriasis. (46) However, that review is less useful for this evidence evaluation because the reviewers' combined results of studies using PUVA and BB-UVB, rather than reporting outcomes separately for these treatment modalities.

Psoralens and Ultraviolet A (PUVA) versus Narrow Band-Ultraviolet B (NB-UVB)
A 2012 industry-sponsored systematic review by Archier et al. focused on studies comparing PUVA to NB-UVB in patients with chronic plaque psoriasis. (47) Pooled analysis of 3 RCTs found a significantly higher psoriasis clearance with PUVA than with NB-UVB (OR=2.79; 95% CI, 1.40 to 5.55). In addition, significantly more patients remained cleared at 6 months with PUVA than with NB-UVB (OR=2.73: 95% CI, 1.18 to 6.27).

PUVA versus Topical Steroids
In 2012, Amirnia et al. published a study in which 88 patients with moderate plaque psoriasis were randomized to receive PUVA or topical steroids. (48) Treatment was continued for 4 months or until clearance was achieved. Clearance was defined as disappearance of at least 90% of baseline lesions. All patients in both groups achieved clearance within the 4-month treatment period. Recurrence (defined as a resurgence of at least 50% of the baseline lesions) was reported significantly more often in the topical steroid group (9/44 [20.5%]) than in the PUVA group (3/44 [6.8%]; p=0.007).

PUVA versus UVA Without Psoralens
In 2014, El-Mofty et al. published an RCT comparing PUVA with broadband-UVA (BB-UVA) in 61 patients with psoriasis affecting at least 30% body surface area (BSA). (49) Clinical outcomes were significantly better in the PUVA group than in the BB-UVA groups. For example, complete clearance was obtained by 23 (77%) of 30 patients in the PUVA group, 5 (31%) of 16 patients in the 10 J/cm^2 UVA group, and 5 (33%) of 15 patients in the 15 J/cm^2 UVA group (p=0.020).

In 2009, Sivanesan et al. published a double-blind RCT evaluating the efficacy of 8-methoxypsoralen (8-MOP) PUVA treatment in patients with moderate-to-severe psoriasis affecting at least 10% BSA. (50) The trial included 40 patients randomized to PUVA (n=30) and or UVA plus placebo psoralens (n=10). Patients were treated 3 times weekly for 12 weeks. The primary outcome was a 75% or greater improvement in PASI 75 score. At 12 weeks, 19 (63%) of 30 patients in the PUVA group and 0 (0%) of 10 patients in the UVA plus placebo group achieved the primary outcome measure (p<0.001). There were no serious adverse effects.

Section Summary: PUVA
RCTs and systematic reviews of RCTs have found that PUVA is more effective than NB-UVB, topical steroids, or UVA without psoralens in patients with moderate-to-severe psoriasis. Due to side effects, PUVA is typically restricted to more severe cases.

Other Modalities to Treat Psoriasis, Including at Home
Balneo-Phototherapy

In 2005, Dawe et al. conducted a paired, controlled study of 60 patients to compare NB-UVB alone versus NB-UVB plus Balneo-Phototherapy. They concluded that pretreatment with Dead Sea salt soaks to NB-UVB did not result in a clinically important improvement in clearance of psoriasis. (51)

Peinemann et al. (2021) sought to assess the effects of artificial exposure to UVB light while soaking in an indoor salt bath (balneophototherapy) in patients with chronic plaque psoriasis. (52) CENTRAL, MEDLINE, Embase, and LILACS databases were searched up to June 2019. Researchers included RCTs. The primary efficacy outcome was psoriasis area and severity index (PASI)-75 to detect people with a 75% or more reduction in the PASI score from baseline. The primary adverse outcome was treatment-related adverse events requiring withdrawal. They included 8 RCTs (2105 participants; 1976 analyzed). With respect to PASI-75, 2 studies found that salt bath + UVB may improve psoriasis when compared to UVB alone (risk ratio 1.71, 95% CI 1.24 to 2.35; 278 participants). With respect to treatment-related adverse events requiring withdrawal, 2 other studies found little to no difference when compared to UVB alone (risk ratio 0.96, 95%, CI 0.35 to 2.64; 404 participants). The authors concluded that salt bath + UVB may improve psoriasis when compared to UVB alone, although results are based on a limited number of studies and provide low-certainty evidence. Additional large RCTs are warranted.

PUVA Home Treatment

No studies were identified that compared home-based PUVA with office-based PUVA. A 2010 review of various types of home phototherapies for psoriasis did not discuss any studies on PUVA delivered at home. (53)

Home UVB Phototherapy

Feldman et al. reported on a survey of thirty-one patients who were prescribed a home UVB phototherapy unit to treat psoriasis was performed as a pilot study of home UVB phototherapy usage; 22 patients responded. (54) Generally, respondents reported home UVB phototherapy to be very helpful for their psoriasis. It was concluded that home UVB is an effective and appropriate treatment for many patients with psoriasis, but screening and education of candidates for home UVB phototherapy is important to ensure compliance with the treatment program.

Jordan et al. reported on a study of long-term modified Goeckerman regimen for psoriasis using an ultraviolet B light source in the home. (55) Fifty-six people with extensive psoriasis began the study, 55 completed a modified Goeckerman program starting at 1-minute exposures, with weekly increases of light by 1 minute until 6 or 8 weeks of treatment had elapsed. All patients cleared of psoriasis (scalp not included). Fifty-one patients accomplished the clearance program totally in the home. Over 80% of them remain virtually clear, as they have maintained a 6- to 8-minute tar-light program 2 to 5 times a week. Thirty-seven subjects have used this home UVB unit for over a year. The authors concluded that the modified Goeckerman treatment of psoriasis in the home show that only 6 non-enclosed lamps were needed for the economical clearing and maintenance of many patients with psoriasis and the initial clearing rate using 42 to 60 sub-erythemal treatments is outstanding.

Koek and colleagues (2009) conducted a randomized controlled single-blind trial comparing office-based UVB treatment with home therapy for individuals with plaque or guttate psoriasis. (56) This study involved 196 subjects who were evaluated through the initial therapy, with the first 105 subjects followed for an additional 12 months post-treatment. The authors reported that both treatments provided significant improvement from baseline, with home therapy being non-inferior to office-based treatment as measured by the psoriasis area and severity index (PASI) and the self-administered psoriasis area and severity index (SAPASI). No significant differences between groups were reported with regard to total cumulative radiation dose or short-term side effects.

Unrue and colleagues (2019) conducted a multicenter, prospective, open-label, interventional study to assess the treatment efficacy, adherence, and satisfaction of an ultraviolet home phototherapy system. (57) The study included 8 participants with stable plaque psoriasis. Matched control and study lesions were assessed on each participant. All participants that completed the 10-week study experienced an improvement in the treated lesions with a mean improvement of 57% in Psoriasis Severity Index (PSI; $p<0.0001$ compared to baseline, and $p<0.0002$ compared to the control lesions). Control lesions did not significantly change in PSI over the study period with a mean change of 9% ($p=0.1411$). No adverse events were reported. Participant treatment adherence was 96%. The results indicate that the home phototherapy system was a safe and effective monotherapy to manage plaque psoriasis in this group of participants.

In 2022, Cohen and colleagues performed a systematic review of the use of home-based devices for the treatment of skin conditions. (58) A total of 4 RCTs evaluating home UVB phototherapy for psoriasis were included (Franken, 2015; Koek, 2009; Paul, 1983; Unrue, 2019). Conflicting evidence was identified for the efficacy of home-based UVB compared to traditional clinic-based administration. Three studies reported either significant improvements in PASI or PSI scores with home UVB use compared to controls, or non- inferiority of home therapy to office-based treatment. However, a study by Paul and colleagues (1983) showed the opposite outcome: while 90% of subjects who were treated in a clinic with phototherapy experienced complete clearance of psoriasis lesions, only 40% of subjects treated at home achieved the same result. Similar to the American Academy of Dermatology – National Psoriasis Foundation guidelines, the review gave a grade of recommendation of B for home phototherapy (UVB) devices for psoriasis.

Tanning Beds for Home Phototherapy

Non-therapeutic or cosmetic use of ultraviolet light is the use of a tanning bed. This device emits ultraviolet radiation (typically 95% UVA and 5% UVB) from fluorescent bulbs in the range of 12 to 28 100-watt lamps for home use or 24 to 60 100 to 200-watt lamps for salon use, used to produce a cosmetic tan. The World Health Organization does not recommend the use of UV tanning devices because of the adverse effects (carcinogenic) on human health of overexposure to UV radiation. (59)

Section Summary: Other Modalities to Treat Psoriasis, Including at Home
Clinical trials are limited supporting the utilization, when not meeting specific criteria noted in coverage for alternative modalities and/or phototherapy in the home that would improve health outcomes over office-based treatment.

Urticaria Pigmentosa (UP)
In 2010, Tan et al. reported a prospective New Zealand analysis of 116 patients, under the age of 16 years, having undergone 144 courses of NB-UVB phototherapy for UP and other dermatological conditions. (60) Treatment was effective in the majority of children (72%). Most received only 1 course. For responders, the mean number of treatments was 32.4. The mean dose per treatment to achieve clearance was 886 mJ (millijoule)/cm^2 and the mean maximum treatment dose per treatment was 1328 mJ/cm^2. All children tolerated treatment well with 36% developing brief, minimally symptomatic, erythema.

Vitiligo (Leukoderma)
Targeted Phototherapy
Systematic Reviews
A systematic review by Lopes et al. (2016) identified 3 studies that compared targeted phototherapy using a 308-nm excimer lamp with NB-UVB (315 patients, 352 lesions) and 3 studies that compared the excimer lamp with the excimer laser (96 patients, 412 lesions). (61) No differences between the excimer lamp and NB-UVB were identified for the outcome of 50% or more repigmentation (RR=1.14; 95% CI, 0.88 to 1.48). For repigmentation of 75% or more, only 2 small studies were identified, and they showed a lack of precision in the estimate (RR=1.81; 95% CI, 0.11 to 29.52). For the 3 studies that compared the excimer lamp with the excimer laser, there were no significant differences at the 50% or more repigmentation level (RR=0.97; 95% CI, 0.84 to 1.11) or the 75% or more repigmentation level (RR=0.96; 95% CI, 0.71 to 1.30). All treatments were most effective in lesions located on the face, with the worst response being lesions on the extremities. There was some evidence of an increase in adverse events such as blistering with targeted phototherapy.

Whitton et al. (2015) updated a Cochrane review of RCTs on treatments for vitiligo. (62) The literature search, conducted through October 2013, identified 12 trials on laser light devices: 6 trials evaluated the combination of laser light devices and a topical therapy; 2 evaluated the combination of laser devices and surgical therapy; 3 compared regimens of laser monotherapy; and 1 compared a helium neon laser with a 290- to 320-nm BB-UVB fluorescent lamp. Due to heterogeneity across studies, the reviewers did not pool study findings. In most trials, all groups received laser light treatment, alone or as part of combination therapy, and thus the effect of targeted phototherapy could not be isolated. Adverse event reports across the studies included burning, stinging, moderate-to-severe erythema, itching, blistering, and edema.

Sun et al. (2015) published a systematic review of RCTs that focused on the treatment of vitiligo with the 308-nm excimer laser. (63) In a literature search conducted through April 2014, reviewers identified 7 RCTs (total n=390 patients) for inclusion. None of the studies was conducted in the U.S.; 5 were from Asia and 3 of those 5 are available only in Chinese. Three

trials compared the excimer laser with an excimer lamp, and 4 compared the excimer laser with NB-UVB. One trial had a sample size of only 14 patients and another, published by Yang et al. (2010), (64) did not report repigmentation rates, providing instead, the proportion of patients with various types of repigmentation (perifollicular, marginal, diffuse, or combined). Repigmentation rates at the 75% and 100% level did not differ significantly between groups treated with the excimer laser versus NB-UVB. The reviewers conducted a meta-analysis of the 2 studies not published in English, though results cannot be verified. Results showed that the likelihood of 50% or more repigmentation was significantly higher with the excimer laser than with NB-UVB (relative risk [RR], 1.39, 95% CI, 1.05 to 1.85). Two of the 4 studies discussed adverse events, with itching and burning reported by both treatment and control groups and erythema and blistering reported only by the patient in the laser group.

Randomized Controlled Trials (RCTs)
Four RCTs comparing targeted phototherapy to alternate treatment options are summarized in Tables 1 through 4 below. (65-69) Poolsuwan et al. (2020) compared treatment of 36 paired vitiligo lesions with either targeted phototherapy (308-nm excimer light) or NB-UVB in a single-blind study of 36 patients. (65) Treatment of lesions with targeted phototherapy led to significant reductions in the Vitiligo Area Scoring index (VASI) score and significantly improved repigmentation grade compared to treatment with NB-UVB; however, the difference between groups in these outcomes were marginal and may not be clinically significant. Wu et al. (2019) compared the treatment of 83 paired vitiligo lesions with either 308-nm excimer laser or topical tacrolimus, with both arms receiving concomitant intramuscular betamethasone injections, in a single-blind study of 138 patients. (66) Excimer laser therapy was associated with a significantly higher proportion of patients with at least 50% repigmentation at 3 months compared to topical tacrolimus. However, interpretation of study results is limited by inadequate description of methods and use of per-protocol analysis, with an evident high rate of patient dropout.

An older, open-label study by Nistico et al. (2012) compared 3 different treatment arms in 53 patients with localized or generalized vitiligo: 1) excimer laser plus vitamin E (n=20); 2) excimer laser plus topical tacrolimus ointment 0.1% and vitamin E (n=20); and 3) vitamin E only (control group, n=13). (67) The investigators found that patients treated with targeted phototherapy were significantly more likely to achieve a "good" or "excellent" repigmentation response (55% in group 1 and 70% in group 2) than those who received oral vitamin E alone (0%). The rate of good or excellent responses did not differ significantly between groups that received targeted phototherapy with and without topical treatment (p=0.36). This study was limited by its open-label design and the fact that the comparator group, oral vitamin E, does not reflect optimal standard care for treatment of vitiligo.

In a randomized trial by Oh et al. (2011), matched lesions in 16 patients were randomized to 308-nm excimer laser alone, topical tacalcitol alone, or the combination of excimer laser and topical tacalcitol. (68) Excimer laser therapy alone and in combination with topical tacalcitol were associated with a significantly higher repigmentation response quartile at 16 weeks compared to topical tacalcitol alone. However, interpretation of study results is limited by

inadequate description of methods, and it is unclear whether tacalcitol is comparable to other standard-of-care topical vitamin D_3 analogues.

Table 1. Summary of Key RCT Characteristics Assessing Targeted Phototherapy for Vitiligo

Study (Year)	Countries	Sites	Dates	Participants	Interventions
Poolsuwan et al. (2020) (65)	Thailand	Single Center	NR	Patients 18 to 65 years of age with vitiligo with stable, symmetrically paired lesions who have not had topical therapy for at least 2 weeks or phototherapy of systemic immunosuppressive drugs for ≥ 8 weeks.	• Localized 308-nm excimer light.[a] • 311-nm NB-UVB.[a]
Wu et al. (2019) (66)	China	Single-center	2012 to 2014	Patients 25 to 48 years of age with vitiligo involving the face or neck.	• Intramuscular betamethasone (every 3 to 4 weeks for 3 to 6 months) plus 308-nm excimer laser. • Intramuscular betamethasone (every 3 to 4 weeks for 3 to 6 months) plus topical tacro imus 0.1% twice daily.
Nistico et al. (2012) (67)	Italy	Single Center	NR	Patients 13 to 56 years of age with localized or generalized vitiligo.	• Targeted 308-nm excimer laser plus oral vitamin E 400 IU.[b] • Targeted 308-nm excimer laser plus topical tacrolimus 0.1% ointment plus oral vitamin E 400 IU.[b] • Oral vitamin E 400 IU alone.[b]

Oh et al. (2011) (68)	Korea	Single-center	NR	Patients 15 to 60 years of age with non-segmental vitiligo	308-nm excimer laser alone (twice weekly for 16 weeks) High-concentration topical tacalcitol alone (once daily) 308-nm excimer laser plus high- concentration topical tacalcitol

IU: international units; NB-UVB: narrow-band ultraviolet B; NR: not reported.

[a] Both interventions given for 3 non-consecutive days per week x 48 treatment sessions.

[b] Frequency of interventions were as follows: Targeted 308-nm excimer laser, twice weekly; oral vitamin E, twice daily; tacrolimus ointment, once daily. All interventions given for 12 weeks.

Table 2. Summary of Key RCT Results Assessing Targeted Phototherapy for Vitiligo

Study	Reduction in VASI Score, mean	Repigmentation
Poolsuwam et al. (2020) (65)		
N	36	36
308-nm excimer light	0.55 ±0.39%	2.36±1.15[a]
NB-UVB	0.43±0.39%	1.94±1.19[a]
p-value	<0.001	<0.001
Wu et al. (2019) (66)		
N	NA	83[e]
Betamethasone + 308-nm excimer laser	NA	• Patients with stable vitiligo at baseline: ≥50% repigmentation at 3 months in 40.8% • Patients with active vitiligo at baseline: ≥50% repigmentation at 3 months in 55.8%
Betamethasone + topical tacrolimus	NA	• Patients with stable vitiligo at baseline: ≥50% repigmentation at 3 months in 10.2% • Patients with active vitiligo at baseline: ≥50% repigmentation at 3 months in 32.3%
p value	NA	• Patients with stable vitiligo at baseline: <.001 • Patients with active vitiligo atbaseline:.024

Nistico et al. (2012) (67)		
N	NA	53
Phototherapy + vitamin E	NA	• Good: 6/20 (30%)[b, c] • Excellent: 5/20 (25%)[b, c]
Phototherapy + tacrolimus + vitamin E	NA	• Good: 8/20 (40%)[b, c] • Excellent: 6/20 (30%)[b, c]
Vitamin E alone	NA	• Good: 0/13 (0%)[b, c] • Excellent: 0/13 (0%)[b, c]
p-value	NA	<0.001[d]
Oh et al. (2011) (68)		
N	NA	16
308-nm excimer laser alone	NA	NR
Topical tacalcitol alone	NA	NR
308-nm excimer laser + topicaltacalcitol	NA	NR
p value	NA	Repigmentation quartile at 16 weeks: • Favoring excimer laser alonevs. tacalcitol alone:.008 • Favoring combination vs.excimer laser alone: NS • Favoring combination vs.tacalcitol alone:.006

NA: not applicable; NB-UVB: narrow-band ultraviolet B; NR: not reported; NS: not significant; RCT: randomized controlled trial; VASI: Vitiligo Area Scoring index.

[a] Repigmentation was reported as a graded score from 1 to 4 with 1 being "poor" and 4 being "excellent."

[b] Good repigmentation defined as 51 to 75% repigmentation; excellent repigmentation defined as 76 to 100% repigmentation.

[c] Repigmentation reported as number of patients out of the total number of patients in subgroup (%) for each category.

[d] P-value reported for good to excellent repigmentation response in each intervention group versus control (vitamin E alone).

Table 3. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-up[e]
Poolsuwam et al. (2020) (65)				5,6. Differences in VASI score and repigmentation do not appear	

				to be clinically significant; clinical significance not defined by investigators.	
Wu et al. (2019) (66)	2. Unclear differentiation between stable and active vitiligo.	1. Schedule of excimer laser not defined.		3. Scant reporting of safety outcomes 5. Clinically significant difference not prespecified	
Nistico et al. (2012) (67)			2. Phototherapy groups compared to oral vitamin E, which is not optimal standard care for vitiligo.	5. Clinically significant difference in response was not prespecified.	
Oh et al. (2011) (68)			1. High-concentr tacalcitol not defined. 2. Unclear whether tacalcitol is comparable to other standard topical vitamin D_3 Analogues.	3. Scant reporting of safety outcomes. 4. Definition and relevance of quartile grading for repigmentation unclear; absolute values not reported. 5. Clinically significant difference not prespecified.	

VASI: Vitiligo Area Scoring index.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a.] Population key: 1. Intended use population unclear; 2. Clinical context for treatment is unclear; 3. Study population is unclear; 4. Study population not representative of intended use. 5. Study population is subpopulation of intended use
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator.
[c.] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Not CONSORT reporting of harms; 4. Not established and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.
[e.] Follow-Up key: 1. Not sufficient duration for benefits; 2. Not sufficient duration for harms.

Table 4. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-up[d]	Power[e]	Statistical[f]
Poolsuwam et al. (2020) (65)		1. Single-blinded to investigators only.			1. Power calculations not reported.	
Wu et al. (2019) (66)	2. Allocation not concealed.	1. Single-blinded to evaluators only.		1. High loss to follow-up based on number enrolled versus number evaluated at 1, 3, and 6 months. 6. Both per protocol and intent to treat analyses reported, but intent to treat analysis used last observation carry-forward imputation.	1. Power calculation not reported.	2. Inadequate description of inferential Statistics.

Nistico et al. (2012) (67)	2. Described as an "open" study; does not appear that allocation concealment occurred.	1, 2. Described as an "open" study; does not appear that blinding occurred.			1. Power calculations not reported	
Oh et al. (2011) (68)	2. Allocation not concealed.	1. Single-blinded to evaluators only.	1. Not Registered.		1. Power Calculation not Reported.	2. Inadequate description of inferential Statistics.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a.] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b]. Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c.] Selective reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d.] Follow-up key: 1. High loss to follow up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e.] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

[f.] Statistical key: 1. Test is not appropriate for outcome type: a) continuous; b) binary; c) time to event; 2. Test is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p-values not reported; 4. Comparative treatment effects not calculated.

Retrospective Studies

Fa et al. (2017) published a retrospective analysis of 979 Chinese patients (3478 lesions) treated with the 308-nm targeted laser for vitiligo. (70) Patients had Fitzpatrick skin phototype III or IV and were followed for 2 years after the last treatment. Repigmentation was assessed by 2 dermatologists. A total of 1374 (39%) lesions reached at least 51% repigmentation, with 1167 of the lesions reaching over 75% repigmentation. Complete repigmentation was seen in 219 lesions. Among the cured lesions, the recurrence rate was 44%. Patients with longer disease duration and older age experienced significantly lower efficacy rates. Application of 16 to 20 treatments resulted in higher repigmentation rates than fewer treatments and increasing the number of treatments beyond 21 did not appear to improve repigmentation rates. There was no discussion of adverse events.

In another retrospective analysis, Dong et al. (2017) evaluated the use of a medium-band (304 to 312 nm) targeted laser for treating pediatric patients (age ≤16 years) with vitiligo. (71)

Twenty-seven patients (95 lesions) were evaluated by 2 dermatologists following a mean of 20 treatments (range, 10 to 50 treatments). After 10 treatment sessions, 37% of the lesions reached 50% or more repigmentation. After 20 treatment sessions, 54% of the lesions achieved 50% or more repigmentation. Six children experienced adverse events such as asymptomatic erythema, pruritus, and xerosis, all resolving in a few days.

Section Summary: Targeted Phototherapy

For individuals who have vitiligo who receive targeted phototherapy, the evidence includes systematic reviews of RCTs, 4 individual RCTs, and 2 retrospective studies. Individual studies tend to have small sample sizes, and those designed to isolate the effect of laser therapy suffer from inadequate descriptions of methods and other limitations. Two meta-analyses were attempted; however, results from a meta-analysis could not be verified because the selected studies were not available in English, and 1 estimate was imprecise due to the small number of studies and participants. RCTs have shown targeted phototherapy to be associated with statistically significant improvements in VASI scores and/or repigmentation compared to alternate treatment options. However, 1 of the RCTs only showed marginal differences between groups in these outcomes limiting clinical significance; the second compared phototherapy to oral vitamin E, which is not an optimal comparator. Overall, there is a lack of well-designed clinical trial evidence that compares targeted phototherapy with more conservative treatments or no treatment/placebo.

Psoralens With Ultraviolet A (PUVA)

Systematic Reviews

Bae et al. (2017) published a systematic review and meta-analysis on the use of phototherapy for the treatment of vitiligo. (72) The literature search, conducted through January 2016, identified 35 unique studies for inclusion with 1201 patients receiving NB-UVB and 227 patients receiving PUVA. The category of evidence and strength of recommendation were based on the study design of the selected studies. The outcome of interest was the repigmentation rate. Meta-analytic results are summarized in Table 5. Adverse events were not discussed.

Table 5. Response Rates for NB-UVB and PUVA in the Treatment of Vitiligo by Treatment Duration

Treatment	Duration, mo	≥50% Repigmentation (95% CI), %	≥75% Repigmentation (95% CI), %
NB-UVB	6	37.4 (27.1 to 47.8)	19.2 (11.4 to 27.0)
NB-UVB	12	56.8 (40.9 to 72.6)	35.7 (21.5 to 49.9)
PUVA	6	23.5 (9.5 to 37.4)	8.5 (0 to 18.3)
PUVA	12	34.3 (23.4 to 45.2)	13.6 (4.2 to 22.9)

Adapted from Bae et al. (2017) (72)

CI: confidence interval; mo: month; NB-UVB: narrowband-ultraviolet B; PUVA: psoralens with ultraviolet A.

A Cochrane review by Whitton et al. (2015) which assessed trials on treatments for vitiligo (discussed in the previous section), identified 12 RCTs evaluating PUVA. (62) Four trials assessed

oral PUVA alone and 8 assessed PUVA in combination with other treatments (e.g., calcipotriol, azathioprine, *Polypodium leucotomos*, khellin, or surgical treatment). Seven of the 8 studies used 9-methoxypsoralen. A meta-analysis of 3 studies that compared PUVA with NB-UVB found that a larger proportion of patients receiving NB-UVB achieved >75% repigmentation compared with patients receiving PUVA; however, the difference was not statistically significant (RR=1.60; 95% CI, 0.74 to 3.45). Patients treated with NB-UVB experienced significantly less nausea (RR=0.13, 95% CI, 0.02 to 0.69) and erythema (RR=0.73, 95% CI, 0.55 to 0.98) compared with patients receiving PUVA.

A meta-analysis of nonsurgical treatments for vitiligo was published by Njoo et al. (1998). (73) Pooled analysis of 2 RCTs evaluating oral unsubstituted psoralen plus sunlight for generalized vitiligo (n=97 patients) found a statistically significant treatment benefit for active treatment compared with placebo (pooled odds ratio, 19.9; 95% CI, 2.4 to 166.3). Pooled analysis of 3 RCTs, 2 of oral methoxsalen plus sun and 1 of oral trioxsalen plus sunlight (n=181 patients), also found a significant benefit for active treatment versus placebo for generalized vitiligo (odds ratio, 3.8; 95% CI, 1.3 to 11.3). Adverse events included nausea, headache, dizziness, and cutaneous pruritus. All studies were published before 1985, had relatively small sample sizes (CIs were wide), and used sun exposure rather than artificial UVA.

Randomized Controlled Trial (RCT)
Yones et al. (2007) published an RCT that used a psoralen formulation available in the U.S. (74) This trial was included in both the Bae et al. (2017) (72) and Whitton et al. (2015) (62) systematic reviews. The trial enrolled 56 patients in the United Kingdom (U.K.) who had nonsegmental vitiligo. Outcome assessment was blinded. Patients were randomized to twice-weekly treatments with methoxsalen hard gelatin capsules PUVA (n=28) or NB-UVB therapy (n=28). The NB-UVB treatments were administered in a Waldmann UV500 cabinet containing 24 Phillips 100 NB-UVB fluorescent tubes. In the PUVA group, the starting dose of irradiation was 0.5 J/cm^2, followed by 0.25 J/cm^2-incremental increases if tolerated. Patients were evaluated after every 16 sessions and followed for up to 1 year. All patients were included in the analysis. The median number of treatments received was 49 in the PUVA group and 97 in the NB-UVB group. At the end of treatment, 16 (64%) of 25 patients in the NB-UVB group had 50% or more improvement in BSA affected compared with 9 (36%) of 25 patients in the PUVA group. Also, 8 (32%) of 25 in the NB-UVB group and 5 (20%) of 25 of patients in the PUVA group had 75% or more improvement in the BSA affected. Although the authors did not provide p values in their outcomes table, they stated that the difference in improvement did not differ significantly between groups for the patient population as a whole. Among patients who received at least 48 treatments, the improvement was significantly greater in the NB-UVB group (p=0.007). A total of 24 (96%) patients in the PUVA group and 17 (68%) in the NB-UVB group developed erythema at some point during treatment; this difference was statistically significant (p=0.02).

Section Summary: Psoralens with Ultraviolet A (PUVA)
For individuals who have vitiligo who have not responded to conservative therapy who receive PUVA (photochemotherapy), the evidence includes systematic reviews and RCTs. There is some

evidence from randomized studies, mainly those published before 1985, that PUVA is more effective than a placebo for treating vitiligo. When compared with NB-UVB in meta-analyses, results have shown that patients receiving NB-UVB experienced higher rates of repigmentation than patients receiving PUVA, though the differences were not statistically significant. Based on the available evidence and clinical guidelines, PUVA may be considered in patients with vitiligo who have not responded adequately to conservative therapy.

Other Common Skin Conditions

Other common dermatological conditions include acne vulgaris, alopecia areata, granuloma annulare (GA), hypertrichosis, keloids, and warts.

Published studies were found during a literature search for in patients with of granuloma annulare. (76, 77) The studies were small, 1 being retrospective with 13 patients and the second, a questionnaire, of 20 patients. The systematic review by Lukas et al. (78) stated that most medical literature on the treatment of generalized GA is limited to individual case reports and small series of patients treated without a control group. Randomized controlled clinical studies are missing. While there are case reports of successful treatments in the literature including surgical, medical and phototherapy options, well-designed, RCTs are warranted.

Section Summary: Other Common Skin Conditions

There is a lack of controlled trials demonstrating improved outcomes treating other common skin conditions. Additional large, well designed RCTs are warranted.

Practice Guidelines and Position Statements

American Academy of Dermatology (AAD)

Psoriasis

The AAD 2010 guidelines on the management of psoriasis recommended that patients with psoriasis who are compliant could, under dermatologist supervision, be considered appropriate candidates for home ultraviolet B therapy. (1) Targeted phototherapy was recommended for patients with mild, moderate, or severe psoriasis with less than 10% involvement of the BSA. Systemic PUVA was indicated in adults with generalized psoriasis resistant to topical therapy.

Vitiligo

British Association of Dermatologists (BAD) et al.

In 2015, BAD issued general guidelines on PUVA by stating, PUVA "…remains an important treatment, being the first-line phototherapy for pityriasis rubra pilaris and plaque-stage MF, and a good second-line phototherapy for common chronic dermatoses, including psoriasis (for which it may be more effective than other interventions such as the new biological therapies), atopic eczema and chronic urticaria. For phototherapy units serving small populations the availability of NB-UVB should be the first priority, but all larger phototherapy units should be able to offer PUVA." (79)

- *Atopic Dermatitis/Eczema*
  The 2015 BAD general guidelines on PUVA, included atopic eczema as a condition to be treated by PUVA, if NB-UVB has not been effective. (79)

- *Cutaneous T-Cell Lymphoma (CTCL)*
  The 2015 BAD general guidelines on PUVA, included CTCL as a condition to be treated by PUVA, as a major therapeutic modality. (79)
- *Psoriasis*
  The 2015 BAD general guidelines on PUVA, included chronic plaque psoriasis as a condition to be treated by PUVA, if NB-UVB has not been effective. (79)
- *Vitiligo*
  In 2008, guidelines on the diagnosis and management of vitiligo were published by a collaboration of several U.K. organizations, including the BAD, the Royal College of Physicians of London, and the Cochrane Skin Group. (80) The guidelines included the following statements (see Table 6).

Table 6. British Guidelines on the Diagnosis and Management of Vitiligo

Recommendation	GOE	LOE
PUVA therapy should be considered for treatment of vitiligo only in adults who cannot be adequately managed with more conservative treatments. PUVA is not recommended in children.	D	4
If phototherapy is to be used for treating nonsegmental vitiligo, NB-UVB should usually be used in preference to oral PUVA.	A	1+
A trial of PUVA therapy should be considered only for adults with widespread vitiligo, or localized vitiligo associated with a significant impact on patient's quality of life. Ideally, this treatment should be reserved for patients with darker skin types.	D	3
Before starting PUVA treatment, patients should be made aware that there is no evidence that this treatment alters the natural history of vitiligo. They should also be made aware that not all patients respond, and that some sites on the body, such as the hands and feet, respond poorly in all patients. They should also be informed of the limit to the number of treatments due to possible adverse effects.	D	3

PUVA: psoralens with ultraviolet A; NB-UVB: narrowband ultraviolet B; GOE: grade of recommendation; LOE: level of evidence.

<u>European Dermatology Forum</u>

- *Psoriasis Vulgaris*
  The 2023 guidelines from the European Dermatology Forum offer the following recommendations (81):
  - For patients with recent malignancy we recommend topical therapies, phototherapy (narrow band UVB) *and/or acitretin. *except patients with a recent, and/or high risk of cutaneous malignancy. (↑↑: strong recommendation).
  - In case of inadequate response to topical therapies, phototherapy, (narrow band UVB) and/or acitretin we suggest using MTX in psoriasis patients with a previous history of cancer (↑: weak recommendation).

- Combination therapy with immunosuppressants, including biologics, or phototherapy have not been evaluated.

- *Vitiligo*
  In 2013, the European Dermatology Forum published consensus guidelines on the management of vitiligo. (82) The guidelines state that oral PUVA is commonly used in adults with generalized vitiligo as a second-line treatment. The guidelines also state that targeted phototherapy is indicated for localized vitiligo, particularly small lesions of recent onset and childhood vitiligo, to avoid adverse effects due to total body irradiation and when total body irradiation is contraindicated. The guidelines were based on expert opinion, not a systematic review of the literature.

National Comprehensive Cancer Network (NCCN)

In their 2024 guidelines for the treatment of primary cutaneous lymphomas (83), the NCCN lists phototherapy as treatment option for mycosis fungoides and Sezary syndrome recommending UVB and nbUVB for limited or localized skin involvement and UVB, nbUB, PUVA, or UVA1 for the treatment of generalized skin involvement. Treatment varies based on the disease stage.

The National Cancer Institute

The 2023 National Cancer Institute (84) lists PUVA and narrowband UVB as treatment options for mycosis fungoides and Sezary syndrome with early cutaneous stages achieving the best responses. Treatment options depend on the stage of the disease.

National Psoriasis Foundation (NPF)

In 2017, the NPF published a consensus guidance based on a task force review of the literature on the treatment for psoriasis involving skinfolds (inverse or intertriginous) psoriasis. (85) The treatment guidance for intertriginous or genital psoriasis stated: "…there is anecdotal evidence demonstrating the strong clinical efficacy of biologic treatment; with limited knowledge on the effects of biologics on intertriginous or genital psoriasis." The guidance on inverse psoriasis is provided in Table 7.

Table 7. Recommendations on Treatment of Inverse Psoriasis

Line of Therapy	Recommendation
First-Line Therapy	Low potency topical steroids for periods less than 2-4 weeks
	Other topical therapies to consider are tacrolimus, pimecrolimus, calcitriol, or calcipotriene to avoid steroid side effects with long-term treatment.
Second- and Third-Line Therapies	Antimicrobial therapy, emollients, and tar-based products.
	Axillary involvement can be treated with botulinum toxin injection to reduce perspiration and inhibit inflammatory substance release.
	Excimer laser therapy or systemic agents.

In 2018, the NPF also published recommendations based on a review of the literature on the treatment for psoriasis in solid organ transplant patients. (86) Because organ transplant patients are excluded from RCTs, there are limited data. The recommendations were based on case series (see Table 8).

Table 8. Recommendations on Treatment of Psoriasis for Solid Organ Transplant Patients

Line of Therapy	Recommendation
First-Line Therapy for Mild- to Moderate Psoriasis	Topical therapy.
First-line therapy for moderate-to-severe psoriasis	The choice of therapy is dependent on organ transplanted • Acitretin with narrowband UVB, or • Narrowband UVB alone, or • Acitretin.
Second-Line Therapy	Increasing the current anti-rejection drug dose.
Severe psoriasis or refractory cases	Systemic or biologic therapies.

Vitiligo Working Group

The Vitiligo Working Group is supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, part of the National Institutes of Health. In 2017, the group published guidelines on current and emerging treatments for vitiligo. (75) The Working Group indicated that PUVA has largely been replaced by NB-UVB, but that "PUVA may be considered in patients with darker Fitzpatrick skin phototypes or those with treatment-resistant vitiligo (level I evidence)." The VWG also stated that "Targeted phototherapy (excimer lasers and excimer lamps) can be considered when <10% of body surface area [BSA] is affected (level II evidence)."

American Academy of Dermatology and National Psoriasis Foundation

In 2019, the American Academy of Dermatology (AAD) and the National Psoriasis Foundation (NPF) joint guidelines on the management and treatment of psoriasis with phototherapy give strong recommendations for the use of targeted ultraviolet B (UVB) (Table 9). (15)

Table 9. AAD-NPF Strength of Recommendation for Targeted UVB

No.	Recommendation	Strength
3.1	Targeted UVB phototherapy, including excimer laser, excimer light, and targeted NB-UVB light, for use in adults with localized plaque psoriasis, for individual lesions, or in patients with more extensive disease.	A
3.2	For maximal efficacy, treatment with targeted UVB phototherapy for adults with localized plaque psoriasis should be carried out 2 to 3 times/wk rather than once every 1 to 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 is more efficacious than an excimer light, which is more efficacious than localized NB-UVB light for the treatment of localized plaque psoriasis in adults.	B
3.5	Recommend targeted UVB phototherapy, including excimer laser and excimer light, for use in adults with plaque psoriasis, including palmoplantar psoriasis.	A
3.6	Excimer laser may be combined with topical corticosteroids in the treatment of plaque psoriasis in adults.	B
3.7	Recommend excimer laser in the treatment of scalp psoriasis in adults.	B

Table adapted from Elmets et al. (2019). (15)
MED: minimal erythema dose; NB-UVB: narrowband ultraviolet B; UVB: ultraviolet B; wk: week(s)

The guidelines for home narrowband-UVB therapy state that evidence shows similar results regarding efficacy, quality of life and side effects between patients with mild-to-severe psoriasis who received home treatments and those who received treatments at hospitals. In addition, home treatment was found to significantly lessen the burden on patients who had to travel to a phototherapy center. (15)

The 2020 AAD and NPF joint guidelines on the management and treatment of psoriasis in pediatric patients also provide recommendations for phototherapy (Table 10). (87) The evidence for phototherapy in the pediatric population is limited and generally of low quality.

Table 10. AAD-NPF Strength of Recommendations for Phototherapy/Photochemotherapy

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

Table adapted from Menter et al. 2020. (87)
NB-UVB: narrowband ultraviolet B; PUVA: psoralens and ultraviolet A.

Summary of Evidence

Atopic Dermatitis/Eczema, Cutaneous T-Cell Lymphoma (CTCL), Lichen Planus (LP), Morphea, Photodermatoses, Pityriasis Lichenoides (PL), Pruritic Eruptions in Human Immunodeficiency Virus (HIV) Infection, and Urticaria Pigmentosa (UP)

For individuals who have eczema, CTCL, LP, morphea, photodermatoses, PL, pruritic eruptions in HIV infections, and UP, who are resistant to topical medications and who receive photochemotherapy, as in psoralen plus ultraviolet A (PUVA), the evidence includes small within-subject studies and/or professional guidelines. Relevant outcomes are symptoms, change in disease status, quality of life, and treatment-related morbidity. PUVA has been shown as second-line therapy for resistance disease. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Psoriasis

For individuals who have mild localized psoriasis who receive targeted phototherapy, there is little evidence. The American Academy of Dermatology does not recommend phototherapy for patients with mild localized psoriasis whose disease can be controlled with topical medications. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have mild psoriasis that is resistant to topical medications who receive targeted phototherapy, the evidence includes small within-subject studies. Studies have shown that targeted phototherapy can improve mild localized psoriasis (<10% body surface area) that has not responded to topical treatment. Targeted phototherapy is presumed to be safer or at least no riskier than whole body phototherapy, due to risks of exposing the entire skin to the carcinogenic effects of ultraviolet B (UVB) light. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have moderate-to-severe localized psoriasis who receive targeted phototherapy, the evidence includes randomized clinical trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are symptoms, change in disease status, quality of life, and treatment-related morbidity. Systematic reviews of small controlled trials in patients with moderate-to-severe psoriasis have found that targeted phototherapy has efficacy similar to whole body phototherapy. Targeted phototherapy is presumed to be safer or at least no riskier than whole body phototherapy, due to risks of exposing the entire skin to the carcinogenic effects of UVB light. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have generalized psoriasis who receive PUVA, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, change in disease status, quality of life, and treatment-related morbidity. The available evidence demonstrates that PUVA is more effective than NB-UVB, topical steroids, or UVA without psoralens in patients with generalized psoriasis. Due to side effects, PUVA is typically restricted to more severe cases. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Vitiligo

For individuals who have vitiligo who have not responded to conservative therapy who receive PUVA (photochemotherapy), the evidence includes RCTs and systematic reviews. Relevant outcomes are change in disease status, quality of life, and treatment-related morbidity. There is some evidence from randomized studies, mainly those published before 1985, that PUVA is more effective than placebo for treating vitiligo. When compared with NB-UVB in meta-analyses, results have shown that patients receiving NB-UVB experienced higher rates of repigmentation than patients receiving PUVA, though the differences were not statistically significant. Based on the available evidence and clinical guidelines, PUVA may be considered in patients with vitiligo who have not responded adequately to conservative therapy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have vitiligo who receive targeted phototherapy, the evidence includes systematic reviews of RCTs, individual RCTs and retrospective studies. Relevant outcomes are change in disease status, quality of life, and treatment-related morbidity. Individual studies tend to have small sample sizes, and few were designed to isolate the effect of laser therapy. Two meta-analyses were attempted; however, results from a meta-analysis could not be verified because the selected studies were not available in English, and one estimate was imprecise due to the small number of studies and participants. Randomized controlled trials have shown targeted phototherapy to be associated with statistically significant improvements in VASI scores and/or repigmentation compared to alternate treatment options. However, one of the RCTs only showed marginal differences between groups in these outcomes limiting clinical significance, and the second compared phototherapy to oral vitamin E, which is not an optimal comparator. Overall, there is a lack of clinical trial evidence that compares this technique with more conservative treatments or no treatment/placebo. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	96900, 96910, 96912, 96913, 96920, 96921, 96922, 96999
HCPCS Codes	E0691, E0692, E0693, E0694

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
01/01/2025	Reviewed. No changes.
02/01/2024	Document updated with literature review. Coverage unchanged. Added references 2-4, 6-11, 16, 17, 25, 28-30, 34, 35, 38, 52, 56-58, 78, 81, 83, 84; others updated, some removed.
04/15/2022	Reviewed. No changes.
06/01/2021	Document updated with literature review. Coverage unchanged. References revised; added 43, 57, and 58; some removed.
04/01/2020	Reviewed. No changes
08/01/2018	Document updated with literature review. Rosacea was removed from the experimental, investigational and/or unproven coverage statement as it is currently addressed in THE801.030, Nonpharmacologic Treatment of Rosacea medical policy. The following NOTEs were added to coverage: NOTE 3: This medical policy does not address photodynamic therapy to treat dermatological conditions, such as actinic keratoses, squamous cell carcinoma, or basal cell carcinoma. For that medical policy, refer to THE801.027, Dermatological Applications of Photodynamic Therapy; and, NOTE 4: This medical policy does not address treatment of rosacea. For that medical policy refer to THE801.030, Nonpharmacologic Treatment of Rosacea. The Description, Rationale, and Reference sections were reorganized. References added were: 6, 7, 15, 17-19, 37, 41, 43-46, 49-51, and 54-56. Numerous references removed.
04/15/2017	Reviewed. No changes.
07/01/2016	Document updated with literature review. The following change was made to Coverage the word localized was added to the following Targeted phototherapy statement: Moderate to severe localized psoriasis comprising less than 20% body area for which Narrowband (NB)-UVB or PUVA are indicated.
04/01/2015	Document updated with literature review. Coverage clarified by adding the word localized to the following statement: Targeted phototherapy [e.g., Xenon-Chloride, Excimer (laser UVB)] may be considered medically necessary

	for the treatment of: 1. Mild to moderate localized psoriasis that is unresponsive to conservative treatment; or …
03/01/2013	Document updated with literature review. Coverage clarified to include Targeted phototherapy [e.g., Xenon-Chloride, Excimer (laser UVB)] is considered experimental, investigational and unproven for the treatment of vitiligo.
07/01/2010	Policy updated with literature review. Clarified coverage as follows: Office-based phototherapy and photochemotherapy may be considered medically necessary when criteria is met; • Office-based Goeckerman regimen may be considered medically necessary for psoriasis or atopic dermatitis; • Office-based targeted (laser) phototherapy may be considered medically necessary for psoriasis when criteria is met; • Office-based targeted (laser) phototherapy is experimental, investigational and unproven for stated conditions; • Office-based Goeckerman regimen may be considered medically necessary when criteria is met; • Homebound phototherapy may be considered medically necessary when criteria is met; • Phototherapy in the home setting using UVA or PUVA is considered not medically necessary; Tanning beds are considered not medically necessary.
08/15/2009	New Medical document originating from THE801.025, Targeting Phototherapy for Psoriasis and THE801.018 Ultraviolet (UV) Phototherapy in the Home. Homebound criteria for Home UVB light has been removed. Coverage of UVA and PUVA in the home are considered not medically necessary.