#### **Medical Policy**



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\*Current Policy Effective Date: 9/1/24 (See policy history boxes for previous effective dates)

## Title: Light and Laser Therapy for Vitiligo and Atopic Dermatitis

#### **Description/Background**

#### 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 to be an autoimmune disease. The most common form of the disorder is non-segmental vitiligo in which depigmentation is generalized, bilateral, symmetrical, and increases in size over time. In contrast, segmental vitiligo, 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.

#### **Atopic Dermatitis**

Atopic dermatitis (AD), or atopic eczema, is a chronic skin condition characterized by a dry, itchy rash on the face, elbows, hands, knees, and/or feet. In addition to skin care and avoidance of substances that might irritate the skin, topical ointments and creams, and oral corticosteroid are standard treatment options.

The pathophysiology of AD involves the complex interaction between genetic and environmental factors, which lead to changes in immunoregulation and disruption of the skin barrier. The goal of conventional AD management is to reduce the frequency and severity of flares.

First-line management of AD includes patient education, avoidance of triggering factors, hydration, treatment of flares through anti-inflammatory pharmacologic therapy and nonpharmacologic therapies aimed at compensation of the skin barrier defects.

Phototherapy and photochemotherapy (i.e., UVA, UVB and PUVA) are considered second-line modalities. Given that traditional therapies may not be effective and carry long-term side effects, artificial ultraviolet radiation has been investigated as a treatment adjunct or alternative to conventional treatments.

#### Treatment

There are numerous medical and surgical treatments aimed at decreasing disease progression and/or attaining repigmentation. Topical corticosteroids, alone or in combination with topical vitamin D<sub>3</sub> analogs, is a common first-line treatment 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 ultraviolet B (UVB) and psoralen plus ultraviolet A (PUVA).

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 devices consisted of a Phillips TL-01 fluorescent bulb with a maximum wavelength (lambda max) of 311 nm. Subsequently, xenon chloride 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.

PUVA 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 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. No topical psoralen formulation is currently available in the US.

## **Regulatory Status**

In 2001, XTRAC<sup>TM</sup> (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 vitiligo. The 510(k) clearance has subsequently been obtained for a number of targeted UVB lamps and lasers, including newer versions of the XTRAC system including the XTRAC Ultra<sup>TM</sup>, the VTRAC<sup>TM</sup> lamp (PhotoMedex), the BClear<sup>TM</sup> lamp (Lumenis), the 308-excimer lamp phototherapy system (Quantel Medical) and the Excilite<sup>TM</sup> and Excilite  $\mu^{TM}$  XeCl lamps. The intended use of all of these devices includes vitiligo among other dermatologic indications. Some of the light-emitting devices are handheld. FDA product code: GEX.

The oral psoralen products methoxsalen soft gelatin capsules (previously available under the brand name Oxsoralen Ultra), has been approved by the FDA.

## **Medical Policy Statement**

Psoralen plus ultraviolet A (PUVA), narrowband ultraviolet B (NB-UVB), and targeted phototherapy with excimer laser, with or without the use of oral or topical medications for the treatment of vitiligo are considered established treatments. They may be useful therapeutic options when indicated.

Phototherapy and photochemotherapy (i.e., ultraviolet A [UVA], UVB and PUVA) are considered established treatments with severe cases of atopic dermatitis, contact dermatitis and other eczema when criteria are met.

Home ultraviolet B (UVB) light therapy is considered established for any <u>one</u> of the following diagnoses:

- Atopic dermatitis when topical treatment alone has failed; or
- Pityriasis lichenoides; or
- Pruritus of hepatic disease; or
- Pruritus of renal failure; or
- Psoriasis, when topical treatment alone has failed; or
- Cutaneous T-cell lymphoma including mycosis fungoides and Sézary syndrome.

## **Inclusionary and Exclusionary Guidelines**

#### Inclusions:

Psoralen plus ultraviolet A (PUVA), narrowband ultraviolet B (NB-UVB), and targeted phototherapy with excimer laser, with or without the use of oral or topical medications for the treatment of vitiligo are considered established treatments for the following:

- Vitiligo that is not responsive to other forms of conservative therapy (e.g., topical corticosteroids, coal/tar preparations).
- NB-UVB and excimer laser phototherapy in individuals  $\geq$  3 years of age.
- Topical PUVA can be performed in children ≥ 2 years of age when up to 20% of their body surface area is affected.
- Systemic PUVA or oral PUVA is restricted to children > 12 years who have widespread vitiligo ( ≥ 20% body surface area).
- Treatment of vitiligo is restricted to the face, neck, trunk, and extremities.

Phototherapy and photochemotherapy (i.e., ultraviolet A [UVA], UVB and PUVA) are considered established treatments with severe cases of atopic dermatitis, contact dermatitis and other eczema when criteria are met:

 PUVA and NB-UVB for severe atopic dermatitis, contact dermatitis or eczema not responding to first-line therapy

Home ultraviolet light booth UVB phototherapy is considered established when conditions A and B are met:

A. The treatment is for one of the following conditions:

- 1. Atopic dermatitis when topical treatment alone has failed; or
- 2. Pityriasis lichenoides; or
- 3. Pruritus of hepatic disease; or
- 4. Pruritus of renal failure; or
- 5. Psoriasis, when topical treatment alone has failed; or
- 6. Cutaneous T-cell lymphoma including mycosis fungoides and Sézary syndrome.

#### and

- B. The treatment meets **all** of the following criteria:
  - 1. Treatment is conducted under a physician's supervision with regularly scheduled exams; **and**
  - 2. Treatment is expected to be long term (3 months or longer); and
  - 3. The individual meets **any** of the following:
    - a. The individual is unable to attend office-based therapy due to a serious medical or physical condition (for example, confined to the home, leaving home requires special services or involves unreasonable risk); **or**
    - b. Office based therapy has failed to control the disease and it is likely that homebased therapy will be successful; **or**
    - c. The individual suffers from severe psoriasis with a history of frequent flares which require immediate treatment to control the disease.

#### **Exclusions:**

- Systemic PUVA or oral PUVA is contraindicated in children < 12 years of age.
- Treatment of vitiligo of the acral areas (fingers, palms, soles of feet)
- Laser treatment for atopic dermatitis, contact dermatitis or other eczema
- An in-home UVB light therapy device for all other conditions not mentioned above, including but not limited to vitiligo, and when the criteria above are not met.
- UVA home therapy devices are not appropriate for home therapy. UVA therapy requires the use of photosensitizers, that should only be used under controlled conditions, and under the supervision of a physician.

**CPT/HCPCS Level II Codes** (Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)

Established c	odes:				
96900	96910	96912	96913	96999	E0691
E0692	E0693	E0694			

## Other codes (investigational, not medically necessary, etc.):

N/A

*Note:* The code(s) listed in this policy may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

## Rationale

#### TARGETED PHOTOTHERAPY

#### **Review of Evidence**

#### **Systematic Reviews**

A systematic review 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). No differences between the excimer lamp and NB-UVB were identified for the outcome of 50% or more repigmentation (relative risk [RR],1.14; 95% confidence interval [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 to the excimer laser, there were no significant differences between treatments for either 50% or greater repigmentation (RR=0.97; 95% CI, 0.84 to 1.11) or 75% or greater repigmentation (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.

Sun et al (2015) published a systematic review of randomized controlled trials that focused on treatment of vitiligo with the 308-nm excimer laser. Reviewers identified 7 RCTs (total n=390 patients) for inclusion. None of the studies were conducted in the United States; 5 were from Asia. Three trials compared the excimer laser with an excimer lamp, and 4 compared the excimer laser with NB-UVB. The 4 studies that evaluated NB-UVB are of greatest interest to us. Repigmentation rates did not differ significantly between groups treated. Results showed that the likelihood of a 50% or more repigmentation rate was significantly higher with the excimer laser than with NB-UVB (relative risk [RR], 1.39, 95% confidence interval [CI], 1.05 to 1.85). Reviewers also stated that, in qualitative analysis, neither study showed significant benefit of the excimer laser for achieving a 75% or more repigmentation rate.

#### **Randomized Controlled Trials**

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. 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. 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). 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.

ior vitiligo					
Study (Year)	Countries	Sites	Dates	Participants	Interventions
Poolsuwan et al (2020) <sup>5,</sup>	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 ≥2 weeks or phototherapy or systemic immunosuppressive drugs for ≥8 weeks	<ul> <li>Localized 308-nm excimer light<sup>a</sup></li> <li>311-nm NB-UVB<sup>a</sup></li> </ul>
Nistico et al (2012) <sup>6,</sup>	Italy	Single- center	NR	Patients 13 to 56 years of age with localized or generalized vitiligo	<ul> <li>Targeted 308-nm excimer laser plus oral vitamin E 400 IU<sup>b</sup></li> <li>Targeted 308-nm excimer laser plus topical tacrolimus 0.1% ointment plus oral vitamin E 400 IU<sup>b</sup></li> <li>Oral vitamin E 400 IU alone<sup>b</sup></li> </ul>

# Table 1. Summary of Key Randomized Controlled Trial Characteristics Assessing Targeted Phototherapy for Vitiligo

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

<sup>a</sup> Both interventions given for 3 non-consecutive days per week x 48 treatment sessions

<sup>b</sup> 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 Randomized Controlled Trial Results Assessing Targeted Phototherapy for Vitiligo

Study	Reduct	tion in VASI score, mean	Repigmentation
Poolsuwam et al (2020)			
• N	36		36
<ul> <li>308-nm excimer light</li> </ul>	0.55 ± 0	0.39%	2.36 ± 1.15a
NB-UVB	0.43 ± (	0.39%	1.94 ± 1.19a
• p-value	< 0.001		<0.001
Nistico et al (2012)			
• N	NA		53
<ul> <li>Phototherapy + vitami</li> </ul>	n E NA		Good: 6/20 (30%) <sup>b,c</sup> Excellent: 5/20 (25%) <sup>b,c</sup>
<ul> <li>Phototherapy + tacroli vitamin E</li> </ul>	mus + NA		Good: 8/20 (40%) <sup>b,c</sup> Excellent: 6/20 (30%) <sup>b,c</sup>
• Vitamin E alone	NA		Good: 0/13 (0%) <sup>b,c</sup> Excellent: 0/13 (0%) <sup>b,c</sup>
<ul> <li>p-value</li> </ul>	NA		<0.001d

NA: not applicable; NB-UVB: narrow-band ultraviolet B; NR: not reported; VASI: Vitiligo Area Scoring index

<sup>a</sup> Repigmentation was reported as a graded score from 1 to 4 with 1 being "poor" and 4 being "excellent"

<sup>b</sup> Good repigmentation defined as 51 to 75% repigmentation; excellent repigmentation defined as 76 to 100% repigmentation

<sup>c</sup> Repigmentation reported as number of patients out of the total number of patients in subgroup (%) for each category.

<sup>d</sup> P-value reported for good to excellent repigmentation response in each intervention group versus control (vitamin E alone).

#### Table 3. Study Relevance Limitations

St <b>udy</b>	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	rollow- up <sup>e</sup>
Poolsuwam et al (2020) <sup>5,</sup>				5,6. Differences in VASI score and repigmentation do not appear to be clinically significant; clinical significance not defined by investigators	
Nistico et al (2012) <sup>6,</sup>			2. Phototherapy groups compared to oral vitamin E, which is not optimal standard of care for vitiligo	5. Clinically significant difference in response was 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. <sup>a</sup> 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 <sup>b</sup> Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator. <sup>c</sup> Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not

delivered effectively.

<sup>d</sup> 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.

<sup>e</sup> Follow-Up key: 1. Not sufficient duration for benefits; 2. Not sufficient duration for harms.

#### Table 4. Study Design and Conduct Limitations

Study	Allocation <sup>a</sup>	Blinding <sup>b</sup>	Selective Reporting <sup>c</sup>	Follow- up <sup>d</sup>	Power <sup>e</sup>	Statistical <sup>f</sup>
Poolsuwam et al (2020) <sup>5,</sup>		1. Single- blinded to investigators only			1. Power calculations not reported	
Nistico et al (2012) <sup>6,</sup>	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	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment. <sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

<sup>b</sup> Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

<sup>c</sup> Selective reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

<sup>d</sup> 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).

<sup>e</sup> 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) retrospectively analyzed 979 Chinese patients (3478 lesions) treated with the 308-nm targeted laser for vitiligo. 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 (304-312 nm) targeted laser for treating pediatric patients (age  $\leq$ 16 years) with vitiligo. Twentyseven patients (95 lesions) were evaluated by 2 dermatologists following a mean of 20 treatments (range, 10-50 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.

Alhowaish et al (2013) performed a meta-analysis of the relevant literature pertaining to vitiligo and excimer laser published between 1990 and 2012. Included in the review were all relevant articles about 308-nm excimer laser and light sources assessing their efficacy in the management of vitiligo, as well as their side effects. The value of combination treatment methods was also analyzed. The available studies provide strong evidence that the excimer laser represents the most effective approach to treat vitiligo compared to ordinary phototherapy. It was noted that excimer laser is relatively safe and effective for localized disease. UV-sensitive areas respond best as well as a short duration of the disease. More frequent treatments achieve better results. Compared to other treatment modalities, the excimer laser most likely constitutes the treatment of choice for localized vitiligo. Its efficacy can be further improved in combination with other therapies such as corticosteroids, pimecrolimus, or tacrolimus.

The Italian research group also published a similar 12-week study in 2009 in which topical 4% khellin ointment was used instead of tacrolimus ointment. This study included 48 patients (16 per group), of which 45 (94%) completed treatment. The proportion of patients with a good or excellent response (see previous definitions) was 14 of 16 (88%) in the excimer laser plus vitamin E group, 14 of 16 (88%) in the excimer laser plus khellin plus vitamin E group, and 1 of 16 (6%) in the vitamin E only (control) group. The clinical response rates in the two groups receiving laser treatment were significantly higher than in the control group.

Cassaci et al (2007) sought to compare the effectiveness of NB-UVB phototherapy and 308nm monochromatic excimer light (MEL). The study was done in a randomized, investigatorblinded and half-side comparison design. Twenty-one subjects with symmetrical vitiligo lesions were enrolled in this study. Vitiligo lesions on one body side were treated twice weekly for six months with 308-nm MEL, while NB-UVB phototherapy was used to treat lesions on the opposite side. At the end of the study, six lesions (37.5%) treated with 308-nm MEL and only one lesion (6%) treated with NB-UVB achieved an excellent repigmentation (score 4) while four lesions (25%) treated with 308-nm MEL and five lesions (31%) treated with NB-UVB showed a good repigmentation (score 3). The investigator concluded that 308-nm MEL is more effective than NB-UVB in treating vitiligo lesions and it induces repigmentation more rapidly. Hadi et al (2004) reported on the effectiveness of excimer laser for the treatment of vitiligo. A retrospective chart review of thirty-two patients with 55 spots of vitiligo were enrolled; a population-based sample was studied that included men and women, adults and children, with different ethnic backgrounds. The treatment was started with the lowest dose, 100 mJ/cm<sup>2</sup> (comparable to one minimal erythema dose value and one multiplier). Depending on Fitzpatrick skin type, the dose was raised gradually in a stepwise fashion. In skin types I to II, the same does was repeated twice before going up to avoid burns. Patients were treated for 30 sessions, or 75% repigmentation, whichever occurred first. Overall, 55 spots were treated: 29 (52.8%) had 75% pigmentation or greater, and 35 (63.7%) had 50% pigmentation or greater. The best results were on the face: of the 21 spots treated 15 (71.5%) had 75% pigmentation, and 16 (76.2%) had 50% pigmentation or greater. Other areas (neck, extremities, trunk, and genitals) had moderate response in comparison to the face. The least response was on the hands and feet; of the 5 spots treated only 20% showed 50% pigmentation or more. The researchers concluded that "slightly more than 50% of the patients tested showed 75% or more pigmentation of their lesions, after 30 treatments or less; most of the responders had Fitzpatrick skin type III and above. All the untreated patches (controls) remained unchanged. This demonstrates that the 308-nm excimer laser is an effective method of treatment for vitiligo."

#### Section Summary: Targeted Phototherapy

Published studies evaluating targeted excimer laser phototherapy for vitiligo include systematic reviews of RCTs, individual RCTs, and retrospective studies. Positive findings have been demonstrated. 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. Excimer laser phototherapy increased the level of repigmentation in a greater percentage of patients over a shorter duration compared with standard therapy.

## HOME ULTRAVIOLET B (UVB) LIGHT THERAPY

#### Atopic dermatitis (AD)

The initial treatment of AD typically consists of topical and non-pharmacological therapies as well as modifications in individual environments or occupations. Phototherapy is limited to those whose symptoms are not adequately controlled by the initial treatment modalities. There are numerous treatment protocols, but in general, individuals are dosed according to their minimal erythema dose and/or Fitzpatrick skin type. The AAD (2014) notes "Phototherapy can be administered on a scheduled but intermittent basis over time, or more continuously as maintenance therapy, for patients with refractory or chronic disease."

#### Cutaneous T-cell lymphoma (CTCL)

Non-Hodgkin lymphoma (NHL) includes two types of cutaneous lymphomas, T-cell lymphomas (CTCLs) and B-cell lymphomas (CBCLs), with CTCLs accounting for the majority of cutaneous lymphomas. According to the National Comprehensive Cancer Network<sup>®</sup> (NCCN) Clinical Practice Guidelines (CPGs) in Oncology<sup>®</sup> for Primary Cutaneous Lymphomas, Mycosis Fungoides (MF) accounts for 50% to 70% of CTCL cases and Sézary syndrome (SS) accounts for less than 5% of CTCL cases. MF is considered an indolent malignancy and generally is associated with a slow progression while the median survival of SS is only 32 months from diagnosis (Trautinger, 2006). While CTCLs develop in the skin, the disease can progress and involve other areas such as lymph nodes, blood or visceral organs. Prognosis

and treatment are dependent upon a number of factors including, but not limited to extent and type of skin involvement, overall stage, whether extracutaneous disease is present and peripheral blood involvement (NCCN, 2020).

#### Mycosis Fungoides and Sézary Syndrome

Ultraviolet light therapy is an established treatment of MF and therapies have included UVB (broad-band and narrow-band) and UVA treatments (Hodak, 2015). Phototherapy can be used at various stages of MF, either alone or in combination with systemic therapy (Hodak, 2015). The 2020 NCCN CPGs for Primary Cutaneous Lymphomas include a 2A indication for UVB therapy for patch/thin plaques in MF/SS with limited/localized or generalized skin involvement. In addition, NCCN includes a 2A indication for UVB in stage III MF/SS, noting that while generalized skin directed therapies may not be well tolerated in this population, phototherapy can be used successfully.

Due to the low incidence of MF, there is a dearth of appropriately powered RCTs, and most recommendations are generally based upon small studies, case series or expert opinion. Olsen et al reported on the results of 3 studies which included home broad-based UVB therapy which consisted of a total of 109 individuals who presented with stage 1A or 1B MF. Home treatments included daily phototherapy while office-based treatments were carried out 3 times per week. A total of 58 individuals received home-based therapy, with 48 of these 58 individuals receiving only home-based therapy and the remaining 10 individuals receiving home therapy after office-based therapy. The authors noted that maintenance regimens within the studies varied and likely affected response duration. Relapse was uncommon while individuals were on maintenance phototherapy (2/18) but was more common once maintenance phototherapy was discontinued (12/23). The authors found that individuals using home-based phototherapy were much more likely to continue maintenance phototherapy than individuals who received office-based phototherapy.

#### Pityriasis lichenoides

UVB has also been recommended as a treatment for several other conditions. Pityriasis lichenoides is a rare collection of skin disorders that have been reported to progress to cutaneous lymphoma or an ulceronecrotic presentation, both of which carry a significant risk of mortality. Treatment is difficult and aggressive approaches are usually recommended. According to one source, the use of UVB phototherapy has been the most successful treatment method and is considered first-line therapy (Khachemoune, 2007).

#### Pruritus of hepatic or renal disease

Pruritus of hepatic disease and renal failure are difficult to treat. Management is primarily focused on the treatment of the underlying symptoms such as pain and itching. Several treatment options are currently used, and UVB phototherapy has become widely accepted as an important tool in the management of these conditions (Wang, 2010).

#### Psoriasis

Koek et al (2009) conducted the first randomized controlled single-blind trial comparing officebased UVB treatment with home therapy for individuals with plaque or guttate psoriasis. 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 noninferior 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.

## Vitiligo

Shan et al (2014) published early results of UVB home phototherapy for vitiligo in a prospective uncontrolled trial (n=93). Treatments were administered 3 times each week at variable dosages. Follow-up was conducted every 3 months up to 1 year to evaluate repigmentation and any complications. At 1 year of follow-up, 35 subjects (38%) achieved excellent repigmentation, 16 (17%) achieved good repigmentation, 15 (16%) showed moderate repigmentation, 16 (17%) had poor repigmentation, and 11 (12%) had no repigmentation. A total of 25 (27%) individuals discontinued treatment due to poor repigmentation. This study was hampered by several design limitations, including a lack of randomization, and lack of appropriate comparator groups.

Eleftheriadou (2014) conducted a pilot trial to determine the feasibility of conducting a multicenter randomized controlled trial (RCT) to assess the safety and effectiveness of home hand-held NB-UVB phototherapy compared with topical treatments for repigmentation of vitiligo. Results showed that a larger RCT evaluating home hand-held phototherapy is feasible and acceptable to participants and healthcare providers. This trial was not intended as an efficacy trial.

A prospective cohort trial enrolled 94 individuals with non-segmental vitiligo to evaluate the efficacy and safety of home and outpatient narrowband UVB therapy. Over a period of 6 months, 48 participants received treatment at home while 46 received outpatient treatment. Primary outcomes included efficacy, quality of life and adverse events. Overall, results were similar at 6 months between groups with higher efficacy seen on some measures for the outpatient group (Zhang, 2019). Further investigation of the efficacy and safety of NB-UVB as a home-treatment for non-segmental vitiligo, in the setting of a randomized trial, is warranted.

Liu et al (2020) published the results of a randomized pilot trial to determine the efficacy and safety of narrowband UVB phototherapy at home compared to hospital management of limited new-onset vitiligo. A total of 100 individuals with new-onset vitiligo (< 3 months) and < 5% body surface area involvement were randomized to either a home-based or a hospital-based treatment group and administered UVB phototherapy 3 times a week. At study-end (8 weeks), home- and hospital-based treatment showed similar efficacy but the frequency of adverse events, such as painful erythema, burning, blistering, and excessive hyperpigmentation, were increased in the home-based.

The current evidence does not support the safety and efficacy of home-based UVB phototherapy devices compared with in-office or alternative treatments for vitiligo. The published literature does not show that use of a home-based UVB phototherapy device provides additional benefits to the individual user.

#### Summary: UVA home therapy devices

The use of UVA as a home therapy has not been shown to be safe and effective when compared to the other alternatives, such as office or facility-based treatment UVA therapy or UVB therapy. The American Academy of Dermatology (AAD) 2014 notes that given the limited number of head-to-head trials, there is no definitive recommendation regarding which form of phototherapy is more effective. UVA therapy requires the concurrent use of photosensitizers, which greatly increase the risk of complications. UVB therapy does not involve the use of photosensitizers.

#### **PSORALENS WITH ULTRAVIOLET A**

#### **Systemic Reviews**

Bae et al (2017) published a systematic review and meta-analysis on the use of phototherapy for the treatment of vitiligo. 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 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.

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Treatment	Duration, mo.	≥50% Repigmentation (95% CI), %	≥75% Repigmentation (95% Cl), %
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 Dec	at al (0017) 9	· · · · · · · · · · · · · · · · · · ·	· · · · · · · · · · · · · · · · · · ·

Table 5. Resi	ponse Rates to NE	-UVB and PUVA in	the Treatment of	f Vitiliao bv 1	reatment Duration
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Adapted from Bae et al (2017).9.

CI: confidence interval; NV-UVB: narrowband ultraviolet B; PUVA: psoralens with ultraviolet A.

#### **Randomized Controlled Trials**

Bansal et al (2013) evaluated the efficacy of psoralen-NB-UVB (P-NB-UVB) vs. NB-UVB in vitiligo in a randomized study. Forty-five Indian patients (over age 13 years) with vitiligo involving more than 5% body surface area were randomly assigned to receive either NB-UVB or P-NB-UVB treatment. Both groups received NB-UVB exposure 3 times weekly, with a total of 60 sessions. The extent of repigmentation achieved was calculated on the basis of Vitiligo Area Severity Index (VASI) scoring. Forty patients were available for analysis at the end of the study. The extent of repigmentation in the P-NB-UVB group was statistically significantly greater in face and neck (P=.006, t-test) and hands (P=.007, t-test) in comparison with the NB-UVB group (t-test). Percentage reduction in VASI scores was statistically significantly greater in the P-NB-UVB group (29.2% vs. 21.7%, P=.043, t-test). The response to P-NB-UVB therapy started earlier than the response to NB-UVB. After excluding sunlight as a confounding factor, treatment response was also significantly better in the P-NB-UVB group (P=.005). Investigators concluded addition of psoralen increased the extent of repigmentation due to NB-UVB therapy in vitiligo.

Sapam et al (2012) compared the efficacy and adverse effects of NB-UVB with oral psoralen PUVA therapy in the treatment of vitiligo in a parallel-group, assessor blinded, randomized, controlled trial. Patients aged 13-70 years with vitiliginous lesions involving more than 5% body surface area were eligible for the study. In total, 56 patients were randomized in a 1:1 ratio to oral PUVA or NB-UVB phototherapy groups. Patients were assessed for the percentage of repigmentation over the depigmented areas as the primary outcome measure at each visit during the first 3 months and then monthly within the next 3 months. The incidence of adverse effects was also noted during the study period as the secondary outcome measure. The median repigmentation achieved at the end of the 6-month therapy course was 45% in the NB-UVB group and 40% in the oral PUVA group. Focal vitiligo had the best response in both treatment groups. There were lesser adverse effects within the NB-UVB (7.4%) than in the PUVA (57.2%) group. Two PUVA patients discontinued therapy due to severe dizziness. There was no significant difference in the mean degree of repigmentation; however, NB-UVB carried a greater response rate and might be superior to oral PUVA with better tolerance and color

match with the surrounding normal skin, as well as fewer side effects in the treatment of vitiligo.

Bhatnagar et al (2007) evaluated the efficacy of NB-UVB compared to trimethylpsoralen PUVA. In this randomized, open, prospective study, 50 patients were divided equally in PUVA and NB-UVB groups. The mean degree of repigmentation attained in the NB-UVB group was 52.24% over a mean treatment period of 6.3 months, whereas in the PUVA group it was 44.7% in a mean period of 5.6 months (P=0.144). After excluding the results of therapy-resistant sites, that is, hands and feet, the mean degree of repigmentation in the NB-UVB group was 67.57%, whereas in the PUVA group it was 54.2% (P=0.007). The researchers concluded that NB-UVB performed better in comparison to TMP PUVA in terms of mean total repigmentation when traditionally considered therapy-resistant sites were excluded.

Yones et al (2007) published an RCT that used a psoralen formulation available in the United States. The trial enrolled 56 patients in the United Kingdom who had non-segmental vitiligo. Outcome assessment was blinded. Patients were randomized to twice-weekly treatments with methoxsalen hard gelatin capsules (8-MOP) psoralen plus UVA (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<sup>2</sup>, followed by 0.25 J/cm<sup>2</sup> 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 greater than 50% improvement in body surface area affected compared with 9 (36%) of 25 patients in the PUVA group. In addition, 8 (32%) of 25 in the NB-UVB group and 5 (20%) of 25 patients PUVA group had at least 75% improvement in the body surface area affected. Although authors did not provide p values in their outcome 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, 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

There is evidence from multiple studies that PUVA and NB-UVB are effective for treating vitiligo when first-line therapies have failed. Studies comparing PUVA with NB-UVB have had mixed findings. Meta-analyses have shown that patients receiving NB-UVB experienced higher rates of repigmentation than patients receiving PUVA, though the differences were not statistically significant. Patients treated with PUVA experienced higher rates of adverse events such as nausea and erythema. Analyses of treatment duration found that repigmentation rates following 12 months of treatment were higher compared with rates following 6 months of treatment.

## LIGHT THERAPY FOR CHILDREN WITH VITILIGO

Kanwar et al (2012) presented a brief update regarding the various safe therapeutic modalities for vitiligo, for use in children. Vitiligo usually presents in childhood and young adulthood. Approximately one half to one third of cases occurs by 20 years of age, and about 25% develop before eight years, with a mean age of onset between four and five years. Topical steroids are often the first line of treatment because they are an easy and convenient mode of

treatment. If the body surface area (BSA) involved in the child is < 20%, and the disease is not rapidly spreading, then topical therapy is first choice. The only drawback of long-term topical steroid usage is its side effects. Topical calcineurin inhibitors are proving to provide results similar to topical steroid, but their drawback is, it is costly and not recommended for children below two years of age. Results of treatment outcome have been reported to be moderately successful, particularly in patients with localized vitiligo. Narrow band UVB has proven to be effective in vitiligo. Much data of NB-UVB exists in adults. Due to fear of long-term toxicity (because of patients prolonged life expectancy after treatment) there is limited data on treatment in children. In children with vitiligo affecting  $\geq$  20% of body surface area, NB-UVB has shown to be a safe option. Studies have shown positive effects of NB-UVB in children with vitiligo, but there is insufficient data to provide recommendation for the safe maximum dose and duration of therapy of NB-UVB in children.

There is an overall consistency in the clinical literature that systemic PUVA or oral PUVA is contraindicated in children younger than 12 years of age; it is restricted to children of > 12 years and those who have widespread vitiligo (i.e.,  $\geq$  20% BSA); however, topical PUVA can be safely used in children of two years and more who have up to 20% of their body affected.

Ezzedine et al (2016) discussed management strategies for vitiligo in the pediatric population. Authors concluded that a variety of phototherapy modalities exist that have been shown to be beneficial in pediatric vitiligo. Generalized phototherapy is often performed in extensive disease and in disease that is spreading rapidly. Psoralens and UVA (PUVA) has been historically used in vitiligo with good benefit, but there is difficulty with nausea, compliance of evewear, office visits, and many side effects including phototoxic reactions. Therefore, PUVA has been largely replaced by narrowband UVB (NB UVB). Furthermore, in head-to-head study, there has been demonstrable increased repigmentation that was not significant over PUVA. In children, NB UVB has become the therapy of choice and can produce two types of benefits: (1) repigmentation, and (2) stabilization, the latter being an important way to gain control over widespread disease. Some benefit can be achieved with the addition of topical corticosteroids. Other forms of phototherapy that have been described as safe and effective for long-term therapy of pediatric vitiligo include excimer laser, targeted UVB, and targeted UVA. Side effects of phototherapy include itch, burning, erythema, stinging, blistering, and phototoxicity. Targeted phototherapy may not allow for disease stabilization in extensive disease but does limit side effects to the local site treated. Excimer laser is most beneficial in segmental vitiligo when performed early on in disease. Phototherapy is often more effective in darker patients and the benefits of phototherapy in Fitzpatrick type I skin (lightest skin type) do not outweigh the risk. Although long-term follow-up of pediatric patients with vitiligo who received phototherapy has not been conducted, the risk of carcinogenesis after phototherapy probably persists lifelong, requiring on-going full body skin examinations for screening after therapy. As some patients with vitiligo will have circulating ANAs, which could sensitize them, screening for ANAs before systemic phototherapy can be helpful.

Phiske et al (2016) indicate that treatment modalities for vitiligo in children do not differ from those used in adults, but some are age specific. Some treatment modalities with potential serious side effects may not be justified in children. If the body surface area (BSA) involved in the child is < 20%, and the disease is not rapidly spreading, then topical therapy (steroids and topical calcineurin inhibitors) is first choice for lesions over face, neck, and genital areas. Excellent repigmentation rates have been reported with topical steroids, whereas calcineurin inhibitors have comparable efficacy and a better safety profile compared with topical steroids.

PUVA oral psoralen plus UVA is contraindicated in children < 12 years of age (due to long term serious side effects), it is restricted to children of > 12 years and those who have widespread vitiligo (i.e.,  $\geq$  20% BSA). Topical psoralens plus UVA is a safer treatment modality for children with limited vitiligo, children younger than two years of age and who have up to 20% of their body affected. It proves to be effective if administered carefully, as there is no necessity to take precautions for ocular toxicity or for hepatic dysfunction which is needed for oral PUVA. It gives favorable response in segmental vitiligo. If the BSA involved is > 20%, phototherapy should be considered. NB UVB has better overall repigmentation rates and safety profile. A meta-analysis found that NB UVB was the most effective and safest therapy for generalized vitiligo. Long - term NB UVB therapy may carry less risk for skin cancer than PUVA therapy. In children, if no response is observed after six months, further therapy should be discontinued.

Cho et al (2011) retrospectively evaluated the efficacy and safety of 308-nm excimer laser treatment in 30 childhood vitiligo patients. Forty childhood vitiligo lesions were studied, and half of them showed 50% repigmentation and 12.5% had greater than 75% repigmentation. Vitiligo lesions over sun-exposed areas responded better. Side-effects reported with this laser are perilesional hyperpigmentation, burns, and folliculitis.

Hui-Lan et al (2009) investigated 49 pediatric patients in a single-blinded, randomized study comparing 308-nm excimer laser therapy together with topical 1% pimecrolimus cream twice daily (group A) with excimer laser therapy twice per week (group B). Of 48 patients evaluated after 30 weeks of treatment, 71% of patients from group A achieved grade III or IV repigmentation compared with 50% in group B. A significant difference was found between group A and B at the end of 30 weeks of treatment.

Al Otaibi et al (2009) conducted a controlled prospective trial in 34 patients with localized vitiligo (age 3-21 years), treatment was given twice-weekly for a period of 13 weeks with a spot size 15- and 25-mm. Half of the children had at least 50% repigmentation, facial lesions responded better in comparison to other sites.

#### Section Summary: Light Therapy For Children With Vitiligo

The available literature suggests that phototherapy may be considered in children when more than 20% of their body surface is involved. NB-UVB is safer than PUVA and should therefore be the treatment of choice when other conservative measures have failed. Combinations of topical therapy and NB-UVB have shown good results and can be tried in patients who fail to show a good response with NB-UVB alone. It remains unknown how many treatments and what frequencies would increase the risk of developing a treatment-related skin cancer. Children with vitiligo that is limited to focal lesions who do not respond to topical therapy have been shown to benefit from excimer laser phototherapy. Published studies reveal that NB-UVB and excimer laser therapy have been successfully performed in children as young as 3 years of age.

#### **DERMATITIS AND EXCIMER LASER**

The excimer laser system is a hand-held UVB laser light source, which utilizes a xenon chloride gas mixture and emits intense, targeted UVB at a monochromatic wavelength of 308 nm. Compared with traditional UVB therapy, it provides an advantage in that a greater intensity of UVB radiation can be used to target lesions while sparing unaffected areas.

Mehraban (2014) published a systemic review summarizing all the experiments, clinical trials and case reports on 308 nm excimer laser in dermatological disorders. 308-nm excimer laser has currently a verified efficacy in treating skin conditions such as vitiligo, psoriasis, atopic dermatitis, alopecia areata, allergic rhinitis, folliculitis, granuloma annulare, lichen planus, mycosis fungoides, palmoplantar pustulosis, pityriasis alba, CD30+ lymphoproliferative disorder, leukoderma, prurigo nodularis, localized scleroderma and genital lichen sclerosus. Further large-scale studies were recommended in order to fully affirm the safety profile of the 308 nm laser considering the potential risk of malignancy.

Beggs (2015) conducted an extensive literature search to find articles pertaining to dermatologic conditions treated with the 308 nm excimer laser. The outcomes and results were compiled into different dermatologic conditions treated with the excimer laser. The 308 nm excimer laser proved to have a wide range of uses for focal inflammatory and hypopigmented conditions. The authors concluded that larger studies and studies evaluating the long-term effects of the excimer laser are needed.

#### Section Summary: Dermatitis And Excimer Laser

Due to the small sample sizes, lack of ongoing current literature and the few published studies demonstrating the use of excimer laser for atopic dermatitis, efficacy and safety have not been documented. The use of all UV treatments contains a risk for development of skin cancer. With the greater intensity of UVB radiation used by the 308 nm excimer laser, the risk in comparison to standard therapy is unknown. Evidence to support excimer laser therapy for the treatment of atopic dermatitis is lacking, further studies are needed.

#### Summary of Evidence

Light therapy for skin conditions include PUVA, NB-UVB, and targeted excimer laser phototherapy. Overall, studies to date support the safety and efficacy of these light therapies for vitiligo, in both pediatric and adult populations. In most instances where vitiligo is recalcitrant to first-line therapies, NB-UVB and targeted excimer laser, with or without topical medications, have emerged as preferred second-line treatments. The percentage of body surface area affected, age of the patient and the area of treatment should all be considered when determining the best modality for treatment of childhood vitiligo.

Phototherapy and photochemotherapy (i.e., UVA, UVB and PUVA) may be prescribed for adults when severe cases of atopic dermatitis, contact dermatitis and other eczema have failed to respond to immunosuppressants. Evidence to support efficacy and safety of excimer laser therapy for the treatment of atopic or contact dermatitis and other eczema is lacking.

## **Supplemental Information**

#### PRACTICE GUIDELINES AND POSITION STATEMENTS

#### American Academy of Dermatology

The American Academy of Dermatology (AAD) website provides information on vitiligo treatments and includes PUVA and excimer laser as options. There are no practice guidelines or protocols for the use of UVB for vitiligo patients. The AAD also provides patient information on vitiligo treatment and mentions NB-UVB as a treatment option.

The AAD (2014) indicates that the successful use of UV light for atopic dermatitis (AD) has led to the investigation of laser light technology as another possible treatment. Various laser modalities, including excimer, diode, and pulsed dye lasers, have been tested in AD patients, with some improvement in symptoms such as pruritus and quality of life (QOL). Given a very limited number and quality of reports, lasers are not recommended for the treatment of AD at this time.

#### **British Association of Dermatologists**

The British Association of Dermatologists (2008) reviewed and updated in (2021) guidelines on the diagnosis and management of vitiligo were published by a collaboration of several U.K. organizations, including the British Association of Dermatologists, the Royal College of Physicians of London, and the Cochrane Skin Group. The guidelines included the following statements:

### Light and laser monotherapy and combination therapies

R20 Offer NB-UVB (whole body or localized, e.g. home based handheld) as first-line phototherapy to people with vitiligo who have an inadequate response to topical therapy and/or who have extensive or progressive disease. As a prolonged course is generally required, discuss the risk-benefit ratio, particularly for children .<sup>§</sup> This may be combined with topical calcineurin inhibitor† (more evidence for tacrolimus) or potent topical corticosteroid, for localized sites. Counsel patients on the significant risk of loss of response upon treatment cessation.

[§There is lack of data on the skin cancer risk for high cumulative exposures in children with less deeply pigmented skin (Fitzpatrick skin types I–III), hence the risk-benefit ratio needs to be carefully considered. Prior to combination NB-UVB and topical tacrolimus treatment, advise patients that there is a theoretical increased risk of skin cancer with this combination of treatment. A shared decision should be made with the person with vitiligo, taking into account other alternatives, the individual's personal and family history of skin cancer risk and the impact of the vitiligo. The evidence for potent topical corticosteroid is limited. Prior to this combination, consider the risk–benefit ratio of the prolonged use of potent topical corticosteroid.]

R21 Inform people with vitiligo who are eligible for NB-UVB therapy of the requirements (depending on local protocols: a pretherapy assessment, medical photographs taken prior to and during follow-ups at 3–6 months, two to three sessions weekly possibly for up to 1 year), and the likely response depending on the affected anatomical site (e.g. the face and trunk usually achieve better repigmentation than acral sites). Alternatively, body surface area (BSA) and areas affected by vitiligo should be documented, or patients could use personal devices to take photographs if medical photography is not available or not practical.

R22 Only consider PUVA or PUVAsol in adults with vitiligo if treatment with NB-UVB is unavailable or has been ineffective.

R23 Consider excimer laser or light in people with localized vitiligo in combination with topical calcineurin inhibitors (more evidence for tacrolimus). Prior to treatment, advise patients that there is a theoretical increased risk of skin cancer with this combination of treatment. This treatment is not widely available on the NHS, but is available in a limited number of centres with a specialist interest.

R24 Consider CO2 laser in combination with 5-fluorouracil in adults with nonsegmental vitiligo on the hands and feet if other treatments have been ineffective (apply 5-fluorouracil once daily for 7 days per month for 5 months; CO2 laser treatments once a month for 5 months). This treatment is not widely available on the NHS, but can be accessed in a limited number of centres with a specialist interest.

There is insufficient evidence to recommend combination treatment of potent or very potent topical steroid with NB-UVB plus CO2 laser for people with vitiligo.

#### **European Dermatology Forum**

The European Dermatology Forum (2013) published consensus guidelines on the management of vitiligo. The guidelines stated that oral psoralens with ultraviolet A are commonly used in adults with generalized vitiligo as second-line treatment. The guidelines also stated 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.

#### European Task Force on Atopic Dermatitis/EADV Eczema Task Force

In 2020, the ETFAD/EADV Eczema Task Force updated its position paper to indicated that beside natural sunlight, phototherapy for atopic dermatitis (AD) may be useful with different artificial light sources: broad-spectrum UVB (280–315 nm), narrowband UVB (311–313 nm), broadband UVA (UVA) (315–400 nm), UVA1 (340–400 nm), UVA1 cold light (with seawater baths) plus UVB (balneophototherapy) and psoralen plus UVA. UVA1 phototherapy can be applied as moderate-dose (50 J/cm2) and low-dose (10 J/cm<sup>2</sup>) regimen, whereas high dose (130 J/cm<sup>2</sup>) is not recommended anymore for AD treatment. Using 308-nm monochromatic excimer light allows the treatment of only limited areas. Though blue light has been used for AD in an uncontrolled trial, treatment with longer wavelengths has not been carefully studied for AD and is therefore not recommended.

#### Vitiligo Task Force

The international Vitiligo Task Force published a 2023 consensus statement on the management of vitiligo. First-line recommendations include topical corticosteroids or immunomodulators. The task force does not recommend oral psoralen plus ultraviolet A (PUVA), but recommends topical PUVA as an option for localized lesions. The statement includes recommendations for the use of excimer devices in patients with localized disease.

#### Vitiligo Working Group

The Vitiligo Working Group (now the Global Vitiligo Foundation) 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. The Working Group indicated that psoralens with ultraviolet A (PUVA) has largely been replaced by narrowband ultraviolet B, but that "PUVA may be considered in patients with darker Fitzpatrick skin phototypes or those with treatment-resistant vitiligo (level I evidence)." The Working Group also stated that "Targeted phototherapy (excimer lasers and excimer lamps) can be considered when <10% of body surface area is affected (level II evidence)."

#### Government Regulations National:

Treatment of Psoriasis. Pub 100-3; Section 250.1. Version 1

#### Indications and Limitations of Coverage

Psoriasis is a chronic skin disease, for which several conventional methods of treatment have been recognized as covered. These include topical application of steroids or other drugs; ultraviolet light (actinotherapy); and coal tar alone or in combination with ultraviolet B light (Goeckerman treatment).

A newer treatment for psoriasis uses a psoralen derivative drug in combination with ultraviolet A light, known as PUVA. PUVA therapy is covered for treatment of intractable, disabling psoriasis, but only after the psoriasis has not responded to more conventional treatment. The Medicare Administrative Contractor should document this before paying for PUVA therapy.

In addition, reimbursement for PUVA therapy should be limited to amounts paid for other types of photochemotherapy; ordinarily, payment should not be allowed for more than 30 days of treatment, unless improvement is documented.

### Local:

There is no local coverage determination (LCD).

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

## **Related Policies**

N/A

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through April 1, 2024, the date the research was completed.

## Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/1/14	8/19/14	8/22/14	Joint policy established
1/1/16	10/13/15	10/27/15	Routine maintenance
1/1/17	10/11/16	10/11/16	<ul> <li>Routine maintenance</li> <li>JUMP criteria is more specific than BCBSA policy – we address age, systemic and topic treatment and include restrictions as to area of body being treated</li> </ul>
1/1/18	10/19/17	10/19/17	<ul> <li>Routine maintenance</li> </ul>
1/1/19	10/16/18	10/16/18	Routine maintenance
1/1/20	10/15/19		<ul> <li>Routine maintenance</li> <li>Title changed from "Light therapy for vitiligo" to "Light and Laser therapy for vitiligo and atopic dermatitis"</li> <li>Excimer laser for atopic dermatitis /eczema added – INV</li> </ul>
9/1/20	6/16/20		Routine maintenance
9/1/21	6/15/21		Routine maintenance Added HCPCS codes E0691-E0694 to established. References updated – policy statement updated to include: Home ultraviolet B (UVB) light therapy is considered established for any one of the following diagnoses: Atopic dermatitis, when topical treatment alone has failed; or Pityriasis lichenoides; or Pruritus of hepatic disease; or Pruritus of renal failure; or Psoriasis, when topical treatment alone has failed; or Cutaneous T-cell lymphoma including mycosis fungoides and Sézary syndrome.

		Added inclusion/exclusion to include statement Home ultraviolet B (UVB) light therapy. Added section on HOME ULTRAVIOLET B (UVB) LIGHT THERAPY under rationale.
9/1/22	6/21/22	Routine maintenance
9/1/23	6/13/23	<ul><li>Routine maintenance</li><li>Vendor: N/A (ky)</li></ul>
9/1/24	6/11/24	<ul> <li>Routine maintenance</li> <li>Vendor: Codes E0691, E0692, E0693, and E0694 managed by Northwood. (ky)</li> </ul>

Next Review Date: 2<sup>nd</sup> Qtr, 2025

## BLUE CARE NETWORK BENEFIT COVERAGE POLICY: LIGHT AND LASER THERAPY FOR VITILIGO AND ATOPIC DERMATITIS

I. Coverage Determination:

Commercial HMO (includes Self- Funded groups unless otherwise specified)	Covered, policy criteria apply
BCNA (Medicare Advantage)	Refer to the Medicare information under the
	Government Regulations section of this policy.
BCN65 (Medicare	Coinsurance covered if primary Medicare covers
Complementary)	the service.

#### II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.