2.01.86	Targeted Phototherapy and Psoralen with Ultraviolet A for Vitiligo		
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Section:	2.0 Medicine	**Page:**	Page 1 of 11

Policy Statement

Psoralen plus ultraviolet A (PUVA) may be considered **medically necessary** for the treatment of vitiligo that is not responsive to other forms of conservative therapy (e.g., topical corticosteroids, coal/tar preparations, ultraviolet light).

Targeted phototherapy (i.e., laser light devices) is considered **investigational** for the treatment of vitiligo.

Policy Guidelines

During psoralen plus ultraviolet A (PUVA) therapy, the patient needs to be assessed on a regular basis to determine the effectiveness of the 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 the disease. Therefore, psoralen plus ultraviolet A is generally not recommended for home therapy.

Coding

There is no specific CPT code for laser therapy for vitiligo. It should currently be reported using the following unlisted CPT code:

- **96999**: Unlisted special dermatological service or procedure

The following CPT codes might be used for laser therapy for psoriasis

- **96920**: Laser treatment for inflammatory skin disease (psoriasis); total area less than 250 sq. cm
- **96921**: Laser treatment for inflammatory skin disease (psoriasis); 250 sq. cm to 500 sq. cm
- **96922**: Laser treatment for inflammatory skin disease (psoriasis); over 500 sq. cm

Description

Vitiligo is an idiopathic skin disorder that causes depigmentation of sections of skin, most commonly on the extremities. Topical corticosteroids, 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, ultraviolet B, light box therapy and psoralen plus ultraviolet A (PUVA). Targeted phototherapy is also being evaluated.

Related Policies

- Dermatologic Applications of Photodynamic Therapy
- Light Therapy for Psoriasis

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

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

The oral psoralen products Oxsoralen-Ultra® (methoxsalen soft gelatin capsules) and 8-MOP® (methoxsalen hard gelatin capsules) have been approved by the FDA; both are made by Valeant Pharmaceuticals. Topical psoralen products have also received FDA approval (e.g., Oxsoralen® [Valeant]).

Rationale

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 an autoimmune disease. The most common form of the disorder is nonsegmental 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.

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_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 narrowband ultraviolet B 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; they 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 lightbox, 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 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.

Literature Review
Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and 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 a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and 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.

Targeted Phototherapy
Clinical Context and Therapy Purpose
The purpose of targeted phototherapy in patients who have vitiligo is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of targeted phototherapy improve the net health outcome in those with vitiligo?

The following PICOs were used to select literature to inform this review.

Patients
The relevant population of interest are individuals with vitiligo.

Interventions
The therapy being considered is 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.

Targeted phototherapy is administered by skin specialists or dermatologists in an outpatient setting.

Comparators
The following therapies are currently being used to treat vitiligo: topical medications and narrowband ultraviolet B (NB-UVB) light box therapy. The most appropriate comparison for targeted phototherapy is NB-UVB, which is considered a standard treatment for active and/or widespread vitiligo based on efficacy and safety.

Outcomes
The general outcomes of interest are a change in disease status. Progression of vitiligo can lead to extreme sensitivity to sunlight, skin cancer, iritis, and hearing loss. QOL is another relevant outcome (e.g., emotional distress as skin discoloration progresses).

The application of targeted phototherapy can require multiple weekly treatments over several weeks. In time, treatment results can fade or disappear.

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).[1] 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 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.[2] 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 broadband UVB fluorescent lamp. Due to heterogeneity across studies, 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.[3] 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.; five were from Asia and three of those five are available only in Chinese. Three trials compared the excimer laser with an excimer lamp, and four 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),[4] did not report repigmentation rates, providing instead, the proportion of patients with various types of repigmentation (perifollicular, marginal, diffuse, or combined). Repigmentation rates at 75% and 100% level did not differ significantly between groups treated with the excimer laser vs NB-UVB. Reviewers conducted a meta-analysis of the two 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 (RR=1.39; 95% CI, 1.05 to 1.85). Two of the four 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
Zhang et al (2017) published an RCT evaluating the use of the 308-nm targeted laser with and without Yiqiqubai granule for the treatment of vitiligo.[5] Yiqiqubai granule is a therapy in traditional Chinese medicine, which is believed to activate blood circulation. The trial had 3 arms: 75 patients received twice-daily oral Yiqiqubai alone, 78 received weekly laser treatments alone, and 80 received both twice-daily oral Yiqiqubai and weekly laser treatments. All groups received treatment for six months. Two dermatologists not involved in the treatment assessed before and after pictures of the patients. QOL measures consisted of embarrassment, dress,

social, and work components, measured on a 5-point scale. Following the 6 months of treatment, the percentages of patients achieving 50% or more repigmentation were 43%, 47%, and 51% for the Yiqiqubai alone, the laser alone, and combined Yiqiqubai and laser groups, respectively ($p<0.05$). While the QOL improved in all three treatment arms, patients in the combined treatment arm reported significantly larger improvements than the arms receiving laser or Yiqiqubai alone.

An RCT comparing a laser with an alternative treatment was published by Nistico et al (2012).[6] This nonblinded RCT included 53 patients with localized and generalized vitiligo. Patients were randomized to 1 of 3 treatments for 12 weeks: (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). All patients in the two excimer laser groups completed treatment; one patient in the control group dropped out. Before and after treatment, 2 independent clinicians rated clinical response; 51% to 75% repigmentation was considered a "good" response and 75% or more repigmentation was considered an "excellent" response. The proportion of patients with a good or excellent response was 11 (55%) of 20 in the laser plus vitamin E group, 14 (70%) of 20 in the laser plus tacrolimus plus vitamin E group, and 0% in the control group. The rate of good or excellent responses did not differ significantly between groups that received excimer laser therapy with and without topical treatment ($p=0.36$). Response rates were significantly better in both groups receiving laser treatment than in the control group ($p<0.001$).

Retrospective Studies

Fa et al (2017) retrospectively analyzed 979 Chinese patients (3478 lesions) treated with the 308-nm targeted laser for vitiligo.[7] Patients had Fitzpatrick skin phototype III or IV and were followed for two years after the last treatment. Repigmentation was assessed by two 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 ≤16 years) with vitiligo.[8] Twenty-seven 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.

Section Summary: Targeted Phototherapy

A number of RCTs and retrospective analyses have evaluated targeted phototherapy for treating vitiligo. The studies tended to have small sample sizes, and few were designed to isolate the effect of laser therapy. Moreover, studies were heterogeneous (e.g., duration and frequency of therapy sessions, different interventions or combinations of interventions, different comparison interventions). These characteristics made it difficult to pool study findings or to draw conclusions about the efficacy of targeted phototherapy for vitiligo. Two meta-analyses were attempted; however, one 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. Also, studies have suggested a potential for blistering and slight erythema with targeted phototherapy. Larger studies with representative patient populations and standard of care comparators (e.g., NB-UVB) are needed to evaluate the efficacy and adverse outcomes.

Psoralens With Ultraviolet A

Clinical Context and Therapy Purpose

The purpose of PUVA in patients who have vitiligo is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of PUVA improve the net health outcome in those with vitiligo?

The following PICOs were used to select literature to inform this review.

Patients

The relevant population of interest are individuals with vitiligo.

Interventions

The therapy being considered is PUVA.

PUVA is administered by skin specialists or dermatologists in an outpatient setting.

Comparators

The following therapies are currently being used to treat vitiligo: topical medications and NB-UVB light box therapy. The most appropriate comparison for PUVA is NB-UVB, which is considered a standard treatment for active and/or widespread vitiligo based on efficacy and safety.

Outcomes

The general outcomes of interest are a change in disease status. Progression of vitiligo can lead to extreme sensitivity to sunlight, skin cancer, iritis, and hearing loss. QOL is also a relevant outcome (e.g., emotional distress as skin discoloration progresses).

The application of PUVA can require multiple weekly treatments for up to 6 to 12 months.

Systematic Reviews

Bae et al (2017) published a systematic review and meta-analysis on the use of phototherapy for the treatment of vitiligo.[9] 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 1. Adverse events were not discussed.

Table 1. Response Rates to NB-UVB and PUVA in the Treatment of Vitiligo by Treatment Duration

Treatment	Duration, mo	≥50% Repigmentation (95% CI), %	≥75% Repigmentation (95% CI), %
NV-UVB	6	37.4 (27.1 to 47.8)	19.2 (11.4 to 27.0)
NV-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).[9]
CI: confidence interval; NV-UVB: narrowband ultraviolet B; PUVA: psoralens with ultraviolet A.

The Cochrane review by Whitton et al (2015), which assessed trials on treatments for vitiligo (discussed in the previous section), identified 12 RCTs evaluating PUVA.[2] Four trials assessed oral PUVA alone and eight assessed PUVA in combination with other treatments (e.g., calcipotriol, azathioprine, polypodiumleucotomos, khellin, or surgical treatment). Seven of the eight 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 greater than 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).[10] Pooled analysis of 2 RCTs evaluating oral unsubstituted psoralen plus sunlight for generalized vitiligo (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 (181 patients), also found a significant benefit for active treatment vs 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 ultraviolet A.

Randomized Controlled Trial

Yones et al (2007) published an RCT that used a psoralen formulation available in the U. S.[11] This trial was included in both the Bae et al (2017) and Whitton et al (2015) systematic reviews. The trial enrolled 56 patients in the United Kingdom 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). 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 body surface area 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 patients in the PUVA group had 75% or more improvement in the body surface area affected. Although the authors did not provide p-values in their outcomes table, they stated 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: PUVA

There is evidence from randomized studies, published mainly before 1985, that PUVA is more effective than a placebo for treating vitiligo. 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.

Summary of Evidence

For individuals who have vitiligo who receive targeted phototherapy, the evidence includes systematic reviews of RCTs. The relevant outcomes are a change in disease status, QOL, and treatment-related morbidity. The 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. 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 the effects of the technology on health outcomes.

For individuals who have vitiligo who have not responded to conservative therapy who receive PUVA (photochemotherapy), the evidence includes systematic reviews and RCTs. The relevant outcomes are a change in disease status, QOL, and treatment-related morbidity. 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 narrowband ultraviolet B in meta-analyses, results have shown that patients receiving narrowband ultraviolet B 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 a meaningful improvement in the net health outcome.

Supplemental Information

Practice Guidelines and Position Statements

British Association of Dermatologists et al

In 2008, 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.[12] As of October 2019, an update for this guideline is currently in progress. The guidelines included the following statements (see Table 2).

Table 2. Guidelines on the Diagnosis and Management of Vitiligo

Recommendation	GOE	LOE
PUVA therapy should be considered for the 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 a 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

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

European Dermatology Forum

The European Dermatology Forum (2013) published consensus guidelines on the management of vitiligo.[13] The guidelines stated that oral psoralens with ultraviolet A are commonly used in adults with generalized vitiligo as a 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, not a systematic review of the literature.

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.[14] The Working Group indicated that psoralens with ultraviolet A have 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)."

U.S. Preventive Services Task Force Recommendation

Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in October 2019 did not identify any ongoing or unpublished trials that may influence this review.

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15. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 2.01.86 (December 2019).

Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- History and physical and/or consultation notes including:
  - Reason for PUVA therapy

- Prior treatment(s) and response(s) including duration

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

MN/IE
The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

Type	Code	Description
CPT®	96900	Actinotherapy (ultraviolet light)
	96912	Photochemotherapy; psoralens and ultraviolet A (PUVA)
	96920	Laser treatment for inflammatory skin disease (psoriasis); total area less than 250 sq cm
	96921	Laser treatment for inflammatory skin disease (psoriasis); 250 sq cm to 500 sq cm
	96922	Laser treatment for inflammatory skin disease (psoriasis); over 500 sq cm
	96999	Unlisted special dermatological service or procedure
HCPCS	J8999	Prescription drug, oral, chemotherapeutic, NOS

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
07/31/2015	BCBSA Medical Policy adoption
03/01/2016	Policy revision without position change
02/01/2017	Policy revision without position change
02/01/2018	Policy revision without position change
02/01/2019	Policy title change from Light Therapy for Vitiligo Policy revision without position change
02/01/2020	Annual review. No change to policy statement. Literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.