Clinical Policy Title: Phototherapy and photochemotherapy for skin conditions

Clinical Policy Number: CCP.1169

Effective Date: October 1, 2015
Initial Review Date: May 20, 2015
Most Recent Review Date: June 4, 2019
Next Review Date: May 2020

Related policies:
None.

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas considers the use of phototherapy and photochemotherapy (psoralen ultraviolet A, also known as PUVA) to be clinically proven and, therefore, medically necessary for the following skin conditions after conventional therapies have failed (Mehta, 2016; National Institute for Health and Care Excellence, 2012; Olsen, 2016; Sidbury, 2014; Taieb, 2013):

- Severe refractory atopic dermatitis/eczema.
- Mycosis fungoides/Sézary syndrome (cutaneous T-cell lymphoma).
- Psoriasis.
- Vitiligo.

AmeriHealth Caritas considers the use of phototherapy at home to be investigational and, therefore, not medically necessary.

Limitations:
All other uses of psoralen ultraviolet A are not medically necessary, including, but not limited to, treatment for the following conditions:

- Keratosis follicularis.
- Lichen amyloidosis.
- Lichen myxedematosus.
- Melasma.
- Low skin tolerance for sunlight.

**Alternative covered services:**

Biologic systemic agents, nonbiologic systemic agents, and phototherapy including broadband ultraviolet B and narrowband ultraviolet B.

**Background**

Ultraviolet light — a cause of sunburns, wrinkles, and skin cancer — can be used in a medical setting as therapy for certain hard-to-treat skin problems and other medical conditions. The main forms of ultraviolet light are ultraviolet A and ultraviolet B.

Psoralen ultraviolet A is a topical treatment of disease by exposure to light at a specific portion of the solar spectrum, 320 to 400 nanometers in wavelength. Psoralens are chemicals found in plants that can absorb UV light. Psoralen ultraviolet A treatment for various skin conditions typically involves administration of an oral drug (e.g., methoxypsoralen) followed by exposure to ultraviolet A 45 to 60 minutes later. Other forms of psoralen ultraviolet A include:

- Topical psoralen ultraviolet A, with subsequent UVA exposure.
- Bath psoralen ultraviolet A, which is not approved and rarely used in the United States.
- Paint psoralen ultraviolet A, used locally on palms and plantar surfaces of the feet with 8-methoxypsoralen ointment or lotion applied directly to lesions.
- Soak psoralen ultraviolet A, in which the area is immersed in a basin of water containing 8-methoxypsoralen.

Originally, psoralen ultraviolet A was developed for psoriasis, a relatively common skin disorder. It is also used for conditions such as vitiligo and mycosis fungoides (the most common type of T-cell lymphoma). While mild psoriasis can often be controlled by topical medications, severe cases often require treatments involving ultraviolet A light exposure.

Before initiating psoralen ultraviolet A therapy, other types of treatment should be discussed with the patient. The potential for psoralen ultraviolet A to increase the risk of skin cancer, especially when treating psoriasis, should also be discussed. Persons at elevated risk for skin cancer from psoralen ultraviolet A include children and persons with a genetic predisposition, a history of skin cancer, or a history of at least 150 prior psoralen ultraviolet A treatments.
Types of toxicity to psoralen ultraviolet A include erythema, pruritus, xerosis, irregular pigmentation, and gastrointestinal symptoms. Most toxicity can be avoided by altering or dividing the dose. Whether psoralen ultraviolet A raises the risk of melanoma is controversial. When administered to pregnant women, psoralen ultraviolet A has been associated with a rise in low-weight births, but no increase in congenital anomalies. An expert panel concluded that psoralen ultraviolet A is contraindicated for patients with lupus erythematosus, porphyria, or xeroderma pigmentation (Menter, 2010). Caution should be exercised for patients with skin types I and II who tend to burn easily, with a history of arsenic intake, with a likelihood of requiring cyclosporin or methotrexate with previous ionizing radiation therapy, or with a history of melanoma or nonmelanoma skin cancer (Cole, 2017).

Psoralen ultraviolet A-related guidelines are often specific to a patient’s condition, e.g.:

- A 2014 practice guideline by the American Academy of Dermatology on dermatitis treatment recommended phototherapy as a second-line treatment if emollients, topical steroids, and calcineurin inhibitors have failed, and that phototherapy may be considered for home use if patients are unable to receive the treatment in an office setting (Sidbury, 2014).
- A National Institute for Health and Clinical Excellence (2012) guideline on psoriasis from the suggests offering NB-UVB phototherapy to psoriasis patients whose condition cannot be controlled with topical treatments alone, but recommends not using any type of phototherapy as maintenance therapy. A review of guidelines for psoriasis concludes that NB-UVB is an effective treatment option for psoriasis (Mehta, 2016). A American Academy of Dermatology (Menter, 2011) guideline on psoriasis observes that psoralen ultraviolet A is more effective than NB-UVB for thick lesions, while NB-UVB generally results in shorter remission.
- A 2012 guideline on alopecia areata from the British Association of Dermatologists recommends against psoralen ultraviolet A use due to potentially serious side effects and inadequate evidence of efficacy (Messenger, 2012).
- A 2016 guideline on mycosis fungoides and Sézary syndrome, for which ultraviolet light is often used, suggests a more refined guideline based on patient stage and centers, and in combination with other agents in practice and clinical trials (Olsen, 2016).
- A 2013 guideline recommends psoralen ultraviolet A as a second-line therapy (behind NB-UVB) for vitiligo, along with psoralen ultraviolet A in various combination therapies for the disease (Taieb, 2013).

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.
We conducted searches on May 3, 2019. Search terms were: “phototherapy,” “photochemotherapy,” “PUVA therapy,” “UVA,” “UV-B,” “psoriasis,” “vitiligo,” “eczema,” “mycosis,” and “fungoides.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Psoriasis is the condition most studied for phototherapy outcomes. A systematic review of 29 articles (n = 675) of persons with palmoplantar pustular psoriasis found that phototherapy, ciclosporin, and topical corticosteroids each controlled the disease, with psoralen ultraviolet A having greater efficacy than ultraviolet B therapy (Sevrain, 2014). Another meta-analysis of psoriasis (23 studies, n = 765) also found psoralen ultraviolet A to be more efficacious than non-larger targeted ultraviolet B phototherapy, although both treatments had positive outcomes (Almutawa, 2015). Psoralen ultraviolet A’s superiority to narrowband ultraviolet B was also observed in a 2012 meta-analysis of 29 trials (n = 773) and accomplished these results in fewer sessions (Archier, 2012a).

A 2013 Cochrane review of 13 trials (n = 662) on psoriasis found the psoralen ultraviolet A vs. ultraviolet B comparison to be hampered by heterogenous evidence, and could not make a definitive conclusion on which was more effective (Chen, 2013). Phototherapy is generally found to work better as part of combination treatments, rather than as monotherapy, in psoriasis patients (Bailey, 2012). Another systematic review of 41 trials (n = 2416) found that psoralen ultraviolet A was more effective than narrowband ultraviolet B as a monotherapy, and narrowband ultraviolet B worked better than broadband ultraviolet B and bath psoralen ultraviolet A in treating adults with moderate to severe psoriasis (Almutawa, 2013).

A systematic review of 21 randomized controlled trials (RCTs) including 961 patients determined that narrowband ultraviolet B and ultraviolet A1 phototherapy in moderate to severe dermatitis were helpful, but data on psoralen ultraviolet A use and phototherapy in children are scarce (Perez-Ferriols, 2015). Another systematic review of 19 studies (n = 905) found that ultraviolet A1 and narrowband ultraviolet B were the most effective treatments for reducing signs and symptoms of dermatitis (Garritsen, 2014).
Findings from 19 systematic reviews have determined that narrowband ultraviolet B can be used effectively for chronic atopic eczema, and UVA used for acute eczema (Williams, 2008).

A recent meta-analysis of 38 studies of persons with vitiligo compared narrowband ultraviolet B phototherapy (n = 1,201) to psoralen ultraviolet A phototherapy (n = 227). At six and 12 months of treatment, the ultraviolet B group had more “at least mild” responses (74.2 and 75.0 percent) than did the psoralen ultraviolet A group (51.4 and 61.6 percent). Marked responses were more common in the face and neck (44.2 percent) than in the trunk (26.1) and the extremities (17.3) after six months of ultraviolet B phototherapy (Bae, 2017). A literature review found that combination therapies for vitiligo, compared to monotherapy, were more effective, especially when phototherapy was included (Bacigalupi, 2012).

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

Mycosis fungoides is the most common cutaneous T-cell lymphoma, and conventional therapy is not always effective in treating it. A review of 20 papers documents photodynamic therapy as a promising and well-tolerated option for treating localized lesions, with excellent cosmetic outcomes (Xue, 2017). Psoralen ultraviolet A and narrowband ultraviolet B monotherapy were found to be effective first-line interventions for mycosis fungoides; the effectiveness of psoralen ultraviolet A either as maintenance therapy or combined with drugs as first-line therapy is uncertain, but may be beneficial for relapse and late-stage disease (Dogra, 2015). A Cochrane review of 14 studies (n = 675) was unable to determine relative efficacy between types of mycosis fungoides treatments (Weberschock, 2012).

Risk of cancer from psoralen ultraviolet A was the focus of a systematic review of 41 studies of chronic plaque psoriasis. Risk was elevated for non-melanoma skin cancer for squamous cell carcinomas, even at low exposures, with risk persisting after treatment cessation; for basal cell carcinoma in patients receiving more than 100 psoralen ultraviolet A treatments; and for melanoma in persons receiving more than 200 psoralen ultraviolet A treatments. No skin cancer risk was associated with NB-UVB use (Archier, 2012b).

Psoralen ultraviolet A is usually administered in an outpatient setting, but this treatment is also available for home use. Research has yet to demonstrate the efficacy of home phototherapy, which has been used for years despite lack of a consensus on efficacy (Koek, 2006). Rajpara (2010) found home NB-UVB was as safe, effective, and cost-effective as outpatient treatment, was more convenient, and generated higher satisfaction (Rajpara, 2010). One study of home-based phototherapy found narrowband ultraviolet B to be safer than psoralen ultraviolet A (Lapolla, 2011). Regular skin examinations by a dermatologist should be performed as psoralen ultraviolet A home treatments are conducted. However,
a Cochrane review failed to support or refute home-based phototherapy for non-hemolytic jaundice in infants over 37 weeks gestation (Malwade, 2014). Most recently, a systematic review of 23 articles observed high levels of patient satisfaction, high levels of safety, and mostly positive reports of high quality of life after home phototherapy (Franken, 2016). The issue of whether home phototherapy use is safe and effective remains unresolved.

Psoralen ultraviolet A is used, sometimes effectively, for a variety of skin conditions for which the professional medical literature is limited. For example, in a Cochrane review of 16 studies, 11 of which were randomized controlled trials, psoralen ultraviolet A treatment for cutaneous lichen planus had comparable outcomes to a psoralen ultraviolet A bath and narrowband ultraviolet B (Atzmony, 2016). A review of 14 studies (n = 64) of pediatric patients with pityriasis lichenoides determined that broadband ultraviolet B, narrowband ultraviolet B, and psoralen ultraviolet A had initial clearance rates of 90 percent, 73 percent, and 83 percent, respectively, with recurrence rates of 23.1 percent, 0 percent, and 60 percent, respectively (Maranda, 2016).

Policy updates:

A total of two guidelines/other and five peer-reviewed references were added to, and six peer-reviewed references removed from, this policy in March 2018.

In May 2019, we added three guidelines/others and two peer-reviewed publications to the reference list. The policy ID changed from 16.02.04 to CCP.1169.

References

Professional society guidelines/other:


Peer-reviewed references:


Almutawa F, Alnomair N, Wang Y, Hamzavi I, Lim HW. Systematic review of UV-based therapy for


Centers for Medicare & Medicaid Services National Coverage Determinations:

250.1 Treatment of Psoriasis.

Local Coverage Determinations:

L33918 Laser Treatment for Psoriasis.

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comment</th>
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<tbody>
<tr>
<td>96900</td>
<td>Actinotherapy (ultraviolet light)</td>
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<tr>
<td>96912</td>
<td>Photochemotherapy; psoralens and ultraviolet A (PUVA)</td>
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<tr>
<td>96913</td>
<td>Photochemotherapy (Goeckerman and/or PUVA) for severe photoresponsive</td>
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<td></td>
<td>dermatoses requiring at least 4-8 hours of care under direct supervision of</td>
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<td></td>
<td>the physician (includes application of medication and dressings)</td>
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<thead>
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<tbody>
<tr>
<td>C84.00-C84.09</td>
<td>Mycosis fungoides</td>
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<tr>
<td>C84.10-C84.19</td>
<td>Sezary disease</td>
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<td>H02.731-H02.739</td>
<td>Vitiligo of eyelid and</td>
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<tr>
<td></td>
<td>periocular area</td>
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<td>L40.0-L40.9</td>
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<td>L80</td>
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<th>HCPCS Level II Code</th>
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<td>S8948</td>
<td>Application of a modality (requiring constant provider attendance) to one</td>
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<td>or more areas; low-level laser; each 15 minutes</td>
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