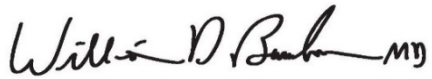


**Prior Authorization Review Panel
MCO Policy Submission**

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: AmeriHealth Caritas Pennsylvania	Submission Date: May 29, 2020
Policy Number: CCP.1303	Effective Date: 3/2018 Revision Date: May 7, 2020
Policy Name: Vitiligo dermatology treatment	
Type of Submission – Check all that apply: <input type="checkbox"/> New Policy <input checked="" type="checkbox"/> Revised Policy* <input type="checkbox"/> Annual Review – No Revisions <input type="checkbox"/> Statewide PDL	
*All revisions to the policy <u>must</u> be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below: Please see revisions below using tracked changes.	
Name of Authorized Individual (Please type or print): William D. Burnham, MD	Signature of Authorized Individual: 

Vitiligo dermatology treatment

Clinical Policy ID: CCP.1303

Recent review date: 5/2020

Next review date: 9/2021

Policy contains: Corticosteroids, excimer laser, photochemotherapy, vitiligo.

AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania's 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 Pennsylvania 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 Pennsylvania's 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 Pennsylvania's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania's clinical policies are not guarantees of payment.

Coverage policy

Treatments for vitiligo are clinically proven and, therefore medically necessary, including the following:

- Monochromatic excimer light laser.
- Narrow-band ultraviolet B phototherapy.
- Topical and oral psoralen photochemotherapy.
- Topical tacrolimus and pimecrolimus (calcineurin inhibitors).
- Topical and systemic corticosteroids (Gawkrodger, 2008; Taieb, 2013; Dillon, 2017).

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Primary care and specialty physician (including surgical) evaluation and management.

All other treatments for vitiligo are considered investigational, and therefore not medically necessary.

Background

Vitiligo is a disorder in which the skin's pigment-making cells (melanocytes) are lost or destroyed. The disease is marked by well-defined white patches on one or multiple parts of the skin, and sometimes head or body hair. Over time, vitiligo affects larger areas of skin. Concerns about appearance and ethnic identity caused by vitiligo

can lead to serious psychological, social, and emotional concerns.

The cause of vitiligo remains unknown. Many persons with vitiligo develop autoimmune thyroid disease or other autoimmune disease. A family trait has been identified in 18% of persons with vitiligo (Gawkrodger, 2008), but questions remain about multiple genes interacting and potential environmental triggers causing the disorder (Genetic and Rare Diseases Information Center, 2018).

The prevalence of vitiligo has been calculated to range between 0.2% in the population at large to 1.8% in a hospital-based population. The highest prevalence occurs in Africans and among females. Prevalence increases gradually with age (Zhang, 2016).

Vitiligo is linked with psoriasis, another dermatologic disorder. In a meta-analysis of 10 studies consisting of psoriasis (n = 120,866) and vitiligo (n = 79,907), there is a significantly increased risk of vitiligo in psoriasis patients, and vice versa (Yen, 2019). Persons with vitiligo also have an elevated risk of thyroid disease and autoimmune thyroid disease, based on a meta-analysis of 37 trials (n = 78,714) (Fan, 2018).

Diagnosis of vitiligo is typically a straightforward process based on physical symptoms, often made by a dermatologist. Several diseases, most notably versicolor, piebaldism and guttate hypomelanosis, can be mistaken for vitiligo, and should be ruled out by clinicians. Wood's light – a hand-held ultraviolet irradiation device - can be used to identify the extent of areas of pigment loss, and also monitor patient response to treatment (Gawkrodger, 2008).

The major treatments for vitiligo are listed below:

- Topical corticosteroids (moderate- to high-strength) are a first-line vitiligo treatment that dampen the cellular immune response. Among the more commonly used topical steroids, which are creams, are mometasone 0.1% or clobetasol 0.05%.
- Topical tacrolimus and pimecrolimus (calcineurin inhibitors), which are also creams, are another first-line vitiligo treatment.
- Ultraviolet A light therapy has cellular immunosuppressive plus mitogenic and melanogenic properties that promote melanocyte proliferation and melanin synthesis. When combined with psoralen, it helps reverse melanocyte and keratinocyte degeneration in and around lesions.
- Ultraviolet B therapy is able to stimulate depigmentation in vitiligo treatment, and is classified as narrowband (NB-UVB, 311–313nm) or broadband (BB-UVB, 280–320nm).
- Monochromatic excimer laser therapy is similar to focused, high-intensity ultraviolet B light therapy using a wavelength of 308nm. An excimer lamp, with an equivalent wavelength, is used in treating vitiligo (Dillon, 2017).

In some cases, various combinations of the above can be used in vitiligo treatment. Certain surgical procedures are also performed, along with Chinese medicine treatments and other therapies.

Findings

The British Association of Dermatology 2008 guideline on vitiligo treatments recommended steroids for no longer than two months; topical tacrolimus (adults only); topical calcineurin inhibitors (tacrolimus and pimecrolimus); phototherapy (ultraviolet B for children, narrow band ultraviolet B and psoralen ultraviolet A for adults); surgery for cosmetically sensitive sites (adults only); and psychological interventions (Gawkrodger, 2008). Recommendations from the European Dermatology Forum guideline confirmed those of the 2008 version, plus

several combination therapies (Taieb, 2013).

An update of vitiligo treatments, consisting of results of 74 articles, presented strong evidence supporting earlier recommendations, plus support for monochromatic excimer light laser therapy (Dillon, 2017).

A Cochrane review of 96 studies (n = 4,512) on efficacy of vitiligo treatment revealed that most studies had fewer than 50 subjects, and the quality of studies was “poor to moderate at best” due to variations in study design and outcome measures, limiting the ability to measure efficacy (Whitton, 2016).

A review of 54 trials on vitiligo treatment found problems in reporting outcomes. A total of 25 outcomes were reported, and just 22% of studies had clearly stated outcome measures. Aside from re-pigmentation, reported in 96% of trials, other outcomes were not often reported, including quality of life (9%), cessation of disease spread (13%), and patient satisfaction (17%) (Eleftheriadou, 2012).

An early analysis of 25 systematic reviews, randomized controlled trials, and observational studies noted several patterns in vitiligo treatment. Topical corticosteroids for adults and children were safe and effective, while the adverse effects of oral corticosteroids outweighed the benefits. Topical primecrolimus was ineffective in reducing lesion size, while no conclusions could be made on topical tacrolimus. Oral psoralen ultraviolet A treatment is effective, but the topical form of the treatment is unlikely to be effective. Narrow band ultraviolet B in adults and children are safe and effective for moderate to severe vitiligo (Matin, 2011).

A systematic review and meta-analysis of six studies (n = 411, 764 lesions) documented no significant differences in efficacy between excimer lamps and excimer laser, or between excimer lamps and narrow band-ultraviolet B therapy for vitiligo. All were considered effective, and adverse effects for each were mild (Lopes, 2016). A related systematic review of seven studies (n = 390) comparing excimer laser and narrow band-ultraviolet B therapy arrived at similar conclusions (Sun, 2015).

A systematic review of seven studies (n = 232) compared narrow band-ultraviolet B treatment for vitiligo with several other therapies. Using degree of re-pigmentation as a measure of effectiveness, there were no significant differences between narrow band and ultraviolet A, psoralens plus ultraviolet A, and 308-nanometer excimer light/laser treatment. Adverse events were slight (Xiao, 2015).

A systematic review and meta-analysis of eight randomized controlled trials (n = 425) determined that combined therapy of excimer laser/light and topical calcineurin inhibitors was superior to excimer laser/light monotherapy. This indicates that calcineurin inhibitors are effective, but authors caution that numbers are small, and studies are heterogeneous (Bae, 2016).

A meta-analysis of 13 studies showed that, compared to placebo, calcineurin inhibitors was significantly more effective on vitiligo for lesion report ($P = .003$) but not for patient report ($P = .157$). Combining phototherapy with calcineurin in the patient report trials showed higher frequency of lesions on the hand and foot, with insignificant effects (Dang, 2016).

A literature review of 24 articles searched for information on efficacy of targeted phototherapy for vitiligo, which the authors defined as application of light energy directly targeted at the lesion through delivery mechanisms such as fiberoptic cables. The term “targeted phototherapy” includes different technologies such as excimer laser (308 nm), intense pulse light systems and non-laser ultraviolet light sources with improved hand-held delivery systems. Each was found to be effective, some in combination with other treatments (Mysore, 2016).

A systematic review/meta-analysis of vitiligo treatment with phototherapy included 35 studies (n = 1,428) patients treated with narrowband ultraviolet-B or psoralen ultraviolet-A. At three months, ultraviolet B patients had at least mild response and marked response in 62.1% and 13.0% of patients, respectively. Ultraviolet-A patients had a rate of 61.6% for at least mild response, similar to the ultraviolet B group (Bae, 2017).

A systematic review of 15 studies discovered that the most commonly used drugs for vitiligo were tacrolimus alone (or combined with clobetasol), pimecrolimus, corticosteroids, and calcipotriol. However, while effectiveness of these treatments were observed, no conclusion on which were most effective could be made (DeMenezes, 2017).

A meta-analysis of seven randomized controlled studies of vitiligo (n = 240, with 413 lesions) found no significant difference in > 50% and > 75% repigmentation between narrow band ultraviolet B with versus without topical calcineurin inhibitor/vitamin D analogs. Lesions located on the face and neck had better results in $\geq 50\%$ repigmentation with combination therapy (Li, 2017).

A systematic review of 39 studies (n = 1,624) assessing benefits of adding phototherapy to melanocyte transplant to treat vitiligo was conducted. Phototherapy modalities included narrow band ultraviolet B (nine studies), psoralen ultraviolet A (19 studies), ultraviolet A (one study), monochromatic excimer light (four studies), and active sunlight exposure (nine studies). No significant differences were observed in studies directly comparing phototherapy modalities. Study quality was moderate to poor, and heterogeneity between studies was high, limiting comparisons and conclusions on effectiveness (Lommerts, 2018).

A systematic review/meta-analysis of topical calcineurin inhibitors to treat vitiligo included 46 studies to evaluate efficacy (n = 1,499). For monotherapy, after three months, at least mild and marked response rates were 55.0% and 18.1%; when phototherapy were added, these rates increased to 89.5% and 47.5%. Both sets of results led authors to state that either monotherapy or combination therapy should be encouraged (Lee, 2019).

A systematic review of 19 studies (n = 814) of combination treatment for vitiligo revealed narrowband ultraviolet B with tacrolimus is better than without tacrolimus in inducing >75% repigmentation ($P = .02$). Tacrolimus and steroids had similar ability to achieve >75% repigmentation ($P = .98$). Finally, the ability of tacrolimus with or without fractional laser to cause >75% is not significantly different at $P = .10$ (Arora, 2020).

A meta-analysis of 11 studies (n = 509) comparing vitiligo patients treated with calcineurin inhibitors or corticosteroids (both topical) found calcineurin to be less effective for at least 50% repigmentation (risk ratio = 0.72). Similar effectiveness was observed for both groups for 1) at least 75% repigmentation; 2) when corticosteroids were classified as medium-potent and super-potent; and 3) at least 50% and at least 75% repigmentation for pediatric patients (Chang, 2020).

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On February 12, 2020, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “calcineurin inhibitors,” “corticosteroids,” “photochemotherapy,” “steroids,” “vitiligo and psoriasis,” “vitiligo,” and “ultraviolet.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

1/2018: initial review date and clinical policy effective date: 3/2018

5/2020: Seven references added to, five references removed from the policy.