Clinical Policy Title: Vitiligo dermatology treatment

Clinical Policy Number: CCP.1303

Effective Date:	**June 1, 2017**
Initial Review Date:	April 19, 2017
Most Recent Review Date:	May 7, 2019
Next Review Date:	May 2020

Policy contains:

- Corticosteroids.
- Excimer laser.
- Photochemotherapy.
- Vitiligo.

Related policies:

None.

CCP.1169 Phototherapy and photochemotherapy for skin conditions.

ABOUT THIS POLICY: *Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina'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 Select Health of South Carolina 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. Select Health of South Carolina'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. Select Health of South Carolina's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina's clinical policies are not guarantees of payment.*

Coverage policy

Select Health of South Carolina considers the use of treatments for vitiligo to be clinically proven and, therefore, medically necessary for 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:

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

Alternative covered services:

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

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 percent of persons with vitiligo (Gawkrodger, 2008), questions remain about multiple genes interacting and potential environmental triggers (Genetic and Rare Diseases Information Center, 2018).

The prevalence of vitiligo has been calculated to range between 0.2 percent in the population at large to 1.8 percent 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. 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 percent or clobetasol 0.05 percent.

- 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 repigmentation 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.

Searches

Select Health of South Carolina searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality.
- The Centers for Medicare & Medicaid Services.
- Cochrane reviews.

We conducted searches on February 28, 2019. Search terms were: “calcineurin inhibitors,” “corticosteroids,” “photochemotherapy,” “steroids,” “vitiligo,” and psoriasis,” “vitiligo,” and “ultraviolet.”

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

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 earlier version, plus several combinations (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 = 4512) 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, severely 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 percent of studies had clearly stated outcome measures. Aside from re-pigmentation, reported in 96 percent of trials, other outcomes were not often reported, including quality of life (nine percent), cessation of disease spread (13 percent), and patient satisfaction (17 percent) (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 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 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 heterogenous (Bae, 2016).

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 ban-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 of 39 studies n = 1624) assessing benefits of adding phototherapy to melanocyte transplant 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 concusions on effectiveness (Lommerts, 2018).

There are other methods of treating vitiligo which have been the subject of systematic reviews, but have not demonstrated a consistent pattern of efficacy to large patient populations. These include:

- A systematic review and meta-analysis of 15 studies (n = 401) compared treatments (erbium laser, carbon dioxide laser, and fractional carbon dioxide laser) for vitiligo with and without ablation therapy. Results for combination therapy were more effective than monotherapy for ≥ 50 percent repigmentation, ≥ 75 percent repigmentation, and patient satisfaction (King, 2018).

- A systematic review and meta-analysis of six studies (n = 85) of fractional carbon dioxide as an add-on treatment for vitiligo was significantly more effective than conventional treatment for re-pigmentaion ($P = .03$), physician improvement ($P < .001$), < 25 percent re-pigmentation ($P = .002$), and patient satisfaction ($P < .001$). Side effects were minor (Kim, 2018).

- A systematic review and meta-analysis of five studies (n = 513) assessed the effectiveness of narrow ban ultraviolet B treatment for vitiligo, with and without oral Chinese herbal medicine. The combineation was significantly more effective than monotherapy ($P < .00001$). The quality of the five trials was low, and only mild adverse effects were reported (Chen, 2016).

- A systematic review of 165 articles showed that topical vitamin D, used in combination with corticosteroids or photherapy, was moderately to very effective in treating vitiligo (Wat, 2014).

- A systematic review of surgery for children and adults with vitiligo found just four studies that qualified, making it difficult to reach an evidence-based judgement on efficacy and safety (Matin, 2015).

Policy updates:

A total of four guidelines/other and 17 peer-reviewed references were added to, and one guideline/other 23 peer-reviewed references removed from this policy in February 2019.

The clinical policy number was changed from CP#16.02.08 to CCP.1303 in February, 2019.

References

Professional society guidelines/other:

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Centers for Medicare & Medicaid National Coverage Determinations:

No National Coverage Determinations identified as of the writing of this policy.

Local Coverage Determinations:

No Local Coverage Determinations identified as of the writing of this policy.

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.

CPT Code	Description	Comments
96910	Photochemotherapy; tar and ultraviolet B (Goeckerman treatment) or petrolatum and ultraviolet B	
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 dermatological service or procedure (excimer laser)	

ICD-10 Code	Description	Comments
L80.0	Vitiligo	

HCPCS Level II Code	Description	Comments
J0702	Injection, betamethasone acetate 3 mg and betamethasone sodium phosphate 3 mg	
J1020	Injection, methylprednisolone acetate, 20 mg	
J1030	Injection, methylprednisolone acetate, 40 mg	
J1040	Injection, methylprednisolone acetate, 80 mg	
J1094	Injection, dexamethasone acetate, 1 mg	
J1100	Injection, dexamethasone sodium phosphate, 1 mg	
J1700	Injection, hydrocortisone acetate, up to 25 mg	
J1710	Injection, hydrocortisone sodium phosphate, up to 50 mg	
J1720	Injection, hydrocortisone sodium succinate, up to 100 mg	
J2650	Injection, prednisolone acetate, up to 1 ml	
J2920	Injection, methylprednisolone sodium succinate, up to 40 mg	
J2930	Injection, methylprednisolone sodium succinate, up to 125 mg	
J3301	Injection, triamcinolone acetonide, NOS, 18 mg	
J3302	Injection, triamcinolone diacetate, per 5 mg	
J3303	Injection, triamcinolone hexacetinodie, per 5 mg	
J7509	Methylprednisolone, oral per 4 mg	
J7510	Prednisolone, oral, per 5 mg	
J7512	Prednisone, immediate reease or delayed release, oral, 1 mg	
J8540	Dexamethaone, oral 0.25 mg	