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: Keystone First Community Health Choices	**Submission Date**: 5/26/2023
Policy Number: ccp.1303	**Effective Date:** 3/2018 **Revision Date:** May 1, 2023
Policy Name: Excimer laser for vitiligo	

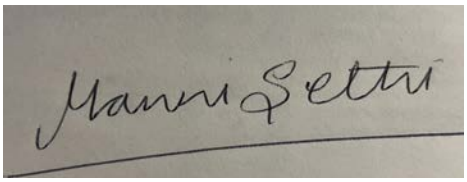
Type of Submission – Check all that apply:

New Policy
x Revised Policy*
Annual Review – No Revisions
Statewide PDL

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

. Reactivation of a previously withdrawn Policy.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Keystone First
Community HealthChoices

Excimer laser for vitiligo

Clinical Policy ID: CCP.1303

Recent review date: 5/2023

Next review date: 9/2024

Policy contains: Excimer laser; vitiligo.

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

Coverage policy

Monochromatic excimer laser light therapy (i.e., wavelength 308 nanometers) is clinically proven and, therefore, may be medically necessary for repigmentation of localized vitiligo, when all of the following criteria are met (Ludmann, 2022; Taieb, 2013).

- Lesions located on the face and neck.
- Failure, intolerance, or contraindication to at least one topical corticosteroid and at least one topical calcineurin inhibitor.
- To avoid side effects associated with total ultraviolet B irradiation or when conventional narrow-band ultraviolet B irradiation is contraindicated.

For any determinations of medical necessity for medications, refer to the applicable state approved pharmacy policy.

Limitations

An initial regimen of monochromatic excimer laser therapy for vitiligo considered medically necessary is generally administered two to three times per week for up to 12 weeks but may be extended if repigmentation is reoccurring (Taieb, 2013).

Monochromatic excimer laser therapy is investigational/not clinically proven and, therefore, not medically necessary if (Taieb, 2013):

- No repigmentation occurs within the first 12 weeks of treatment.
- There is an unsatisfactory response (< 25% repigmentation) after 24 weeks of treatment.
- Treatment duration exceeds 104 weeks.

Alternative covered services

- Primary care and specialty physician (including surgical) evaluation and management.
- Narrow-band ultraviolet B phototherapy.
- Topical and oral psoralen photochemotherapy plus ultraviolet A radiation.
- Topical tacrolimus and pimecrolimus (calcineurin inhibitors).
- Topical and systemic corticosteroids.

Background

Vitiligo is a chronic disorder in which the skin's 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, which can spread over time. Concerns about appearance and ethnic identity caused by vitiligo can lead to serious psychological, social, and emotional concerns (Bergqvist, 2020).

Vitiligo is the most common cause of skin depigmentation. The prevalence of vitiligo ranges between 0.2% in the population at-large to 1.8% in a hospital-based population. The highest prevalence occurs in African Americans and among females. Prevalence increases gradually with age (Zhang, 2016).

The cause of vitiligo remains unknown, but several mechanisms have been implicated in melanocyte destruction. These include genetic, autoimmune responses, oxidative stress, inflammatory mediators, and melanocyte detachment mechanisms. There is consensus on the multifactorial and autoimmune nature of vitiligo, but not on the contribution of specific individual factors (Bergqvist, 2020). Individuals with vitiligo are at risk for developing autoimmune thyroid disease, thyroid cancer, and psoriasis (Fan, 2018; Yen, 2019).

Diagnosis of vitiligo is typically a straightforward process based on physical symptoms, often made by a dermatologist. Several diseases, such as tinea versicolor, progressive macular hypomelanosis, and idiopathic 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 to monitor patient response to treatment (Ahmed jan, 2022).

Vitiligo is classified into segmental or nonsegmental subtypes, each with prognostic and treatment implications. The available treatments are not curative but may halt disease progression and produce repigmentation, often with acceptable cosmesis (Ahmed jan, 2022). The major nonsurgical treatments for vitiligo are listed below, used alone or in combination (Dillon, 2017):

- First-line treatments are topical corticosteroids (moderate- to high-strength) that dampen the cellular immune response (e.g., mometasone 0.1% or clobetasol 0.05%) and topical calcineurin inhibitors (e.g., tacrolimus and pimecrolimus).
- 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 (311–313nm) or broadband (280–320nm).
- Monochromatic excimer laser or lamp therapy is targeted phototherapy, similar to focused, high-intensity ultraviolet B light therapy using a wavelength of 308nm. Several excimer laser systems have received 510(k) premarket approval (U.S. Food and Drug Administration, 2022).

Surgical methods such as tissue grafts, cellular grafts, cultured epidermal suspensions, and hair follicle transplantation may be options for patients with refractory disease. Emerging treatments include prostaglandins, Janus kinase inhibitors, and nonsteroidal systemic immunosuppressives (Bergqvist, 2020).

An initial regimen of monochromatic excimer laser therapy for vitiligo is generally administered two to three times per week for up to 12 weeks. If repigmentation is occurring, monochromatic excimer laser therapy beyond the initial 12 weeks may be needed as long as, and generally for up to 104 continuous weeks (Taieb, 2013).

Findings

The American Academy of Dermatology Association lists excimer laser among available vitiligo treatments. Excimer laser is recommended for small areas, and lamps are recommended for larger areas. Patients typically need several treatments. Excimer laser may be combined with other treatments (Ludmann, 2022).

The European Dermatology Forum recognizes vitiligo as an immune-mediated disease with a silent inflammatory phase. The Forum recommends targeted phototherapies for localized vitiligo, particularly for small lesions of recent onset and childhood vitiligo. These interventions are designed to avoid the side effects from total body irradiation with ultraviolet B and when total body irradiation using conventional narrow band ultraviolet B is contraindicated (e.g., risk for skin cancer, photoaggravated disease, etc.). Limited, low quality evidence suggested excimer laser combined with topical medications may be more effective than laser monotherapy. Contraindications have not been well elucidated (Taieb, 2013).

There was no consensus on the optimum treatment duration. Experts advised targeted phototherapy may be continued as long as repigmentation is occurring up to a maximum period of one or two years. Treatment is typically discontinued if no repigmentation occurs within the first three months of treatment or if there is an unsatisfactory response (< 25% repigmentation) after six months of treatment. Maintenance treatment is not recommended (Taieb, 2013).

In a Cochrane review update of 12 studies of laser phototherapy, most studies had fewer than 50 subjects, and very few included children or participants with segmental vitiligo. The primary outcomes were quality of life (one study), percentage of repigmentation > 75% (six studies), and adverse effects (six studies). The majority of participants achieving > 75% repigmentation were administered combination interventions that included some form of excimer phototherapy. Most adverse effects were short-lived and did not interfere with continued treatment. No studies reported on secondary outcomes of cessation of spread or long-term repigmentation (at two years' follow up). Study quality was "poor to moderate at best" due to variations in study designs and outcome measures, limiting the ability to measure efficacy (Whitton, 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 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 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).

In 2022, we added an American Academy of Dermatology Association (Ludmann, 2022) statement to the policy. We narrowed the focus of the policy to address excimer laser only, as the other treatments for vitiligo are either pharmaceuticals or phototherapy options addressed in clinical policy CCP.1169. We added two systematic reviews and meta-analyses comparing the efficacy of phototherapy as either monotherapy or combination therapy for repigmentation of vitiligo. The results suggest combination therapy using either narrowband-ultraviolet B phototherapy or excimer laser with tacrolimus (Chang, 2021), or narrowband ultraviolet B, psoralen ultraviolet A, or excimer laser with calciprotriol (Hu, 2021), may provide greater clinical improvement than phototherapy alone. Heterogeneous selection criteria and treatment protocols prevent determination of the optimal candidate or treatment administration. Their findings are consistent with the previous policy findings.

In 2023, we deleted older references and added a new study. Results of a meta-analysis of six randomized controlled trials (n = 302) suggest excimer laser combined with platelet-rich plasma may be more efficacious than excimer laser alone when comparing total response rates, no response rates, and adverse effects. However, platelet-rich plasma is not the standard of care for vitiligo, and lack of long-term outcomes data and moderate-to-high bias in the studies call for further study (Chen, 2022).

We modified medical necessity criteria to align with the American Academy of Dermatology Association recommendations, which omit a lower age limit and recommend excimer laser when topical creams or other phototherapy options have failed or are not tolerated (Ludmann, 2022).

References

On May 2, 2023, 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 “”hypopigmentation/therapy” (MeSH), “lasers, excimer” (MeSH), “phototherapy,” “excimer laser,” and “vitiligo.” 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.

Ahmed jan N, Masood S. Vitiligo. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Feb-. https://www.ncbi.nlm.nih.gov/books/NBK559149/. Updated February 16, 2023.

Bae JM, Hong BY, Lee JH, Lee JH, Kim GM. The efficacy of 308-nm excimer laser/light (EL) and topical agent combination therapy versus EL monotherapy for vitiligo: A systematic review and meta-analysis of randomized controlled trials (RCTs). *J Am Acad Dermatol*. 2016;74(5):907-915. Doi: 10.1016/j.jaad.2015.11.044.

Bergqvist C, Ezzedine K. Vitiligo: A review. *Dermatology.* 2020;236(6):571-592. Doi: 10.1159/000506103.

Chang HC, Sung CW. Efficacy of combination therapy of narrowband-ultraviolet b phototherapy or excimer laser with topical tacrolimus for vitiligo: An updated systematic review and meta-analysis. *Photodermatol Photoimmunol Photomed.* 2021;37(1):74-77. Doi: 10.1111/phpp.12593.

Chen J, Yu N, Li H, Tang Y, Zhu H. Meta-analysis of the efficacy of adding platelet-rich plasma to 308-nm excimer laser for patients with vitiligo. *J Int Med Res*. 2022;50(9):3000605221119646. Doi: 10.1177/03000605221119646.

Dillon AB, Sideris A, Hadi A, Elbuluk N. Advances in vitiligo: An update on medical and surgical treatments. *J Clin Aesthet Dermatol*. 2017;10(1):15-28. https://www.ncbi.nlm.nih.gov/pubmed/?term=Dillon+AB+Sideris+A+Hadi+A. Published 2017.

Fan KC, Yang TH, Huang YC. Vitiligo and thyroid disease: A systematic review and meta-analysis. *Eur J Dermatol*. 2018;28(6):750-763. Doi: 10.1684/ejd.2018.3449.

Hu M, Liao K, Lei W, Zhang R, Tu C. The addition of topical calcipotriol to phototherapy enhance the efficacy of treatment in patients with vitiligo: A systematic review and meta-analysis. *Int Immunopharmacol.* 2021;98:107910. Doi: 10.1016/j.intimp.2021.107910.

Lommerts JE, Uitentuis SE, Bekkenk MW, de Rie MA, Wolkerstorfer A. The role of phototherapy in the surgical treatment of vitiligo: A systematic review. *J Eur Acad Dermatol Venereol*. 2018;32(9):1427-1435. Doi: 10.1111/jdv.14950.

Lopes C, Trevisani VF, Melnik T. Efficacy and safety of 308-nm monochromatic excimer lamp versus other phototherapy devices for vitiligo: A systematic review with meta-analysis. *Am J Clin Dermatol*. 2016;17(1):23-32. Doi: 10.1007/s40257-015-0164-2.

Ludmann P. Vitiligo: Diagnosis and treatment. American Academy of Dermatology Association website.https://www.aad.org/public/diseases/a-z/vitiligo-treatment. Published 2022. Ludmann P. Vitiligo: Overview. The American Academy of Dermatology Association. https://www.aad.org/public/diseases/a-z/vitiligo-overview. Last updated June 29, 2022.

Sun Y, Wu Y, Xiao B, et al. Treatment of 308-nm excimer laser on vitiligo: A systemic review of randomized controlled trials. *J Dermatolog Treat*. 2015;26(4):347-353. Doi: 10.3109/09546634.2014.991268.

Taieb A, Alomar A, Bohm M, et al. Guidelines for the management of vitiligo: The European Dermatology Forum consensus. *Br J Dermatol*. 2013;168(1):5-19. Doi: 10.1111/j.1365-2133.2012.11197.x.

U.S Food and Drug Administration. 510(k) Premarket Notification database searched using product code FTC. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm.

Whitton M, Pinart M, Batchelor JM, et al. Evidence-based management of vitiligo: Summary of a Cochrane systematic review. *Br J Dermatol*. 2016;174(5):962-969. Doi: 10.1111/bjd.14356.

Xiao BH, Wu Y, Sun Y, Chen HD, Gao XH. Treatment of vitiligo with NB-UVB: A systematic review. *J Dermatolog Treat*. 2015;26(4):340-346. Doi: 10.3109/09546634.2014.952610.

Yen H, Chi CC. Association between psoriasis and vitiligo: A systematic review and meta-analysis. *Am J Clin Dermatol*. 2019;20(1):31-40. Doi: 10.1007/s40257-018-0394-1.

Zhang Y, Cai Y, Shi M, et al. The prevalence of vitiligo: A meta-analysis. *PloS One*. 2016; 11(9): e0163806. Doi: 10.1371/journal.pone.0163806.

Policy updates

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

5/2019: Policy references updated. Policy number changed to CCP.1303.

5/2020: Policy references updated.

5/2021: Policy references updated.

5/2022: Policy references updated. Coverage modified.

5/2023: Policy references updated. Coverage modified.