Clinical Policy Title: Alopecia areata

Clinical Policy Number: CCP.1134

Effective Date: January 1, 2015
Initial Review Date: September 17, 2014
Most Recent Review Date: August 1, 2018
Next Review Date: August 2019

Related policies:

CCP.1169 Phototherapy and photochemotherapy (PUVA) for skin conditions

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

Coverage policy

Prestige Health Choice considers alopecia areata to be a medical condition, and the use of treatments specified in this policy to be clinically proven and, therefore, medically necessary when the following criteria are met:

- Confirmed diagnosis of alopecia areata by a dermatologist (i.e., clinical evaluation, skin biopsy).
- Treatment for less than 50 percent hair loss:
  - Topical corticosteroids (glucocorticoids).
  - Intralesional corticosteroids (glucocorticoids). Note: If significant hair regrowth is not demonstrated after six months, continued use is not medically necessary.
- For members with more than 50 percent hair loss who have failed a trial of corticosteroid therapy, one of the following:
  - Topical immunotherapy (i.e, squaric acid dibutyl ester and diphenylcyclopropenone).
  - Topical anthralins (dithranol).
- Photochemotherapy: psoralen plus ultraviolet A therapy for extensive alopecia areata, when provided by a physician in a clinic or outpatient setting.
- Systemic corticosteroids (oral prednisone).

**Limitations:**

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website may be accessed at http://ahca.myflorida.com/Medicaid/.

All other treatments for alopecia areata are not medically necessary.

The following treatments are considered cosmetic and/or not medically necessary:

1. Laser therapy, including excimer laser treatment in any setting, is considered cosmetic and not medically necessary. Services that are cosmetic are not covered under most benefit plans.
2. Hair growth stimulants that do not modify disease or affect the underlying condition, including, but not limited to, minoxidil (Rogaine®) and finasteride (Propecia®).
3. All other medications, treatments and products for alopecia areata not specifically noted above in the policy coverage section of this policy (Messenger, 2012).

**Alternative covered services:**

Consultation with a network dermatologist.

**Background**

Alopecia areata is the most frequent cause of inflammation-induced hair loss, affecting an estimated 6.8 million people in the United States, with a calculated lifetime risk of 2.1 percent (National Alopecia Areata Foundation, 2017; Villasante Fricke, 2015). Alopecia areata affects both children and adults and hair of all colors. The majority of cases of the disease manifest between ages 30 and 60. Alopecia areata is associated with an increased overall risk of other autoimmune disorders, including lupus, rheumatoid arthritis, thyroid disease, ulcerative colitis, and vitiligo (Cole, 2007).

Alopecia areata is an autoimmune condition characterized by a T-cell mediated attack on the hair follicle. The inciting antigenic stimulus is unknown. A dense peribulbar lymphocytic infiltrate and reproducible immunologic abnormalities are hallmark features of the condition. The cellular infiltrate primarily consists of activated T-lymphocytes and antigen-presenting Langerhans cells. T-lymphocytes play a critical role in the pathogenesis of disease. The observance of hair regrowth in those with alopecia areata who are treated with cyclosporine, a known inhibitor of T-cell function, further confirms the central role of the T-lymphocytes in the development of the disease.
A meta-analysis of ten studies (n=764) observed that patients with alopecia areata had a lower average serum level of zinc and selenium than healthy controls (both \( P < .00001 \)). No significant difference between patients and controls existed in the levels of serum copper (\( P = 0.81 \)), serum iron (\( P = 0.36 \)), serum ferritin (\( P = 0.37 \)) and serum magnesium (\( P = 0.07 \)) (Jin, 2017).

Psoriasis is a disorder with nearly double the risk of having at least two other autoimmune diseases, with rheumatoid arthritis having the strongest link (Wu, 2012). Psoriasis is a T-cell mediated disorder that shares many immunologic features with alopecia areata. Accordingly, treatments that are effective in psoriasis often prove to be beneficial in alopecia areata. Anthralin, topical and intralesional steroids and cyclosporine are among several therapeutic agents that have efficacy in both disorders. Based on the impressive therapeutic responses seen in those with psoriasis treated with alefacept, a similarly beneficial outcome is tentatively anticipated with treatment of those with alopecia areata. Patients with alopecia areata also have a significantly increased risk of atopic dermatitis (Mohan, 2015).

Alopecia areata can be classified according to its pattern, as follows:
- Reticular — Hair loss is more extensive and the patches coalesce.
- Ophiasis — Hair loss is localized to the sides and lower back of the scalp.
- Sisaipho (ophiasis spelled backwards) — Hair loss spares the sides and back of the head.
- Alopecia totalis — Hair loss is 100 percent on the scalp.
- Alopecia universalis — Complete loss of hair on all hair-bearing areas.

Counseling is an important part of management of alopecia areata. Some patients are profoundly upset by their alopecia and may require psychological support. An individual’s reaction to alopecia will vary depending on his or her own perceptions of body image, self-esteem, coping strategies and personality traits, as well as the individual’s social support network. Commonly, people may feel self-conscious, conspicuous, angry, rejected, embarrassed or different, and they may behave in a shy, cautious, aggressive, retreating, evasive or defensive manner. It is important to mention self-acceptance, particularly in those with long-standing, extensive and persistent alopecia areata.

A number of treatment options are available for alopecia areata:
- No treatment
- Corticosteroids (glucocorticoids)
  - Topical corticosteroids (glucocorticoids)
  - Intralesional corticosteroids
  - Systemic corticosteroids (prednisone)
- Contact immunotherapy
- Photochemotherapy psoralen plus ultraviolet A, Photo therapy
- Minoxidil
- Anthralin (Dithranol, Drithocreme)
- Calcineurin inhibitors
- Biologic drugs
- Other treatments
  - Sulfasalazine
  - Methotrexate
  - Isoprinosine
- Laser therapy
  - Cyclosporine
- Other treatments
  - Aromatherapy
  - Hypnotherapy
  - Tacrolimus
  - Interferon
  - Dapsone
  - Methotrexate
  - Wigs and prostheses (Messenger, 2012).

Spontaneous remission occurs in up to 80 percent of patients with limited patchy alopecia areata within one year (Ito, 2012). Therefore, not all patients of alopecia areata simplex/multiplex need extensive treatments, and "wait and see" is one of the choices for some patients. However, once the hair loss shows a progressive course, it is difficult to manage well and may be recalcitrant to any treatment in some cases.

**Searches**

Prestige Health Choice searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.

We conducted searches on May 31, 2018. Search terms were “alopecia areata,” “hair loss,” and “psoriasis.” 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**
Guidelines for treatment of alopecia areata have been published by the British Association of Dermatologists (Messenger, 2012), National Alopecia Areata Foundation (Olsen, 2004), Japanese Dermatological Association (Tsuboi, 2012), and American Academy of Dermatology (Alkaifah, 2010).

Early reviews of the literature on alopecia areata treatments focused on short-term effects of corticosteroids (topical, intralesional, and systemic), topical sensitizers (diphenylcyclopropenone), psoralen and ultraviolet A phototherapy, minoxidil and dithranol, all of which showed improvements in outcomes (Garg, 2009; Delamere, 2008).

A systematic review of 29 randomized controlled trials examined efficacy of treatments of alopecia areata, including anthralin, antidepressants, biologics, calcineurin inhibitors, corticosteroids (topical and systemic), minoxidil, prostaglandin analogs, sensitizers, and a miscellaneous group of topical and oral drugs with less scientific evidence (aromatherapy, photodynamic therapy, azelaic acid, garlic gel, bexarotene, triiodothyronine, inosiplex, and total glucosides of paeony). Authors concluded the majority of these trials were of moderate quality. Some were effective; topical and oral corticosteroids and the sensitizing agents diphenylcyclopropenone and dinitrochlorobenzene were cited (Hordinsky, 2014). No studies of long-term results of alopecia areata treatments exist (Miteva, 2012).

Other systematic reviews on efficacy of particular treatment for alopecia areata also appear in the peer-reviewed literature:

- A review of 11 studies (n=1986) of patients with alopecia areata revealed consistently poor health-related quality of life scores, comparable to those in patients with the skin diseases psoriasis or atopic dermatitis (Liu, 2016).

- A meta-analysis of 21 studies (n=2530) also documented significantly reduced health-related quality of life scores within the alopecia areata population, across the role-emotional, mental health and vitality domains (P < 0.001). Wearing a wig had a positive impact, while scalp involvement, anxiety and depression had a negative impact on quality of life. Conflicting results were found regarding the association between quality of life and age, sex, marital status and disease duration (Rencz, 2016).

- A review of 28 studies (n=1252) concluded that antidepressants resulted in a reduced burden of dermatological symptoms in conditions including alopecia areata, due to their anti-inflammatory properties (Eskeland, 2017).

- A review on efficacy of platelet rich plasma treatment on non-scarring hair loss included 14 articles addressing androgenic alopecia and four on alopecia areata found low-quality evidence and controversial results, and could not conclude that this therapy was or was not effective (Ayatollahi, 2017).

- A review of janus kinase inhibitors on skin disorders, consisting of 134 articles, found favorable results for psoriasis, but also for alopecia areata (Shreberk-Hassidim, 2017). Another systematic
review of tofacitinib, a janus kinase inhibitor, reflected these advances, but also expressed concern about the safety profile of the drug on diseases including alopecia areata (Kostovic, 2017).

- Perhaps the first systematic review of the efficacy of laser therapy on alopecia areata documented hair regrowth in eight of ten clinical trials, using a 308-nm excimer laser/light in men, women, and children (Darwin, 2018).

Because there is no known cure for alopecia areata, some patients resort to alternative treatments. A review of 13 studies was undertaken, but lack of valid data precluded researchers from making conclusions on efficacy (van den Biggelaar, 2010).

The difficulties encountered in systematic reviews to make conclusions about efficacy of alopecia areata treatment is partly due to the limited number of randomized controlled trials. Only a minority of trials include substantial numbers of subjects, including:

- A trial of 90 subjects given topical minoxidil five percent solution, platelets rich plasma injections, or placebo showed both treatment groups had significantly greater hair growth after three months, and that the platelet rich plasma group had a faster response (El Taieb, 2017).

- A trial of 226 patients aged 18 - 50 years with localized alopecia areata received intralesional triamcinolone acetonide (10 mg/ml) or topical betamethasone valerate cream 0.1 percent twice daily. After 12 weeks, hair re-growth was significantly greater in the intralesional steroid group, 74.3 versus 46.9 percent, \( P < .001 \) (Devi, 2015).

- A trial of 90 subjects (60 with alopecia areata, 30 healthy controls), divided the treatment patients into those given 0.05 percent clobetasol propionate cream, and 20 patients were given petrolatum (placebo) for 12 weeks. Ophiasic pattern and nail involvement were observed more frequently in patients with atopy (\( P < 0.05 \)). Relapse was more frequent in patients with atopy (\( P = 0.002 \)) and nail involvement (\( P = 0.02 \)) (Utak, 2014).

**Policy updates:**

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

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tr>
<td>Liu (2016)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Alopecia areata and Health Related Quality of Life issues</td>
<td>• Systematic review of 11 studies (n=1986) on Health Related Quality of Life of patients with alopecia areata.</td>
</tr>
<tr>
<td></td>
<td>• Subjects consistently demonstrated poor Health Related Quality of Life scores, with greater</td>
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<td>Content, Methods, Recommendations</td>
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<td></td>
<td>• Health Related Quality of Life experienced by patients with alopecia areata is similar to that seen in patients with other chronic skin diseases including atopic dermatitis and psoriasis.</td>
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<tr>
<td>Efficacy of intralesional steroids on alopecia areata</td>
<td>Key points:</td>
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<td>• Randomized controlled trial of 226 subjects age 18-50 with alopecia areata.</td>
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<tr>
<td></td>
<td>• Group A received intralesional triamcinolone acetonide (10 mg/ml) and Group B received topical betamethasone valerate cream 0.1 percent (%) twice daily.</td>
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<tr>
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<td>• Hair re-growth was seen in 84 (74.3%) of the intralesional steroid group and in 53 (46.9%) of the topical betamethasone group ($P &lt; .001$).</td>
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<tr>
<td>Hordinsky (2014)</td>
<td>Key points:</td>
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<tr>
<td>Assessment of treatments for alopecia areata</td>
<td>• Systematic review of 29 trials on efficacy of alopecia areata treatments.</td>
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<tr>
<td></td>
<td>• Review included anthralin, antidepressants, biologics, calcineurin inhibitors, corticosteroids (topical and systemic), minoxidil, prostaglandin analogs, sensitizers, and topical and oral drugs with less scientific evidence (aromatherapy, photodynamic therapy, azelaic acid, garlic gel, bexarotene, triiodothyronine, inosiplex, and total glucosides of paeony).</td>
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<td>• A majority of Randomized Controlled Trials had only moderate quality of evidence.</td>
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<td>• Effective treatments included topical and oral corticosteroids and the sensitizing agents diphenylocyclopropenone and dinitrochlorobenzene.</td>
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<td>Delamere (2008)</td>
<td>Key points:</td>
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<tr>
<td>Short term effects of corticosteroids on alopecia areata</td>
<td>• Cochrane review of 17 studies (n=540), persons with alopecia areata.</td>
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<td>• There were no RCTs on the use of diphencyprone, dinitrochlorobenzene, intralesional corticosteroids or dithranol, which are commonly used for treating alopecia areata.</td>
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<td>• No convincing evidence exists that (widely-prescribed) topical steroids and minoxidil are beneficial in the long-term.</td>
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**References**

**Professional society guidelines/other:**


Peer-reviewed references:


**Centers for Medicare & Medicaid Services National Coverage Determinations:**

No National Coverage Determinations found for treatment of alopecia areata.

**Local Coverage Determinations:**

No Local Coverage Determinations found for treatment of alopecia areata.

**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.
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**Appendix A**

PerformRx
Published April 30, 2018 Last accessed June 11, 2018
No PerformRx policy identified as of the writing of this policy.