Clinical Policy Title: Alopecia areata

Clinical Policy Number: 16.02.03

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Related policies:
None.

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Coverage policy

Select Health of South Carolina 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 (ILC; glucocorticoids).
    **Note:** If significant hair regrowth is not demonstrated after six months, continued use of ILC 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 [SADBE] and diphenylcyclopropenone [DPCP]).
  - Topical anthralins (dithranol).
- Photochemotherapy: psoralen plus UVA therapy (PUVA) for extensive alopecia areata, when provided by a physician in a clinic or outpatient setting.
- Systemic corticosteroids (oral prednisone).

**Limitations:**

All other treatments for alopecia areata are not medically necessary.

A. 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. Hair growth stimulants that are not disease modifying and do not affect the underlying condition, including, but not limited to Minoxidil (Rogaine) and Finasteride (Propecia).
4. All other medications, treatments and products for alopecia areata not specifically noted above in the policy coverage section of this policy.

All other medications, treatments and products for alopecia areata not specifically noted.

**Alternative covered services**

Consultation with a network dermatologist.

**Background**

Alopecia areata is the most frequent cause of inflammation-induced hair loss, affecting an estimated 4.5 million people in the United States. Depending on ethnic background and area of the world, the prevalence of alopecia areata is 0.1 percent to 0.2 percent, with a calculated lifetime risk of 2 percent. Alopecia areata affects both children and adults and hair of all colors. Although the disorder is uncommon in children under 3 years of age, most patients are relatively young — up to 66 percent are younger than 30 years old, and only 20 percent are older than 40 years of age. Alopecia areata is associated with an increased overall risk of other autoimmune disorders (16 percent). For example, it is accompanied by lupus erythematosus in 0.6 percent of patients, vitiligo in 4 percent, and autoimmune thyroid disease in 8 percent to 28 percent.

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.

Activation of T-cells is initiated by interaction of the T-cell receptor with the antigen/major histocompatibility complex on the antigen-presenting cells. Co-stimulatory interactions occur secondarily, including binding of the T-cell CD2 receptor to the antigen-presenting cell ligand lymphocyte function-associated antigen-3 CD58 (LFA-3). Induction of a molecular signaling cascade with resultant T-cell activation and proliferation ensues. Abrogation of this activation may result in diminished or aborted
expression of disease, and thus suggests a potential therapeutic role for alefacept in the treatment of alopecia areata. Alefacept is a bioengineered LFA-3/immunoglobulin fusion protein that binds to the CD2 T-cell receptor and interferes with the ligation of LFA-3. Binding of the immunoglobulin portion of the fusion protein to the FCy receptor on antigen-presenting cells potentiates apoptosis of CD-2 T-cells to thereby reduce the population of activated T-cells.

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 intralosomal 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.

Hair follicles are preserved in alopecia areata and the potential for recovery of hair growth is maintained, even in longstanding disease. One study from Japan reported that spontaneous remission within one year occurred in 80 percent of patients with a small number of circumscribed patches of hair loss. Data from secondary and tertiary referral centers are less favorable, indicating that 34 percent – 50 percent of patients will recover within one year. Almost all will experience more than one episode of the disease, and 14 percent – 25 percent progress to total loss of scalp hair (alopecia totalis) or loss of the entire scalp and body hair (alopecia universalis), from which full recovery is unusual (< 10 percent). Disease severity at presentation is the strongest predictor of long-term outcome. In an Italian study, 191 patients with alopecia areata who presented to a university dermatology clinic between 1983 and 1990 were contacted by telephone in 2005 to give self reports of their clinical status. Six patients with less severe disease at presentation were more likely to report being free of disease at follow up (68 percent with less than 25 percent hair loss initially; 32 percent with 25 percent – 50 percent hair loss initially; 8 percent with more than 50 percent hair loss initially). Patients with more severe disease initially were also more likely to report worsening patterns of alopecia, such as alopecia totalis and alopecia universalis.

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.

An overriding consideration in the management of alopecia areata is that, although the disease may have a serious psychological effect, it has no direct impact on general health that justifies the use of hazardous treatments, particularly those of unproven efficacy. In addition, many patients, although by no means all, experience spontaneous regrowth of hair. However, the psychological effects of alopecia may impact on general health and depend on the individual’s coping strategy when dealing with an altered body image, which can result in higher levels of anxiety and a greater risk of depression leading to social, work-related and personal problems. 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 (SCARED) manner. It is important to mention self-acceptance, particularly in those with long-standing, extensive and persistent alopecia areata.
A number of treatments can induce hair growth in alopecia areata but none has been shown to alter the long-term course of the disease. The high rate of spontaneous remission makes it difficult to assess efficacy, particularly in mild forms of the disease. Some trials have been limited to patients with severe alopecia areata where spontaneous remission is unlikely. However, these patients tend to be resistant to all forms of treatment and the failure of a treatment in this setting does not exclude efficacy in mild alopecia areata. There are numerous case reports and uncontrolled case series claiming response of alopecia areata to diverse treatments. However, few treatments have been subjected to randomized controlled trials (RCTs) and, except for contact immunotherapy, there are few published data on long-term outcomes. A Cochrane review of 17 RCTs in alopecia areata concluded that only one trial (of topical steroid) gave evidence of short-term benefit and none showed long-term benefit. However, the review did not consider contact immunotherapy or intralesional corticosteroid treatment due to the absence of RCTs for these modalities.

**Treatment options:**

- **No treatment:**
  - Leaving alopecia areata untreated is a legitimate option for many patients. Spontaneous remission occurs in up to 80 percent of patients with limited patchy hair loss of short duration (< 1 year). Such patients may be managed by reassurance alone, with advice that regrowth cannot be expected within three months of the development of any individual patch. The prognosis in longstanding extensive alopecia is poor, and a wig may be a better option in such patients than indulging in treatments unlikely to be effective in this group.

- **Corticosteroids (glucocorticoids) treatment:**
  - **Topical corticosteroids (glucocorticoids)** — Very potent topical steroids are widely used to treat alopecia areata but the evidence for their effectiveness is limited. In a RCT of 0.25 percent desoximetasone cream in 70 patients with patchy alopecia areata, more patients treated with the corticosteroid experienced at least minor improvement compared with a placebo, but the result failed to reach statistical significance. In a trial of 0.05 percent clobetasol propionate foam, 34 patients with moderate to severe alopecia areata were randomly assigned to treatment to one side of the scalp or the other. After 12 weeks of treatment, more sites treated with clobetasol had at least 50 percent regrowth of hair (seven of 34 vs. one of 34). Clobetasol propionate applied under an occlusive dressing may be effective in some patients. In a study of 28 patients who had alopecia totalis or alopecia universalis for a mean duration of seven years, 0.05 percent clobetasol propionate ointment applied under an occlusive plastic film on six out of seven nights for six months resulted in long-term hair regrowth in five patients (18 percent). The study initially had patients use the treatment on only one side of the scalp, and no hair regrowth occurred on the untreated side. Folliculitis is a common side effect of treatment with potent topical steroids.
  - **Intralesional corticosteroids** — Depot corticosteroid injected intralesionally stimulates hair regrowth at the site of injection in some patients. Porter and Burton reported that tufts of hair grew in 33 out of 34 sites injected with triamcinolone hexacetonide in 11 patients with alopecia areata, and in 16 of 25 sites injected with triamcinolone acetonide in 17 patients. The effect lasted about nine months. Multiple injections may be given, the main limitation being patient discomfort. Intralesional corticosteroids may also be administered by a needleless device (e.g., Dermojet®; Dermojet UK, Crawley, U.K.). The device should be sterilized between patients. Abell and Munro reported 52 of 84 patients (62 percent) showed regrowth of hair at 12 weeks after three injections of triamcinolone acetonide using the Porto Jet needleless device compared with one of 15 (7 percent) control subjects injected with isotonic saline. The results were less favorable in alopecia totalis than in
localized alopecia. Skin atrophy at the site of injection is a consistent side effect of intralesional steroid therapy, particularly if triamcinolone is used, but this usually resolves after a few months. Repeated injection at the same site or the use of higher concentrations of triamcinolone should be avoided, as this may cause prolonged skin atrophy. There is a risk of cataract and raised intraocular pressure if intralesional corticosteroids are used close to the eye, (e.g., for treating eyebrows).

- Systemic corticosteroids (prednisone) — Long-term daily treatment with oral corticosteroids will produce regrowth of hair in some patients. One small, partly controlled study reported that 30 percent — 47 percent of patients treated with a six-week tapering course of oral prednisolone (starting at 40 mg daily) showed more than 25 percent hair regrowth. Unfortunately, in most patients, continued treatment is needed to maintain hair growth and the response is usually insufficient to justify the risks.

- Contact immunotherapy:
  - Contact immunotherapy was introduced by Rosenberg and Drake in 1976. The contact allergens used in the treatment of alopecia areata include: 1-chloro, 2, 4, dinitrobenzene (DNCB); squaric acid dibutylester (SADBE); and 2, 3- diphenylcyclopropenone (DPCP). DNCB fell from favor when it was found to be mutagenic against Salmonella typhimurium in the Ames test. Neither SADBE nor DPCP are mutagenic. One DPCP precursor is mutagenic and batches should be screened for contaminants by the supplier. DPCP is more stable in solution and is usually the agent of choice. A review of all the published studies of contact immunotherapy concluded that 50 percent – 60 percent of patients achieve a worthwhile response but the range of response rates was very wide (9 percent – 87 percent). Patients with extensive hair loss are less likely to respond. Other reported adverse prognostic features include the presence of nail changes, early onset and a positive family history. In most studies, treatment has been discontinued after six months if no response is obtained. Contact immunotherapy is an unlicensed treatment that uses a nonpharmaceutical-grade agent. Patients should be fully informed about the nature of the treatment, be given an information sheet and provide signed consent.

- Photochemotherapy psoralen plus ultraviolet A, Photo therapy:
  - There are several uncontrolled studies of psoralen plus ultraviolet A (PUVA) treatment for alopecia areata, using all types of PUVA (oral or topical psoralen, local or whole body UVA irradiation) claiming success rates of up to 60 percent – 65 percent. Two retrospective reviews have reported low response rates or suggested the response was no better than the natural course of the disease, although these observations were also uncontrolled. The relapse rate following treatment is high, and continued treatment is usually needed to maintain hair growth, which may lead to an unacceptably high cumulative UVA dose.

- Minoxidil:
  - An early double-blind study reported a significantly greater frequency of hair regrowth in patchy alopecia areata in patients treated with topical 1 percent minoxidil compared with a placebo. Subsequent controlled trials in patients with extensive alopecia areata using 1 percent or 3 percent minoxidil failed to confirm these results. Two of these studies reported a treatment response during an extended but uncontrolled part of the trial. In one study comparing 5 percent and 1 percent minoxidil in extensive alopecia areata, regrowth of hair occurred more frequently in those receiving 5 percent minoxidil but few subjects obtained a cosmetically worthwhile result. Topical minoxidil is ineffective in alopecia totalis or universalis.

- Anthralin (Dithranol, Drithocreme):
  There are a small number of case report series of dithranol (anthralin) or other irritants in the treatment of alopecia areata. The lack of controls makes the response rates difficult to evaluate but
only a small proportion of patients seem to achieve cosmetically worthwhile results. In one open study, 18 percent of patients with extensive alopecia areata achieved cosmetically worthwhile hair regrowth. The published data indicate dithranol needs to be applied sufficiently frequently and in a high enough concentration to produce a brisk irritant reaction in order to be effective. Staining of hair limits its use in fair-haired individuals.

- **Calcineurin inhibitors:**
  - The dual properties of ciclosporin as an immunosuppressive drug and as a hypertrichotic agent make it a logical choice in treating alopecia areata, and this is supported by animal studies. Although there are only a small number of published uncontrolled trials with low patient numbers, the evidence that ciclosporin does stimulate hair regrowth in some patients with alopecia areata is convincing. However, as ciclosporin has to be given orally (it is not active topically), side effects are a major consideration and, in patients with severe alopecia areata, the cosmetically worthwhile response rate is probably too low to justify the risks. No response to treatment was seen in a case series of 11 patients with moderate to severe alopecia areata treated with topical tacrolimus for 24 weeks.

- **Biologic drugs:**
  - The response of alopecia areata to biologic drugs has so far proved disappointing. Evidence to date indicates that antitumor necrosis factor (TNF) biologic drugs are ineffective. There are several reports of alopecia areata occurring in patients receiving anti-TNF biologic drugs for other conditions, and in an open-label study in 17 patients with moderate to severe alopecia areata there was no response to treatment with etanercept. In an RCT in 45 patients with chronic severe alopecia areata, there was no significant response to alefacept, an anti-T-cell biologic, compared with placebo.

- **Other treatments:**
  - Partial evidence of efficacy, either from uncontrolled case series or from single controlled or partially controlled trials, exists for a number of treatments.
  - Sulfasalazine — Several uncontrolled case series have claimed response to sulfasalazine. In an uncontrolled study of 26 patients with severe alopecia areata (> 40 percent hair loss), of whom completed the treatment, six showed complete recovery and a further nine had partial regrowth of hair. Partial or complete relapse occurred in 10 of the 15 responders.
  - Methotrexate — In a retrospective review of 22 patients with alopecia totalis or universalis treated with methotrexate 15 mg – 25 mg per week with or without prednisolone 10 mg – 20 mg daily, 14 achieved complete regrowth of hair, including three of six patients treated with methotrexate alone.
  - Isoprinosine — Isoprinosine (Newport Pharmaceuticals, Swords, Ireland) is an old drug that has immunostimulatory and antiviral properties. Early uncontrolled studies of its use in alopecia areata reported mixed positive and negative results. A more recent RCT in 32 patients with recalcitrant alopecia areata reported complete remission at 12 weeks in 50 percent of patients taking Isoprinosine compared with none in the placebo control group.
  - Laser therapy — An infrared diode laser was used to treat patchy alopecia areata in 16 patients. Complete or partial regrowth was seen in 32 of 34 treated patches, whereas no growth occurred in patches left untreated. In 18 adults, 42 patches of alopecia areata were treated twice weekly for 12 weeks with a 308-nm excimer laser. Regrowth was seen in 17 patches. Similar results (60 percent response rate) were observed in a study of excimer laser treatment in nine children with alopecia areata. Patches left untreated failed to regrow hair.

- **Cyclosporine** — Topical cyclosporine has not proven to be effective in severe alopecia areata because no patient (of 10) showed benefit with application of a 10 percent cyclosporine A (CsA) solution twice per day for 12 months. Another study of 14 patients using a 5 percent solution of
cyclosporine twice per day for four to six months reported vellus growth in three of 14 patients and normal hair growth in three patients with patchy alopecia areata. No regrowth was seen in eight of the patients. Neither study showed systemic absorption of CsA; routine blood examination showed only a transient increase of hepatic enzymes in one patient. Oral cyclosporine was effective in the DEBR model for alopecia areata. All rats had a full pelage by five weeks of treatment with 10 mg/kg/d, five d/wk. for seven weeks. Studies in humans also have proven efficacy with doses of 6 mg/kg/d for three months in six patients. All patients experienced regrowth; three out of six had cosmetically acceptable regrowth. Unfortunately, all patients relapsed within three months of discontinuation of cyclosporine. No evidence indicates that CsA can prevent hair loss during an active episode, because reports have described patients taking CsA who developed alopecia areata while under treatment for unrelated conditions. The mechanism of action of cyclosporine remains unclear. It may act through its immunosuppressive effect, because, in patients who regrew hair, clearance of immune cells from the hair follicles and alteration in the balance of regulatory lymphocytes occurred (i.e., decrease of the CD4/CD8 ratio). Cyclosporine causes hypertrichosis in patients treated for conditions unrelated to hair loss. The mechanism by which cyclosporine stimulates hair growth remains unknown. In conclusion, topical cyclosporine has shown limited efficacy. Although systemic CsA appears to be effective in alopecia areata, the adverse effect profile, the recurrence rate after treatment discontinuation and, thus, the inability to produce long-term remissions makes CsA unattractive for the treatment of alopecia areata.

- Aromatherapy — In a nonrandomized double-blind trial, 19 out of 43 (44 percent) patients receiving aromatherapy showed a treatment response at seven months, compared with six out of 41 (15 percent) patients in the control group.
- Hypnotherapy — In a nonrandomized trial comparing 20 patients (most with severe alopecia areata) treated by hypnotherapy with 21 untreated control patients, the treated group showed a significant reduction in scores for depression and anxiety, but there was no difference between groups in terms of hair regrowth. Despite the negative influence on hair growth, this study highlights the role of non-pharmacological treatments in helping patients with alopecia areata.
- Tacrolimus — Regrowth was shown on the application site of topical tacrolimus in two studies using the DEBR model. Oral tacrolimus was ineffective. No benefit was shown in the use of topical tacrolimus for alopecia areata in a small 2005 study by Price et al. that included 11 patients.
- Interferon — A study of 11 patients with alopecia areata ranging from patchy alopecia areata to alopecia universalis showed no benefit using intralesional interferon alfa-2 (1.5 million international units (IU), three times per wk. for three weeks.).
- Dapsone — Dapsone at 50 mg twice per day was used in a six-month, double-blind, placebo-controlled study. Of patients in the study, 54 percent (7 of 13) withdrew from the dapsone group because of adverse effects, such as malaise. Of the remaining six patients, three experienced generalized growth of terminal hair, compared with four (four of 13) patients in the placebo group, who experienced only sparse patchy regrowth of vellus hair. The authors concluded that although dapsone showed some efficacy, the high incidence of adverse effects rendered it unacceptable. Another study showed a rate of success comparable to the occurrence of spontaneous regrowth reported in the literature.
- Methotrexate — Joly reported 22 patients with longstanding severe alopecia areata who responded well to methotrexate, with or without systemic corticosteroids. Although the results from that study are surprisingly good, a more standardized study involving more patients is needed because other dermatologists have not had such good efficacy with methotrexate.
Wigs and prostheses — Coping with the impact of alopecia areata depends on the individual’s ability to deal with an altered body appearance and their perceptions of themselves. When wearing prostheses, individuals often have an underlying fear of being discovered, particularly when discussions about hair arise from social conversation, as many do not feel at ease disclosing their condition. Wigs, integrated systems, hairpieces, headscarves, hats, false eyelashes and semi permanent make-up can be used as effective ways to cope with alopecia areata. However, choosing to wear a hair prosthetic can be an overwhelming experience due to the variety of different options and suppliers to choose from. Choice can be limited depending on an individual’s financial circumstance, as wigs range in price from $50 to $5,000. Synthetic acrylic wigs are the most affordable option. Monofilament acrylic wigs are constructed to give the appearance of hair growing from the scalp; they are light, look natural and come in a variety of colors, lengths and styles. However, all synthetic wigs become damaged near heat, such as when opening oven doors and using patio heaters, and, if worn daily, will need replacing every three to four months to maintain the appearance of the acrylic fibers in good condition and the illusion of hair. Human hair wigs vary; quality depends on where the hair has been sourced and the construction of the cap; i.e., if the wig is pre-sized or made to measure. Human hair looks very natural and will last longer if kept in good condition, typically one to two years. Manufacturing techniques in wig cap construction give some wigs the ability to stay in place while sleeping, exercising, swimming and showering. However, they are expensive, and careful consideration is required when choosing a supplier, particularly when purchasing online or abroad. The U.K. National Health Service (NHS) policy on entitlement for a prescription for human hair wigs is only available to patients who are allergic to acrylic or who have a skin condition made worse by acrylic.

Advances in the management of alopecia areata:

Spontaneous remission occurs in up to 80 percent of patients with limited patchy alopecia areata within one year. 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. Hair loss is not life-threatening but severely decreases quality of life. There are two widely known guidelines for alopecia areata from the British Association of Dermatologists and the National Alopecia Areata Foundation (USA). These guidelines have been substantial in providing clues for dermatologists, but they need to be updated. Recently, the Japanese Dermatological Association also published a guideline for the management of alopecia areata. This guideline suggests treatments followed by recommendations and evidence levels. Several new treatments are added, such as corticosteroid pulse therapy and antihistamine drugs, in addition to Japanese historical therapies. Although the highly recommended therapies are still contact immunotherapy and local injection of corticosteroid, it may result in improvement of alopecia areata may be improved by use of appropriate treatments decided by age, hair loss type, disease course and desire of the alopecia areata patient.

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’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).
We conducted searches on August 8, 2016. 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**

In summary, the future of hair loss treatment shows great promise, from new medications, such as dutasteride, to advances in cloning and gene therapy. But many of these treatments are years, and maybe decades, away from commercial use. Current treatment methods, including cosmetic products, drugs such as Propecia, and surgical procedures such as follicular unit micrografts are currently available. Various therapeutic agents have been described for the treatment of alopecia areata, but none are curative or preventive. The aim of alopecia areata treatment is to suppress the activity of the disease. The high rate of spontaneous remission and the paucity of randomized, double-blind, placebo-controlled studies make the evidence-based assessment of these therapies difficult.

**Policy updates:**

Added:


2016:

Added new clinical trials and updated reference links.

**Summary of clinical evidence:**

<table>
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<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tr>
<td>Civas E, et al. (2010) Therapy-resistant alopecia areata of the scalp and eyebrows:</td>
<td><strong>Key points:</strong></td>
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<tr>
<td></td>
<td>• Alopecia areata is a common skin disorder of presumed autoimmune etiology, and it usually shows an unpredictable course. Treatment of alopecia areata is challenging.</td>
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<td>• There is very little information on the use of surgical therapies for the treatment of alopecia areata in the medical published work.</td>
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<td>• A 24-year-old male patient was referred to a private hair transplantation clinic owned by one of the authors for the treatment of therapy-resistant alopecia areata affecting both eyebrows. He had quickly lost all body hair</td>
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four years prior, beginning from the scalp. He received psoralen and ultraviolet A (PUVA) therapy for alopecia universalis and all body hair regrew except his eyebrows. Alopecia areata was stable for the 18 months following the last medical treatment he received.

- Because there was no response to various medical therapeutic agents, researchers decided to transplant occipital hairs to the eyebrow area. After the patient understood and accepted all risks, occipital hairs were transplanted to the eyebrows by using the follicular unit extraction technique.
- Postoperatively, the patient did not receive any topical or systemic therapies for alopecia areata. Although 40% hair regrowth was detected in his eyebrows at one year postoperation, this rate was 80% by two years postoperation.
- However, there was resistance to regrowth in the medial eyebrow regions. New eyebrows grew as occipital hairs and required trimming. His satisfaction from the surgical procedure was 90% at the end of the 24th postoperative month. Surgical treatment of diseases like alopecia areata is still controversial. This case report offers an additional contribution to the published work on the surgical methods used in the treatment of stable alopecia areata.

### Shapiro J, et al. (1993)

**Topical diphenylcyclopropenone (DPCP) and minoxidil have been used in the treatment of alopecia areata with variable results.**

**Key points:**

- **Objective:** This study was designed to evaluate the efficacy of DPCP alone or in combination with topical 5% minoxidil for the treatment of chronic severe alopecia areata. The effect of therapy on cutaneous T-cell and Langerhans cell subpopulations and intercellular adhesion molecule-1 (ICAM-1) expression was also examined.
- **Methods:** Fifteen patients with chronic (more than two years), severe (more than 50% scalp involvement) alopecia areata participated in a 24-week trial. Half of the scalp was treated with DPCP once weekly and with either 5% minoxidil solution or a vehicle solution twice daily in a randomized double-blind design. Skin biopsy specimens from each half of the scalp were obtained before therapy and after 12 weeks and 24 weeks of therapy for histologic and immunophenotypic analysis.
- **Results:** Thirteen patients completed the study. Five of 13 patients (38%) showed marked regrowth of coarse terminal hair after 24 weeks of treatment with DPCP. The addition of topical 5% minoxidil did not produce any significant clinical benefit in this 24-week trial. Immunophenotypic analysis showed no differences between responders and nonresponders at baseline. During treatment, Leu-4, Leu-2, Leu-3, and keratinocyte ICAM-1 expression were significantly reduced in biopsy specimens of responders vs. nonresponders.
- **Conclusion:** DPCP treatment showed a 38% success rate in producing cosmetically acceptable regrowth in patients with chronic severe alopecia areata.


**Key points:**

- **Background:** Decades ago, alopecia areata was regarded as a well-known...
example of psychosomatic disease. The poor development of measurement methods and criteria for the classification of psychiatric disorders at that time was probably partly to blame for the lack of methodologic validity of some studies.

- Methods: We studied a random sample of 32 patients with alopecia areata (patchy form). Sociodemographic, dermatologic and psychiatric variables were collected. Psychiatric examination was carried out by standardized interviews — Schedules for Clinical Assessment in Neuropsychiatry (SCAN), International Personality Disorders Examination (IPDE) and Psychological Adjustment to Illness Scale (PAIS) — using the Research Diagnostic Criteria of the International Classification of Diseases, 10th edition, to assess the diagnosis. A descriptive and association study was performed, correlating the patient’s adjustment and adaptation to the illness to various factors (linear regression techniques and analysis of variance).
- Results: Sixty-six percent of patients presented with psychiatric comorbidity, mainly adjustment disorders (F.43.2), generalized anxiety disorders (F.41.1) and depressive episodes (F.32). Overall adaptation to the illness, however, was satisfactory, showing few repercussions in family or social life, work or sexual adjustment. Poor adjustment was associated with a dependent personality (Pearson’s r = 0.66), antisocial personality (r = 0.39), generalized anxiety (P = 0.003) and depression (P = 0.02).
- Conclusions: There is a high psychiatric comorbidity in alopecia areata (anxiety and mood disorders), requiring systematic psychiatric evaluations of these patients. A satisfactory overall adaptation to mild/moderate forms of the disease is the norm, but adaptation and comorbidity in severe forms (totalis, universalis) are unknown. A dermatology/liaison psychiatry setting could improve the management of alopecia areata.

Glossary

Alopecia — Loss of hair as a result of illness, functional disorder or hereditary disposition. The medical term for hair loss.

Alopecia areata (AA) — A disease that causes the body to form antibodies against some hair follicles. It can result from such factors as stress, genetics and the immune system. Alopecia areata causes sudden smooth, circular patches of hair loss.

Alopecia totalis (AT) — A condition that results in no hair on the scalp. It may begin as alopecia areata or some other cause.

Alopecia universalis (AU) — A condition that results in no hair on any part of the body, this includes eyelashes, eyebrows and scalp hair. It may develop as alopecia areata or result from another cause.

Anagen — The growing phase of hair usually lasts between one and seven years.

Anagen effluvium — Loss of hair that is supposed to be in the anagen or growing phase. This is the type of hair loss associated with chemotherapy or radiation treatment.
Androgenetic alopecia — Hair loss resulting from a genetic predisposition to effects of dihydrotestosterone (DHT) on the hair follicles. Also termed female pattern baldness and male pattern baldness, hereditary alopecia, and common baldness.

Catagen — The intermittent stage between the growing (anagen) and resting (telogen) phases of the hair's growth cycle.

Cicatricial (scarring) alopecia — A group of rare disorders that destroy the hair follicle and replace it with scar tissue, thereby causing permanent hair loss. It occurs worldwide in otherwise healthy men and women of all ages.

Diazoxide — A drug that dilates blood vessels by opening potassium channels and also promotes hair growth.

Dihydrotestosterone (DHT) — A male hormone suggested to be the main cause for the miniaturisation of the hair follicle and for hair loss. DHT is formed when the male hormone testosterone interacts with the enzyme 5-alpha reductase.

Dutasteride — A 5-alpha-reductase inhibitor medication by GlaxoSmithKline. Dutasteride inhibits both type-I and type-II 5-alpha reductase.

5-alpha-reductase inhibitors — Prevent the body from converting testosterone to DHT by blocking the action of the enzyme 5-alpha reductase.

Finasteride — The generic name of the brand-name drug Proscar®. Proscar is manufactured by Merck and is US Food and Drug Administration(FDA)-approved for the treatment of benign prostate enlargement; 1 mg tablets of finasteride have been marketed under the brand name Propecia as a treatment for hair loss. It is an antiandrogen that blocks the formation of dihydrotestosterone by inhibiting the enzyme 5 alpha-reductase.

Frontal alopecia — Hair loss at the front of the head.

Medically Necessary- A service or benefit is Medically Necessary if it is compensable under the MA Program and if it meets any one of the following standards:

- The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
- The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- The service or benefit will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.
**Minoxidil** — A prescription medication taken orally for the treatment of high blood pressure and used topically to retard hair loss and/or encourage hair growth. Generic name for Rogaine.

**Nonscarring alopecia** — A broad category of different types of hair loss, including androgenetic alopecia. The hair follicle remains intact, thus increasing the likelihood that hair loss can be reversed.

**Norwood scale** — A scale for the classification of hair loss.

**Patchy hair loss** — Small or large areas of hair loss on the scalp.

**Phototherapy** — Utilizes UVB light, categorized as either wide-band or narrow-band, which refers to the wavelengths included in the UV light source. The Goeckerman regimen combines UVB treatments with coal tar applications.

**Photochemotherapy** — Utilizes UVA in conjunction with a photosensitizer called psoralen (also known as psoralen with ultraviolet A, or PUVA). The photo-sensitizer is a medication that can be applied directly to the skin or taken orally and makes the skin more sensitive to the ultraviolet light. PUVA is usually a second-line treatment, reserved for patients who have failed to improve with conventional therapy. PUVA may be used to treat psoriasis, atopic dermatitis (eczema) and other conditions. Complications of PUVA may include skin damage, premature skin aging, cataracts and increased risk of melanoma and squamous cell carcinoma.

**Polysorbate 80** — An emulsifying agent that has been marketed extensively by private companies as a hair growth promoting agent.

**Propecia** — The brand name for 1 mg dose of finasteride, approved for the prevention and treatment of male pattern baldness.

**Retin-A** — A brand name for a prescription acne medication. Has in some cases shown to be effective against hair loss, particularly when combined with minoxidil; however, can cause extreme scalp irritation that can make hair loss worse.

**Rogaine** — The brand name for minoxidil topical hair growth solution, available over the counter in 2 percent solution and 5 percent extra-strength solution.

**Scarring alopecia** — Patchy hair loss with obvious sign of scalp inflammation.

**Senescent alopecia** — The type of hair loss that naturally occurs with age. During the process of aging, both the duration of hair growth and the diameter of the hair follicle decrease.

**Telogen** — The resting phase of the hair cycle, which usually lasts approximately three months.
Telogen effluvium — The second most common form of hair loss (androgenetic alopecia is the first). A condition that causes an increased number of hairs to enter the telogen or resting phase. The additional shedding usually occurs in response to various stresses, such as emotional trauma, pregnancy, illness, major surgery and certain medications. Telogen effluvium can be delayed (occurring a few months after the stressful incident) or chronic (unresolved).

Telogen loss — Loss of hair during resting phase of hair or natural loss.

Traction alopecia — Hair loss which occurs due to traction placed on hair. Traction alopecia is commonly seen with braids, pony tails and other hairstyles which create traction on the scalp.

Trichotillomania — A type of alopecia caused by the constant pulling and twirling of a specific area of scalp. The hair loss usually improves once the habit is precluded; however, in some severe cases it is permanent.

References

Professional society guidelines/others:


Peer-reviewed references:


**Clinical trials:**

Searched clinicaltrials.gov on August 9, 2016 using terms “alopecia areata,” “hair loss” | Open Studies. 64 studies found, four relevant.


**CMS National Coverage Determinations (NCDs):**

No NCDs found for treatment of alopecia areata.

**Local Coverage Determinations (LCDs):**

No LCDs 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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