Clinical Policy Bulletin:
Alopecia Areata

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Policy

I. Aetna considers the following treatments medically necessary for mild alopecia areata (less than 50% loss of scalp hair):
   A. Anthralin (Dithranol, Drithocreme);
   B. Glucocorticoid (topical, intralesional).

II. Aetna considers the following treatments medically necessary for extensive alopecia areata (greater than 50% loss of scalp hair):
   A. Anthralin (Dithranol, Drithocreme);
   B. Glucocorticoid (oral, topical, intralesional);
   C. Psoralen (oral or topical) photochemotherapy (PUVA).

III. Aetna considers topical immunotherapy (i.e., diphenylcyclopropenone [DPCP/DCP], squaric acid dibutyl ester [SADBE]) medically necessary for extensive alopecia areata (greater than 50% loss of scalp hair) when conventional therapies have failed.

IV. Aetna considers the following treatments experimental and investigational for alopecia areata:
   A. Finasteride (Propecia)
   B. Topical minoxidil (Rogaine).

   Both topical minoxidil and finasteride are hair growth stimulants that do not affect the underlying pathogenesis of this condition and are used mainly for the treatment of androgenetic alopecia (male pattern baldness). Neither has been proven effective in the treatment of alopecia areata, as they do not affect the underlying pathogenesis of this condition.

V. Aetna considers the following therapies experimental and investigational for alopecia areata as their effectiveness has not been established by the peer-reviewed medical literature:
Alopecia areata is a disease characterized by hair cycle dysfunction and the presence of peribulbar and perifollicular mononuclear cell infiltrates. The diagnosis of this condition is made by observation. The majority of patients is under 40 years old and report the rapid onset of one or several defined, usually round, 1 to 4 cm areas of scalp hair loss. A common feature is the presence of “exclamation-mark” hairs that may be present at the margins of the bald patch. “Exclamation-mark” hairs are broken, short hairs that taper proximally. Some patients with alopecia areata also exhibit nail pitting. The disease may affect any hair-bearing area, but most commonly affects the scalp, eyebrows, eyelashes, and beard. Hair loss may be patchy or extensive. In extreme cases, the disease may result in total loss of scalp hair (alopecia totalis) or scalp and body hair (alopecia universalis).
Although the etiology of alopecia areata is unknown, most evidence supports the hypothesis that the disease is immunologically mediated. Circulating autoantibodies and follicular deposits of C3 and IgG have been reported. Alopecia areata usually occurs as an isolated condition, but may occur in conjunction with pernicious anemia, thyroid disease, ulcerative colitis, Addison's disease, vitiligo, lupus erythematosus, and Down syndrome.

Treatment success depends on the age of onset of the disease and the extent of hair loss. The prognosis tends to be worse in more extensive cases (alopecia totalis or universalis), or when alopecia areata begins in early childhood. In all cases, hair regrowth may occur spontaneously without treatment, even after months or years. In both mild and extensive cases of alopecia areata, topical corticosteroids of medium to very high potency are used.

The most common treatment for mild cases of alopecia areata (involving less than 50% loss of scalp hair) is direct intradermal injection of corticosteroids (e.g., cortisone or triamcinolone acetonide) into patches of hair loss. Multiple injections are administered monthly to the skin in and around the bare patches; an average of 4 to 6 monthly injections are usually required for significant improvement. The prognosis for total permanent regrowth in cases with limited involvement is excellent. Topical glucocorticoid therapy may be used alone or in combination with other therapies, such as anthralin or injected glucocorticoids.

Anthralin (Drithocreme, Dithranol) is a synthetic, tar-like substance that has been widely used for psoriasis. Anthralin's effectiveness in inducing hair regrowth may be due to a non-specific immunomodulating effect. It is potentially irritating and may cause redness, itching, and scaling; therefore, it is often applied and then removed 20 to 60 mins later (short-contact therapy).

Therapy for extensive alopecia areata (involving more than 50% loss of scalp hair) may be prolonged and difficult. Systemic corticosteroids are seldom used due to their adverse effects; however, they may be required depending on the severity of the condition and the adequacy of the response to topical therapy. Treatments usually need to be continued until remission of the disease occurs; however, if there is no significant response after 6 months of treatment, oral corticosteroids are unlikely to be effective.

Psoralen phototherapy (psoralen and ultraviolet light A or PUVA) is another immunosuppressant treatment that is used for alopecia areata. The psoralen is administered topically or orally and is followed by 1 or 2 hours with UVA (ultraviolet A); however, between 40 and 80 treatments may be required before hair regrowth occurs. The need for long-term therapy, along with concern about increased risk of photodamage/photoaging and skin cancer, make PUVA therapy less than satisfactory. In addition, its effectiveness has been questioned in the literature. Healy and Rogers (1993) reported on the results of 102 alopecia areata patients treated with PUVA and concluded that the results achieved with PUVA differed little from what would be expected with no treatment. Furthermore, there is a high relapse rate when PUVA treatment is discontinued. Despite these limitations, PUVA is still considered standard practice of care by the American Academy of Dermatology.

Topical immunotherapy has been used in Canada and Europe with reported hair growth rates of 40 to 60% among patients with scalp hair loss of 50 to 99%. Topical immunotherapy with DPCP/DCP and SADBE is offered only at a few centers in the United States due to the investigational status of these drugs for alopecia areata. Initial responses are generally seen after 12 weeks of therapy with cosmetically acceptable results in 24 weeks. If there is no response by the end of 24 weeks, immunotherapy is discontinued. Over the long-term, approximately 1/3 of patients eventually stop responding to therapy.
Topical minoxidil (Rogaine) and oral finasteride (Propecia) are indicated for androgenetic alopecia (male-pattern hair loss); they have not been approved by the Food and Drug Administration (FDA) for treatment of alopecia areata.

Gundogan et al (2004) described the use of the excimer laser in 2 patients with alopecia areata with evidence of hair regrowth and good tolerability. However, these investigators stated that this new means of treatment has yet to be discussed in medical literature. The investigators concluded that large prospective studies are needed to evaluate the potential clinical value of the excimer laser in treating alopecia areata.

Tacrolimus ointment is a steroid-free topical immunomodulator developed for the treatment of atopic dermatitis. By inhibiting T-cell activation and cytokine production, topically applied tacrolimus modulates inflammatory responses in the skin. Many studies have shown that it is effective and well-tolerated for the treatment of atopic dermatitis. Moreover, it has been suggested that tacrolimus ointment may be effective treatment for a variety of other inflammatory skin disorders such as alopecia areata. Price and colleagues (2005) reported their findings on the use of topical tacrolimus for patients with alopecia areata. These researchers found that 11 patients with alopecia areata affecting 10 to 75 % of the scalp with an average duration 6 years had no terminal hair growth in response to tacrolimus ointment 0.1% applied twice-daily for 24 weeks.

In a review on the diagnosis and treatment of iron deficiency and its potential relationship to hair loss, Trost et al (2006) stated that there is insufficient evidence to recommend universal screening for iron deficiency in patients with hair loss. In addition, there is insufficient evidence to recommend giving iron supplementation therapy to patients with hair loss and iron deficiency in the absence of iron deficiency anemia.

Willemsen et al (2006) noted that only limited data exist on the role of psychotherapy in alopecia areata. These investigators sought to document the influence of hypnotherapy on psychological well-being and clinical outcome in patients with alopecia areata. Hypnosis was used in 28 patients with extensive alopecia areata who were refractory to previous conventional treatments. It was added as a complementary treatment or used as the only treatment. In all, 21 patients (9 with alopecia totalis or alopecia universalis and 12 with extensive alopecia areata) were analyzed during a 5-year period. After treatment, all patients had a significantly lower score for anxiety and depression. Scalp hair growth of 75 % to 100 % was seen in 12 patients after 3 to 8 sessions of hypnotherapy. Total growth occurred in 9 of these 12 patients, including 4 patients with alopecia universalis and 2 with ophiasis. In 5 patients, a significant relapse occurred. The authors concluded that hypnotherapy may enhance the mental well-being of patients with alopecia areata and it may improve clinical outcome. However, they noted that this is a preliminary study with a limited number of patients, and a larger randomized controlled trial is need to validate these early findings.

In a phase II, placebo-controlled trial, Price and associates (2008) evaluated the safety and effectiveness of efalizumab in the treatment of moderate-to-severe alopecia areata. A total of 62 patients were enrolled into this study, which consisted of three 12-week periods -- (i) a double-blind treatment period, (ii) an open-label efalizumab treatment period, and (iii) a safety follow-up. There were no statistical differences between treatment groups in percent hair regrowth, quality-of-life measures, or changes in biologic markers of disease severity after 12 or 24 weeks. In both groups, there was an approximately 8 % response rate for hair regrowth (at 12 weeks). Efalizumab was well-tolerated. The authors concluded that a 3- to 6-month trial of efalizumab was not effective in promoting hair regrowth in this small cohort of patients with moderate-to-severe alopecia areata.

In a Cochrane review on interventions for alopecia areata, Delamere and colleagues
(2008) evaluated a range of interventions that included topical photodynamic therapy and topical minoxidil. Overall, none of the interventions showed significant treatment benefit in terms of hair growth when compared with placebo.

In a randomized, multi-center, double-blind, placebo-controlled study, Strober and colleagues (2009) evaluated the effectiveness of alefacept for the treatment of severe alopecia areata. A total of 45 individuals with chronic and severe alopecia areata affecting 50 % to 95 % of the scalp hair and resistant to previous therapies were included in this study. Main outcome measure was improved Severity of Alopecia Tool score over 24 weeks. Subjects receiving alefacept for 12 consecutive weeks demonstrated no statistically significant improvement in alopecia areata when compared with a well-matched placebo-receiving group (p = 0.70). The authors concluded that alefacept is ineffective for the treatment of severe alopecia areata.

Faghihi and associates (2009) noted that latanoprost is an analog of prostaglandin F(2-alpha) that is used to treat glaucoma. Increases in eyelash number, thickness, and pigmentation have been reported as latanoprost side effects. These investigators examined if topical use of this drug can be used as a treatment of alopecia areata of eyebrows and eyelashes or not. In an experimental study, 26 patients with symmetrical eyelash and eyebrow alopecia areata were treated over 4 months with topical latanoprost for one side and the other side was not treated with any drug. The results were compared. Only 1 of the latanoprost-treated cases showed partial hair regrowth on the treated side. The relationship between hair regrowth and latanoprost application was not statistically significant (p = 1) by Fisher test. Based on these findings, topical latanoprost is not effective in the treatment of alopecia areata. The authors stated that more studies with a larger sample size, longer study duration, and higher concentration of medication are needed.

In a 2-year, prospective, non-blinded, non-randomized, controlled study, Coronel-Pérez et al (2010) examined the effectiveness of latanoprost in eyelash alopecia areata. These investigators conducted a survey of 54 subjects with alopecia areata universalis; control group comprised 10 subjects who received injections of 0.5 mg/cm(2) of triamcinolone acetonide (TAC) in their eyebrows and 1 mg/cm(2) of TAC injections in affected scalp. The treatment group included 44 subjects who received the same treatment as the control group in scalp and eyebrows but they also applied a drop of latanoprost 0.005 % (50 microg/ml) ophthalmic solution in their eyelid margins every night. Subjects were reviewed every 3 months for 2 years. A total of 40 subjects finished the study and 4 subjects were lost to follow-up. In the treatment arm of this study, the course was well-tolerated and uncomplicated. Both investigators and patients evaluated the regrowth. The results obtained were: complete regrowth in 17.5 %, moderate regrowth in 27.5 %, slight regrowth in 30 % and without response in 25 %. Moderate and total regrowth constituted a cosmetically acceptable response. The therapy was continuous and the response remained without any side effects. No patients had cosmetically acceptable eyelash regrowth in the control group. The authors concluded that latanoprost may be an effective drug in the treatment of eyelash alopecia areata because it induces acceptable responses (total and moderate) in 45 % of the patients. They stated that a formal, blinded, prospective unilateral controlled study will permit further understanding about this promising therapeutic agent for eyelash alopecia areata.

In a review on alopecia areata, Alkhalifah and co-workers (2010) noted that several reports of multiple biologics, including adalimumab, efalizumab, etanercept, and infliximab failed to show improvement in patients with alopecia areata. Furthermore, these investigators stated that the use of topical calcineurin inhibitors (e.g., pimecrolimus and tacrolimus) in alopecia areata was unsuccessful. In a single study, bexarotene 1 % gel resulted in a 26
% hair regrowth rate; dermal irritation is a common side effect. These researchers stated that the effectiveness of bexarotene needs to be confirmed in randomized, placebo-controlled trials. Capsaicin was previously reported to induce vellus hair regrowth in alopecia areata. More recently, a study showed that topical capsaicin and clobetasol 0.05% are comparable. Moreover, these investigators stated that these findings should be supported by randomized, placebo-controlled trials before capsaicin use is added to the therapeutic armamentarium of alopecia areata. Ustekinumab, a fully human monoclonal antibody to the shared p40 subunit of interleukin-12 and interleukin-23, has been shown to be effective in plaque psoriasis, and studies are ongoing to evaluate its long-term safety and effectiveness. The authors stated that ustekinumab may be tried on patients with alopecia areata in the future. In addition, these researchers noted that the relation between vitamin D levels and the development of alopecia areata, and whether vitamin D supplementation helps in the treatment of alopecia areata represent an attractive area of research, the results of which may prove that vitamin D is a safe and helpful choice in the treatment of alopecia areata.

In a pilot study, Farshi et al (2010) evaluated the safety and effectiveness of azathioprine as a systemic monotherapy for moderate-to-severe alopecia areata. A total of 20 patients (14 men [70 %] and 6 women [30 %]) with minimum 6 months history of alopecia areata were included. The extent of scalp hair regrowth during and after the completion of the 6 months treatment was evaluated by the Severity of Alopecia Tool (the SALT score). The daily drug intake was calculated as 2 mg/kg of body weight. Mean duration of current episode of scalp hair loss was 26.4 (26.4 +/- 17) months. Mean regrowth percentage was 52.3 % (52.3 +/- 38.4). Mean hair loss percentage before treatment was 72.7 % (72.7 +/- 28.3) compared with 33.5 % (33.5 +/- 30.7) after 6 months of azathioprine treatment. This showed a highly significant statistical difference (paired t-test, confidence interval [CI]: 95 %: 21.5 to 54.1). Mean hair loss score (S(0) to S(5)) before treatment was 3.9 (3.9 +/- 1.6) and after 6 months of azathioprine treatment was 1.8 (1.8 +/- 1.3). Assessment showed significant difference from baseline score (sign test, p < 0.0001). No significant statistical difference was observed with respect to gender before and after azathioprine treatment. Treatment with azathioprine as a systemic monotherapy clinically produces relevant improvement in moderate-to-severe alopecia areata. The authors concluded that generally azathioprine is a low-cost and well-tolerated drug and with controlled studies on larger number of patients, long-term safety and effectiveness of this treatment should be investigated.

Cho and colleagues (2010) examined the safety and efficacy of botulinum toxin type A (BTXA) injections for the treatment of patients with alopecia areata of the scalp. A total of 7 patients with alopecia areata received 10 U of BTXA intradermal injections on each site 3 times. Subjects were classified according to the extent of scalp hair loss into Severity of Alopecia Tool subclasses. Two patients had one patch of alopecia areata; the remaining patients had total or universal type alopecia areata. One patient dropped out of the study after experiencing spontaneous recovery from her alopecia areata. One patient reported aggravation of her alopecia areata following BTXA injections. The remaining patients’ alopecia areata did not change after BTXA injections. The authors concluded that these findings suggested that BTXA injection can not be used as an alternative treatment for recalcitrant alopecia areata. Nevertheless, future studies concerning the treatment efficacy of BTXA for mild-to-moderate alopecia areata are needed.

Bayramgürler and colleagues (2011) stated that although narrow-band ultraviolet B (NB UVB) phototherapy is a well-established treatment in many dermatosis, there is little evidence of efficacy of this method for alopecia areata (AA) treatment in the literature. These investigators undertook a retrospective review of the 25 AA patients treated with NB UVB. Intra-muscular triamcinolone acetonide injections per month were used as
concomitant treatment in some patients who did not have any contraindication. Eight patients (32%) received monthly intra-muscular corticosteroid injections. Four (22.2%) and 2 (20%) patients achieved excellent response in extensive patchy hair loss patients and entire scalp hair loss patients, respectively. Four of 6 patients who achieved excellent response also received monthly intra-muscular corticosteroid injections. When patients receiving systemic corticosteroid injections were compared with patients given only NB UVB with respect to the treatment responses, a statistically significant difference was seen in patients who achieved excellent response. Narrow-band UVB is not an effective treatment with only 20% excellent treatment responses in patients with severe AA, most of whom were also treated with systemic corticosteroids.

In a double-blind, randomized pilot clinical trial, Nasiri et al (2012) examined the efficacy of topical triiodothyronine in patients with patchy AA. A total of 10 patients with patchy AA were treated with triiodothyronine and placebo applied twice-daily to either of 2 bilaterally symmetrical patches for 12 weeks. The 2 sides were randomly assigned following simple randomization procedure to one of the two treatment groups. The patients and the investigator were blinded to the content of the tubes. Hair regrowth was evaluated every 4 weeks. Blood samples for measurements of complete blood count along with thyroid function (T3, T4 and TSH) and liver function tests were taken at the baseline and at the end of study. After 12 weeks of treatment, there was no statistically significant difference between the outcome in terms of reduction of the patch size and hair regrowth. No adverse effects were noted. The authors concluded that triiodothyronine in the studied dosage and formulation was safe but not more effective than placebo.

Park et al (2013) examined if the combination therapy of cyclosporine and psoralen plus ultraviolet A (PUVA) could be an effective treatment for severe AA. A total of 41 patients with severe AA were treated with oral cyclosporine and topical PUVA. Cyclosporine was given at an initial daily dose of 200 mg for adult and 100 mg for children for periods of up to 16 weeks. Eight-methoxypsoralen (Methoxsalen) was applied topically 20 minutes prior to ultraviolet A (UVA) exposure, and the patients were irradiated with UVA twice-weekly for 16 weeks. Of the total 41 patients, 2 (7.3%) patients were lost to follow-up, and 1 (2.4%) patient discontinued the treatment due to abdominal discomfort. Six (14.6%) patients were treated for less than 12 weeks. Of remaining 32 patients, 3 (9.4%) showed excellent response, 3 (9.4%) showed good response, 12 (37.5%) showed fair response, and 14 (43.7%) showed poor response. The authors concluded that although limited by its uncontrolled character, this study showed that the combination therapy with cyclosporine and PUVA may be an additional choice for severe and recalcitrant AA.

Staumont-Salle et al (2012) evaluated the long-term outcomes of patients with AA who were treated with methylprednisolone bolus. This study included 60 patients treated between 1995 and 2000. The short-term outcomes were analyzed in 2000. The long-term assessment of 30 patients was performed in 2010 by phone questionnaire. Significant hair regrowth was observed in 10/30 patients at 6 months after the bolus treatment. Half of the plurifocalis AA patients were responders at 6 months, but less than 25% of alopecia totalis (AT) and alopecia universalis (AU) patients responded. Long-term outcomes were assessed after a mean duration of 12.3 years; 8/10 initial responders had mild or no disease, and 14/20 initial non-responders had severe AA. The authors concluded that this study confirmed the low efficiency, both short- and long-term, of this treatment for AT and AU.

Bin Saif et al (2012) examined the safety and effectiveness of oral mega pulse methylprednisolone for patients with severe therapy resistant AA. Patients with AU, AT, or alopecia ophiasis (AO) were assigned to one of the 3 treatment groups: Group A received oral mega pulse methylprednisolone (MP) for 3 consecutive days once every 2 weeks for
24 weeks; Group B received 2 consecutive daily pulses every 3 weeks; and Group C received 3 consecutive daily pulses every 3 weeks. Patients who showed regrowth of 75% or more at 24 or 36 weeks continued their treatment, while intervals were increased gradually. A total of 42 patients were included in this study, and 52.4% of them had atopic diathesis, while 35.7% had autoimmune thyroiditis. At 36 weeks, 12 (28.6%) patients had adequate response, 9 (21.4%) had inadequate response, and 21 (50%) patients had poor response. The response rate showed no statistically significant difference between treatment groups. There were statistically significant differences in age of onset, duration of the disease, and presence of subclinical hypothyroidism between different response groups. At follow-up: 13 (38.2%) patients relapsed; 5 (14.7%) patients developed moderate hair fall; 3 (8.8%) patients developed mild hair fall; 7 (20.1%) patients maintained their hair regrowth; and 6 (17.6%) patients were lost in follow-up. Treatment was relatively well-tolerated among subjects in groups B and C. The authors concluded that oral mega pulse MP use in severe forms of AA has relative effectiveness and tolerance; but with high relapse rate.

In a retrospective case-series study, Droitcourt et al (2012) examined the safety and effectiveness of combination of systemic pulse corticosteroids and methotrexate in the treatment of severe AA. Patients were treated with intravenous 500 mg methylprednisolone per day for 3 consecutive days monthly during 3 months plus methotrexate initiated at the end of the second pulse regimen. These investigators reviewed all case notes of patients who received this regimen between January 1 2007 and December 1 2010. A total of 20 patients were treated. Data on hair regrowth at month 12 were available for all patients; 14 patients were still receiving the treatment on December 1 2010, 2 patients were lost in follow-up, and 4 patients had stopped the treatment. Of the 14 patients who were still receiving the treatment regimen at month 18, 10 (10/20, 50%) had total hair regrowth and 4 (4/20, 20%) had incomplete but satisfactory hair regrowth. The treatment was well-tolerated. The authors concluded that the initial treatment by pulse intravenous corticosteroids may influence the overall response. They stated that this approach should be evaluated in a larger series of patients.

Acikgoz et al (2014) examined the effect of pulse methylprednisolone therapy for the treatment of adult AA. Demographic features of all patients were recorded before the treatment. Patients received methylprednisolone 500 mg intravenously in 3 consecutive days by monthly for 3 months. Patients were followed-up for 3 months. Treatment responses were defined by complete regrowth (100%), significant regrowth (more than 50%) and minimal regrowth (less than 50%). A total of 15 patients enrolled in this study. At the end of the study, 2 patients had significant regrowth and 1 patient had minimal regrowth in multi-focal AA (n = 4); 1 patient had significant regrowth and 1 patient had minimal regrowth in alopecia universalis (n = 8); 3 patients had no regrowth in alopecia totalis (n = 3). The authors concluded that these findings suggested that pulse methylprednisolone therapy might be a therapeutic option for severe multi-focal AA. However, for patients with alopecia totalis or universalis, treatment results were unsatisfactory. These preliminary findings need to be validated by well-designed studies.

Waldmann (2013) noted that interleukin-15 (IL-15) has a pivotal role in life and death of natural killer (NK) and CD8 memory T cells. IL-15 signals through a heterotrimeric receptor involving the common gamma chain (γc) shared with IL-2, IL-4, IL-7, IL-9, and IL-21, IL-2/IL-15 receptor β (IL-15Rβ) shared with IL-2 and a private IL-15Rα subunit. Interferon (IFN)- or CD40 ligand-stimulated dendritic cells coordinately express IL-15 and IL-15Rα. Cell surface IL-15Rα presents IL-15 in trans to cells that express IL-2/IL-15Rβ and γc. IL-15 is being used to treat patients with metastatic malignancy. However, IL-15 is an inflammatory cytokine involved in immunological memory including that to self, thereby playing a role in autoimmune diseases. These insights provided the scientific basis for
clinical strategies directed toward diminishing IL-15 action. Dysregulated IL-15 expression was demonstrated in patients with rheumatoid arthritis, inflammatory bowel disease, psoriasis, celiac disease, and AA. The monoclonal antibody Hu-Mik-β-1 targets the cytokine receptor subunit IL-2/IL-15Rβ (CD122), blocks IL-15 trans-presentation, and is being used in clinical trials in patients with autoimmune diseases. In parallel, clinical trials have been initiated involving the Janus kinase-1/2 (Jak1/2) inhibitor ruxolitinib and Jak2/3 inhibitor tofacitinib to block IL-15 signaling.

In a randomized, double-blind, placebo- and active-controlled, half-head, parallel-group study, Trink et al (2013) evaluated the safety and effectiveness of platelet-rich plasma (PRP) for the treatment of AA. A total of 45 patients with AA were randomized to receive intralosomal injections of PRP, triamcinolone acetonide (TrA) or placebo on one half of their scalp. The other half was not treated. Three treatments were given for each patient, with intervals of 1 month. The end-points were hair regrowth, hair dystrophy as measured by dermoscopy, burning or itching sensation, and cell proliferation as measured by Ki-67 evaluation. Patients were followed for 1 year. Platelet-rich plasma was found to increase hair regrowth significantly and to decrease hair dystrophy and burning or itching sensation compared with TrA or placebo. Ki-67 levels, which served as markers for cell proliferation, were significantly higher with PRP. No side-effects were noted during treatment. The authors concluded that the findings of this pilot study, which was the first to investigate the effects of PRP on AA, suggested that PRP may serve as a safe and effective treatment option in AA, and calls for more extensive controlled studies with this method.

Also, an UpToDate review on “Management of alopecia areata” (Messenger, 2014) states that “Platelet-rich plasma, which contains growth factors that are important for cell proliferation and differentiation and has antiinflammatory properties, may be beneficial in alopecia areata. In a trial in which 45 patients with chronic recurring alopecia areata of at least two years duration were randomly assigned to intralosomal injections of autologous platelet-rich plasma, triamcinolone acetonide, or placebo administered once per month for three months, platelet-rich plasma injection was most effective for inducing hair regrowth. Platelet-rich plasma therapy also was associated with reductions in symptoms of burning or itching in affected areas. Additional studies are necessary to validate the findings of this trial”. Furthermore, the review does not mention the use of IL-15 blockers (e.g., ruxolitinib and tofacitinib) as therapeutic options.

Mehraban and Feily (2014) stated that 308nm xenon-chloride excimer laser, a novel mode of phototherapy, is an ultraviolet B radiation system consisting of a noble gas and halide. The aim of this systematic review was to investigate the literature and summarize all the experiments, clinical trials and case reports on 308-nm excimer laser in dermatological disorders. 308-nm excimer laser has currently a verified efficacy in treating skin conditions such as vitiligo, psoriasis, atopic dermatitis, alopecia areata, allergic rhinitis, folliculitis, granuloma annulare, lichen planus, mycosis fungoides, palmoplantar pustulosis, pityriasis alba, CD30+ lympho proliferative disorder, leukoderma, prurigo nodularis, localized scleroderma and genital lichen sclerosus. The authors concluded that although the 308-nm excimer laser appears to act as a promising treatment modality in dermatology, further large-scale studies should be undertaken in order to fully affirm its safety profile considering the potential risk, however minimal, of malignancy, it may impose.

Hordinsky and Donati (2014) reviewed all randomized controlled trials (RCTs) on the treatment of AA. These investigators performed a search in the biomedical literature database PubMed, and used the terms “alopecia areata treatment” and article type “randomized controlled trials”. Following this algorithm, they reviewed, analyzed, and reported on 29 trials that examined the efficacy of anthralin, anti-depressants, 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 peony). The authors concluded that using the American College of Physicians Guideline grading system, their assessment was that the majority of published RCTs of AA were only of moderate quality. A number of treatments were found to be effective (e.g., topical and oral corticosteroids and the sensitizing agents diphenylcyclopropenone and dinitrochlorobenzene); however, most studies had major limitations that hinder the interpretation of these results.

In a pilot study, Zaher et al (2015) compared the safety and effectiveness of bimatoprost to those of corticosteroid in the treatment of scalp AA. A total of 30 adult patients with patchy AA (S1) were included. Two AA patches were randomly assigned to treatment either by mometasone furoate 0.1 % cream once-daily (area A) or bimatoprost 0.03 % solution twice-daily (area B) for 3 months. Patients were assessed using the SALT scoring system for hair re-growth. All responding AA patches showed significant reduction in their SALT score after therapy. Area B demonstrated significantly better results regarding rapidity of response in weeks, percentage of hair re-growth and side effects compared to area A. The authors concluded that bimatoprost solution represents a therapeutic option for scalp AA. These preliminary findings from a pilot study need to be validated by well-designed studies.

Lux-Battistelli (2015) noted that spontaneous remission occurs in less than 10 % of patients suffering from AA totalis for more than 2 years. The effectiveness of PUVA therapy is controversial due to recurrence of hair loss after cessation. These investigators reported 2 cases presenting with AA totalis and AA universalis. After hair regrowth, relapse of hair loss occurred upon cessation of PUVA and zinc gluconate combination therapy. However, hair regrowth was noted upon the re-introduction of zinc gluconate and sulfur amino acids without PUVA in the first case and with episodic PUVA in the second case. The chronology of events appeared to support the notion that zinc has a significant effect. These findings suggested the possibility of a subgroup of zinc-responsive patients, but the identification of these patients remains difficult. Metallothioneins and zinc transporters regulating the entrance and exit of zinc in cells might play a key role. Combination therapy with immunomodulators may be administered to facilitate enhanced zinc-targeted action. Taking into account the safety profile of zinc, 30 to 40 mg/day of zinc metal may be used during at least 1 year, although these researchers recommend monitoring its serum and hair levels. The authors concluded that studies with a larger number of patients are needed to further investigate the therapeutic effect of zinc.

An UpToDate review on “Management of alopecia areata” (Messenger, 2015) states that “Further study is necessary to determine whether low-dose recombinant IL-2 therapy should have a role in the treatment of alopecia areata …. Improvement in alopecia totalis during treatment with hydroxychloroquine has been documented in two women with refractory alopecia totalis who were treated with a dose of 200 mg twice daily. Additional studies are necessary to confirm the efficacy of this therapy. In our experiences with small numbers of patients, hydroxychloroquine has not been an effective therapy …. A prospective study of 29 adults with alopecia areata involving 40 to 70 % of the scalp suggests that simvastatin/ezetimibe (40 mg/10 mg) may be beneficial for alopecia areata …. A controlled trial is necessary to confirm efficacy of this therapy …. Complete hair regrowth following multiple treatments with a fractional photothermolysis laser has been reported in a patient with alopecia areata refractory to minoxidil and topical and intralesional corticosteroids. However, further studies are necessary before this approach can be routinely recommended …. Evidence for involvement of neuropeptides in the pathogenesis of alopecia areata and a case report in which alopecia areata associated with neuralgiform head pain improved after botulinum toxin A injection suggested that botulinum toxin might be useful for alopecia areata. However, additional data to support a
beneficial effect are lacking... Further studies are necessary to determine whether botulinum toxin may be effective for some patients with alopecia areata.”

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

11900 Injection, intralesional; up to and including seven lesions
11901 more than seven lesions
96912 Photochemotherapy; psoralens and ultraviolet A (PUVA)

CPT codes not covered for indications listed in the CPB:

0232T Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed
36522 Photopheresis, extracorporeal
96567 Photodynamic therapy by external application of light to destroy pre-malignant and/or malignant lesions of the skin and adjacent mucosa (e.g., lip) by activation of photosensitive drug(s) each phototherapy exposure session
96910 Photochemotherapy; tar and ultraviolet B (Goeckerman treatment) or petrolatum and ultraviolet B

CPT codes related to the CPB:

96372 Therapeutic, prophylactic, or diagnostic injection (specify substance or drug), subcutaneous or intramuscular

HCPCS codes not covered for indications listed in the CPB:

J0135 Injection, adalimumab, 20 mg
J0215 Injection, alefecept, 0.5 mg
J0585 Injection, onabotulinumtoxinA, 1 unit
J0586 Injection, AbobotulinumtoxinA, 5 units
J0587 Injection, rimabotulinumtoxinB, 100 units
J1438 Injection, etanercept, 25 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J1745 Injection, infliximab, 10 mg
J7308 Aminolevulinic acid HCL for topical administration, 20%, single unit dosage form (354 mg)
J7335 Capsaicin 8% patch, per 10 square centimeters
J7336 Capsaicin 8% patch, per square centimeter
Allopecia Areata

J7500  Azathioprine, oral 50 mg
J7501  Azathioprine, parenteral, 100 mg
J7502  Cyclosporine, oral 100 mg
J7515  Cyclosporine, oral 25 mg
J7516  Cyclosporine, parenteral 250 mg
J8610  Methotrexate, oral 2.5 mg
J9250  Methotrexate sodium, 5 mg
J9260  Methotrexate sodium, 50 mg
P9020  Platelet rich plasma, each unit
S0138  Finasteride, 5 mg
S0162  Injection, efalizumab, 125 mg

ICD-9 codes covered if selection criteria are met:

704.01  Alopecia areata

ICD-9 codes not covered for indications listed in the CPB:

704.00  Alopecia, unspecified

The above policy is based on the following references:


