INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Alopecia Areata***
-August 2022-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of agents currently utilized for the treatment of alopecia at the Summer 2022 NPTC meeting. This review focused on therapeutic agents commonly used for alopecia areata (AA). It was determined that other subtypes of alopecia lack effective pharmacologic treatments (e.g., female androgenetic alopecia), are cosmetic in nature (e.g., male androgenetic alopecia), affect a relatively low number of patients, or any combination thereof.[1] The following treatments are common in AA management and include intralesional corticosteroid injections, super-high potency topical corticosteroids, topical immunotherapy, oral corticosteroids, and additional systemic agents for treatment refractory disease (e.g., baricitinib, methotrexate, azathioprine, and cyclosporine).[2,3] Following clinical review and analysis, the NPTC **made no changes** to the IHS National Core Formulary.

Discussion:

AA affects roughly 2% of individuals in the United States. Epidemiological data for the American Indian/Alaska Native population are currently lacking.[4] Varying degrees of hair loss are possible with AA and include patchy scalp hair loss in limited disease and complete scalp and/or total body hair loss in extensive disease. While AA does not cause negative sequelae beyond hair loss, psychosocial and emotional impact on patients can be considerable.

AA is a chronic, nonscarring, relapsing-remitting disease. It does not involve an inflammatory component nor does it cause destruction of hair follicles. The pathophysiology of AA involves a premature transition from the anagen/growth phase of the hair cycle to the catagen or telogen phases which results in sudden hair loss in affected follicles. This transition may be caused by loss of immune privilege within the hair follicle and a T cell-mediated attack on cells within the hair bulb.[5]

Treatment selection for patients experiencing AA is driven by the extent of disease upon presentation, patient age, and disease chronicity. Extent/severity of disease can be determined using diagnostic tools, the most common of these is the Severity of Alopecia Tool (SALT). A SALT score is calculated by determining the percentage of the scalp affected by hair loss (e.g., a SALT score of 50 represents 50% total scalp hair loss). It is generally accepted that a SALT score < 50 represents limited disease and a score of ≥ 50 is considered extensive disease.[6] Patient age must also be considered since pediatric patients are unlikely to tolerate intralesional therapy. Treatment recommendations also vary based on disease chronicity at presentation with acute disease defined as a current episode lasting <12 months and chronic disease ≥ 12 months. An estimated 50% of limited AA cases will resolve spontaneously without any treatment. Conversely, extensive disease is much less likely to resolve without therapeutic management.[7]

In general, *limited* disease is treated with local treatments (e.g., intralesional triamcinolone, potent topical corticosteroids, minoxidil, and/or ophthalmic prostaglandin analogues). Group 1/Class I topical corticosteroids such as augmented betamethasone dipropionate, clobetasol propionate 0.05%, and halobetasol propionate 0.05% have better efficacy data than lower potency agents.[2] Recommended treatments for *extensive* disease include topical immunotherapy, intralesional corticosteroids targeting areas of high disease activity, potent topical corticosteroids, oral corticosteroids, and anthralin which is reserved for second-line use.[2,3] Patients experiencing *treatment refractory* AA may receive treatment with systemic treatments including methotrexate, azathioprine, and cyclosporine.[8]

Several AA treatment guidelines are available, all of which consistently note a lack of high-quality evidence for commonly used treatments. However, a recent phase 3 study comparing baricitinib to placebo for the treatment of AA led to the FDA approval of baricitinib for this indication in June 2022. The BRAVE trial utilized a parallel, randomized, double-blind design with two parallel treatment groups receiving either baricitinib 2mg

daily, baricitinib 4mg daily, or placebo randomized 2:3:2 respectively.[9] The primary outcome of this trial was improvement in SALT score from a baseline of 50 or greater to 20 or less at 36 weeks. Statistical significance was achieved for both the 2mg/day and 4mg/day doses with a number needed to treat of 7 and 4, respectively. The trial was sponsored by the manufacturer of baricitinib and included a total of ~1,200 patients. While this study did have notable limitations (e.g., small sample size, industry-sponsored, and short duration), the results were promising and will likely lead to further studies of baricitinib for the management of AA. At present, baricitinib is the only FDA-approved treatment for AA.

Three systematic reviews and meta-analyses evaluating treatment modalities for AA were also discussed. Recommendations stemming from these reviews were based on low quality evidence from multiple studies, a small number of which were randomized or placebo-controlled. Authors for each study acknowledged the weakness of these recommendations and clearly stated that additional high-quality trials are needed with consistently defined treatment outcomes to facilitate future comparison.

Six treatment guidelines from the British Association of Dermatologists [2012], Japanese Dermatologic Association [2017], Italian Society of Dermatology [2019], Australian College of Dermatology [2019], Brazilian Society of Dermatology [2020], and the AA Consensus of Experts study [2020] were also discussed. While each guideline provided similar recommendations for the treatment of AA, there was significant variability among guidelines regarding their place in therapy when considering disease severity, age of the patient, and chronicity of disease.[10]

Findings:

The most common treatments for limited AA include intralesional corticosteroids (triamcinolone acetonide most commonly used), potent topical corticosteroids, minoxidil, and topical prostaglandin analogues. Efficacy data supporting use of these agents are of low quality which led to inconsistent recommendations in AA treatment guidelines. Extensive disease is most often managed with topical immunotherapy, limited use of intralesional corticosteroid injections, potent topical corticosteroids, and oral corticosteroids. Anthralin may be used as second-line treatment for patients experiencing extensive disease. Limited data support the use of methotrexate, azathioprine, and cyclosporine for treatment refractory cases of AA. Baricitinib represents a new treatment approach with more robust efficacy data, but further study is needed to solidify its place in therapy. Of these agents, Group 1/Class I topical corticosteroids, prednisone, and ophthalmic prostaglandin analogues are currently on the IHS National Core Formulary. Considering the overall lack of efficacy data for other AA treatments including triamcinolone acetonide injection, minoxidil, anthralin, and baricitinib, no new agents were recommended for addition to the IHS National Core Formulary for management of AA.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

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