hydrocortisone (Alkindi Sprinkle™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO212

Description

Hydrocortisone (Alkindi Sprinkle) is a an orally administered corticosteroid.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
hydrocortisone (Alkindi Sprinkle)	0.5mg capsules	Adrenocortical insufficiency	10 mg/m^2/day*
	1mg capsules		
	2mg capsules		
	5mg capsules		

*limited to three capsules a day

Initial Evaluation

I. **Hydrocortisone (Alkindi Sprinkle)** may be considered medically necessary when the following criteria below are met:
   A. The member is 17 years of age or younger; **AND**
   B. The medication is prescribed by, or in consultation with, an endocrinologist; **AND**
   C. A diagnosis of an **Adrenocortical insufficiency** (e.g. primary adrenal insufficiency, Addison's Disease, secondary adrenal insufficiency) and the following are met:
      1. The request is for hydrocortisone (Alkindi Sprinkle) 0.5 mg, 1 mg, or 2 mg capsules; **AND**
         i. Each individual dose is less than 5 mg (of note, when a 5 mg dose is reached, member is required to transition to generic hydrocortisone oral tablets, unless contraindicated); **AND**
         ii. Treatment with hydrocortisone compound formulation (solution or suspension) has been ineffective, contraindicated, or not tolerated; **OR**
      2. The request is for hydrocortisone (Alkindi Sprinkle) 5 mg capsules;
         i. Treatment with generic hydrocortisone oral tablet is contraindicated (documentation must be attached); **AND**
         ii. Treatment with hydrocortisone compound formulation (solution or suspension) has been ineffective, contraindicated, or not tolerated

II. Hydrocortisone (Alkindi Sprinkle) is considered not medically necessary when the following are met:
   A. Total daily dose requirement for hydrocortisone may be met using hydrocortisone (Cortef) oral tablets (5 mg, 10 mg, or 20 mg) or hydrocortisone compound (solution or suspension)
   B. Treatment requiring hydrocortisone (Alkindi Sprinkle) 5 mg capsules

III. Hydrocortisone (Alkindi Sprinkle) is considered investigational when used for all other conditions, including but not limited to:

   A. Treatment of members 18 years of age or older, requiring hydrocortisone therapy
   B. Chemotherapy induced nausea and vomiting

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. The request is for hydrocortisone (Alkindi Sprinkle) 0.5 mg, 1 mg, or 2 mg capsules; **AND**
   - Each individual dose is less than 5 mg (of note, when a 5 mg dose is reached, member is required to transition to generic hydrocortisone oral tablets, unless contraindicated); **AND**
   - Treatment with hydrocortisone compound formulation (solution or suspension) has been ineffective, contraindicated, or not tolerated; **OR**
IV. The request is for hydrocortisone (Alkindi Sprinkle) 5 mg capsules;
   - Treatment with generic hydrocortisone oral tablet is contraindicated (documentation must be attached); **AND**
   - Treatment with hydrocortisone compound formulation (solution or suspension) has been ineffective, contraindicated, or not tolerated
V. Provider attests that the member remains ineligible to transition to generic hydrocortisone tablets and compounded hydrocortisone products (solution or suspension); **AND**
VI. Member has exhibited improvement or stability of disease symptoms (e.g. improved cortisol levels over baseline, improvement in symptoms such as hypotension, hyponatremia)

Supporting Evidence

I. Hydrocortisone (Alkindi Sprinkles) is a corticosteroid, indicated as a replacement therapy in pediatric patients (less than 17 years of age) with adrenocortical insufficiency. Alkindi Sprinkle is a granular formulation of hydrocortisone, which was designed to overcome the barrier of inaccuracy of dosing (when using currently available hydrocortisone formulations) for younger patients.

II. Pediatric patients (neonate to <17 years old) usually require less than 5 mg of total daily dose of hydrocortisone. The daily dose of hydrocortisone is usually divided into two to three doses with initial dose of 8mg/m^2 to 10mg/m^2 per day. Hydrocortisone (Alkindi Sprinkle) is supplied in a pack size of 50 capsules to be stored in the original bottle (unbreakable package). Quantity limit for hydrocortisone (Alkindi Sprinkles) is based on total daily dose divided into two to three individualized doses and should be rounded up to the nearest pack size.

III. Currently there are no published clinical trial or treatment regimens for children with Primary Adrenal Insufficiency (PAI). The Journal of Endocrinology and Metabolism guideline recommends that treatment in children is aimed at managing and controlling symptoms of adrenal insufficiency with optimal doses that allow for growth and pubertal development. Because PAI is a complex disease state, management and treatment monitoring of PAI in pediatric patients must be in consultation with an endocrinologist or a healthcare provider with endocrine expertise.

IV. Differential diagnose of PAI requires confirmation with the Corticotropin simulation test, which is considered the gold standard due to its higher degree of specificity and sensitivity. A confirmed diagnosis of PAI is determined by low morning serum cortisol concentrations (≤ 140 *n*Mol/L) and high adrenocorticotropic hormone (ACTH) levels (≥ 66 *p*mol/L).

V. While glucocorticoid monotherapy is a typical initial treatment approach, many patients also require a mineralocorticoid as an add-on agent. The Journal of Endocrinology and Metabolism guideline recommends use of 100 µg per day of fludrocortisone. Mineralocorticoids are essential in maintaining water and electrolyte homeostasis; however, use in PAI has not been studied systematically. The rationale is to dose fludrocortisone in the mornings to mimic aldosterone levels, which are generally high in the morning due to circadian rhythms.

VI. Patients with PAI are at high risk of developing Adrenal crisis, an acute etiology that develops due to inability of the adrenal gland to produce enough cortisol in response to an increased need. Clinical features of adrenal crisis consist of volume depletion and hypotension. In such cases, parenteral injections (50mg/m^2) of hydrocortisone may be required.

VII. Hydrocortisone (Alkindi Sprinkle) received FDA approval for pediatric patients (<17 years of age) based on the ease of dosing and proposed accuracy of dosing as it is available in smaller doses (0.5 mg, 1 mg, 2 mg, and 5 mg). Hydrocortisone (Alkindi Sprinkle) was granted FDA-approval as a new dosage form of hydrocortisone and was limited to the indication of adrenocortical insufficiency. There are no independent prospective clinical trials to support efficacy and safety of hydrocortisone (Alkindi Sprinkle) for any other conditions. As such, until now, patients requiring a daily dose of hydrocortisone > 5 mg per day have been managed using

hydrocortisone (Cortef) oral tablets (intact or crushed and mixed with liquid), or compounded formulations of hydrocortisone (oral solution or suspension). Notably, the compounded formulations of hydrocortisone have been successfully used in pediatric populations to fulfill the need for optimum daily doses less than 5 mg. These formulations provide accuracy of dosing as well as ease of administration. Although hydrocortisone (Alkindi Sprinkle) is a new formulation that provides administrative convenience, use of this formulation is cost-prohibitive. Given the long-standing efficacy, safety, accuracy of dosing, cost, and clinical experience, compounded formulations of hydrocortisone are considered standard and practical high-value treatment options in this space and should be preferred over hydrocortisone (Alkindi Sprinkle).

Investigational or Not Medically Necessary Uses

I. There are no direct head-to-head clinical trials comparing efficacy and safety of glucocorticoid drugs used in in long term treatment of PAI in children. The Endocrine Societal Guidelines recommend children should be treated with hydrocortisone because of its optimal pharmacokinetic profile, and short half-life, furthermore overtreatment should be avoided. Doses of ≥ 5mg daily are considered not medically necessary for children aged less than 17 years of age due to risk of growth retardation. Therefore, close monitoring of glucocorticoid dosing is advised in children with increasing body surface area.

II. Hydrocortisone (Alkindi Sprinkle) is not considered medically necessary in any other disease state other than adrenocortical insufficiency. Epidemiology in this setting largely involves pediatric population. Based on the scope of FDA-approval, hydrocortisone (Alkindi Sprinkle) is deemed medically necessary only for pediatric patients diagnosed with adrenocortical insufficiency, for whom, the total daily dose requirement may not be met using generic hydrocortisone tablets or compounded hydrocortisone formulations.

III. Use of hydrocortisone has been widely recommended in many inflammatory conditions including chemotherapy induced nausea, prostate cancer, chronic lung disease and gout. However, it should be noted that typical daily dose requirement of hydrocortisone in the treatment of these conditions is higher than 5 mg per day. As such, use of hydrocortisone (Alkindi Sprinkle) in these settings over traditionally used hydrocortisone formulations (e.g. generic Cortef oral tablet) is not practical and FDA-approved, given the lack of the clinical superiority data for the former, as well as, higher cost of therapy.

IV. Efficacy and Safety of hydrocortisones (Alkindi Sprinkle) for treatment of conditions other than adrenocortical insufficiency have not been studied and remain unknown.

References

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Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	12/2020