

09-J5000-22

[Original Effective Date](#): 10/01/25

[Reviewed](#): 08/13/25

[Revised](#): 00/00/00

Subject: Hydrocortisone (Khindivi) Oral Solution

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Adrenal insufficiency results from impaired production or action of glucocorticoids and/or mineralocorticoids, which are typically synthesized by the adrenal cortex, and is characterized primarily by a cortisol deficiency. In children, adrenal insufficiency may present with unexplained volume depletion, hypotension, hyponatremia, hyperkalemia, fever, abdominal pain, hyperpigmentation, hypoglycemia, or non-specific symptoms such as fatigue, dizziness, or anorexia. Diagnosis is confirmed through measuring basal and/or stimulated serum cortisol and plasma ACTH levels. Low cortisol plus high ACTH levels suggest primary adrenal insufficiency, and low cortisol plus low or low-normal ACTH levels suggest secondary or tertiary adrenal insufficiency. For management, replacement therapy with oral hydrocortisone therapy is recommended with a goal of controlling symptoms and allowing for adequate growth and pubertal development while trying to avoid drug-related adverse effects. Common adverse reactions for corticosteroids include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite, and weight gain. Various forms of oral hydrocortisone are available and include tablets, granules, and suspensions. On May 28, 2025, the FDA approved hydrocortisone (Khindivi) oral solution as a replacement therapy in pediatric patients 5 years of age and older with adrenocortical insufficiency.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an

outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of hydrocortisone (Khindivi) oral solution **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Diagnosis of adrenocortical insufficiency
2. Age 5 to less than 18 years of age
3. Therapy is for replacement maintenance and not stress dosing
4. Member has a documented intolerance or inability to take (e.g., unable to swallow) **ALL** of the following hydrocortisone dosage forms: - documentation must be submitted
 - a. Tablet formulation
 - b. Compounded suspension
 - c. Sprinkles
5. Prescribed by, or in consultation with, a prescriber who manages adrenocortical insufficiency (e.g., endocrinologist)

Approval duration: 6 months

Continuation of hydrocortisone (Khindivi) oral solution **meets the definition of medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization for the requested agent has been previously approved by Florida Blue or another health plan in the past 2 years (if another health plan, documentation of a health plan-paid claim during the 90 days before the authorization request must be submitted), OR the member has previously met ALL indication-specific initiation criteria.
2. Member has a clinical meaningful response (e.g., improvement in cortisol and/or ACTH levels) without any significant adverse events that require discontinuation (e.g., hyperosmolarity, metabolic acidosis, hypoglycemia, hepato-renal injury, and/or central nervous toxicity from polyethylene glycol 400)
3. Age 5 to less than 18 years of age
4. Therapy is for replacement maintenance and not stress dosing
5. Member continues to have a documented intolerance or inability to take (e.g., unable to swallow) **ALL** of the following hydrocortisone dosage forms: - documentation must be submitted
 - a. Tablet formulation
 - b. Compounded suspension
 - c. Sprinkles
6. Prescribed by, or in consultation with, a prescriber who manages adrenocortical insufficiency (e.g., endocrinologist)

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Hydrocortisone (Khindivi) is a corticosteroid indicated as replacement therapy in pediatric patients 5 years of age and older with adrenocortical insufficiency.
- When stress dosing is needed use a different hydrocortisone containing drug product.
- The recommended starting replacement dosage of hydrocortisone (Khindivi) is 8 to 10 mg/m² daily. Individualize the dose, using the lowest possible dosage. Use of lower starting doses may be sufficient in patients with residual but decreased endogenous cortisol production. Higher doses may be needed based on the patient's age and symptoms of the disease.
- Divide the total daily dose into 3 doses and administer 3 times daily. Older patients may have their daily dose divided by 2 and administered twice daily.
- When switching from other oral hydrocortisone formulations, use the same total daily hydrocortisone dosage. If symptoms of adrenal insufficiency occur, increase total daily dosage.

Dose Adjustments

- Dosage adjustments may be necessary with the following drug interactions:
 - CYP3A4 Inhibitors: concomitant administration may require a decrease in the hydrocortisone (Khindivi) dose.
 - CYP3A4 Inducers: concomitant administration may require an increase in the hydrocortisone (Khindivi) dose.
 - Estrogen and Estrogen-Containing Products: concomitant administration may require an increase in the hydrocortisone (Khindivi) dose.
 - Antidiabetic agents: excessive doses may increase blood glucose concentrations. Dose adjustment of antidiabetic agents may be required.
 - NSAIDs: concomitant administration increases risk of gastrointestinal adverse reactions.

Drug Availability

- Hydrocortisone (Khindivi) is supplied as a colorless to slightly yellow colored, clear viscous 1 mg/mL solution (473 mL bottle: NDC 71863-116-16).

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Hypersensitivity to hydrocortisone or any component of the product

Precautions/Warnings

- **Adrenal Crisis:** Undertreatment, sudden discontinuation of therapy, or switching from another oral hydrocortisone formulation may lead to adrenocortical insufficiency, adrenal crisis and death. Adrenal crisis may also be induced by stress events such as infections or surgery. During periods of stress switch to another oral hydrocortisone product and increase the dose. Switch patients who are vomiting, severely ill or unable to take oral medications to parenteral corticosteroid formulations.
- **Systemic Adverse Reactions Due to Inactive Ingredients:** Hydrocortisone (Khindivi) contains the inactive ingredients polyethylene glycol 400, propylene and glycol, and glycerin, which may cause hyperosmolarity, metabolic acidosis, hypoglycemia, hepato-renal injury, central nervous toxicity, gastrointestinal adverse reactions. Discontinue hydrocortisone (Khindivi) oral solution and switch to another hydrocortisone product if these adverse reactions occur.
- **Immunosuppression and Increased Risk of Infection with Use of a Dosage Greater Than Replacement:** Use of a greater than replacement dosage can suppress the immune system and increase the risks of new infections or exacerbation of latent infections with any pathogen, including viral, bacterial, fungal, protozoan, or helminthic infections. Monitor patients for signs and symptoms of infections.
- **Growth Retardation:** Long-term use in excessive doses may cause growth retardation. Use the minimum dosage of hydrocortisone (Khindivi) to achieve desired clinical response and monitor the patient's growth.
- **Cushing's Syndrome Due to Use of Excessive Doses of Corticosteroids:** Prolonged use with supraphysiologic doses may cause Cushing's syndrome. Monitor patients for signs and symptoms of Cushing's syndrome every 6 months.
- **Decrease in Bone Mineral Density:** Corticosteroids decrease bone formation and increase bone resorption which may lead to inhibition of bone growth and development of osteoporosis. Use the minimum dosage of hydrocortisone (Khindivi) to achieve desired clinical response.
- **Psychiatric Adverse Reactions:** Use may be associated with severe psychiatric adverse reactions such as euphoria, mania, psychosis with hallucinations and delirium or depression. Symptoms typically emerge within a few days or weeks of starting the treatment. Most reactions resolve after either dose reduction or withdrawal, although specific treatment may be necessary. Monitor patients for behavioral and mood disturbances during treatment. Instruct caregivers and/or patients to seek medical advice if psychiatric symptoms develop.
- **Ophthalmic Adverse Reactions:** Cataracts, glaucoma and central serous chorioretinopathy have been reported with prolonged use of high doses. Monitor patients for blurred vision or other visual disturbances and if they occur, refer them to an ophthalmologist.
- **Gastrointestinal Adverse Reactions:** Increased risk in patients with certain gastrointestinal disorders. Signs and symptoms may be masked.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, not otherwise specified
-------	--

ICD-10 Diagnosis Codes That Support Medical Necessity

E27.1	Primary adrenocortical insufficiency
E27.40	Unspecified adrenocortical insufficiency
E27.49	Other adrenocortical insufficiency

REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: The following National Coverage Determination (NCD) was reviewed on the last guideline revised date: Self-administered Drug List (A54770). No Local Coverage Determination (LCD) was found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at [Coverage Protocol Exemption Request](#).

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2025. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed 7/30/25.
2. DRUGDEX System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2025 July 30].

3. DynaMed [database online]. Ipswich, MA: EBSCO Information Services.; 2025. URL <http://www.dynamed.com>. Accessed 7/30/25.
4. Khindivi (hydrocortisone) oral solution [package insert]. Cranbury, NJ: Eton Pharmaceuticals, Inc.; June 2025.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 08/13/25.

GUIDELINE UPDATE INFORMATION:

10/01/25	New Medical Coverage Guideline: Hydrocortisone (Khindivi) oral solution for replacement therapy in pediatric patients 5 to less than 18 years of age with adrenocortical insufficiency who are unable to tolerate or take an alternate dosage forms (e.g., tablets, compounded suspension).
----------	---