



KHINDIVI A HYDROCORTISONE DRUG

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ABSTRACT

Khindivi (Oral Solution of Hydrocortisone) Khindivi is an oral hydrocortisone formulation designed specifically for children with adrenocortical insufficiency who are five years of age or older. Khindivi, a synthetic glucocorticoid, supports immunologic, metabolic, and stress-response processes by restoring low cortical levels. The formulation, which is designed for age-specific titration and variable dosage, provides 1 mg/mL hydrocortisone in a glycerin-based solution. Since Khindivi is not authorized for stress dosage during acute events, unlike other hydrocortisone medications, alternate corticosteroid therapies are required in emergency situations. In order to replicate the diurnal cortical rhythm, clinical use requires customized dose based on body surface area (8–10 mg/m²/day), split into two or three administrations. Adverse reactions include hepato-renal issues, central nervous system toxicity, and metabolic acidosis, particularly in individuals who are hypersensitive to excipients like propylene glycol and polyethylene glycol 400. Khindivi's pharmacokinetic profile and tolerability underscore its importance in long-term endocrine therapy; cautious monitoring is required to avoid adrenal crisis during formulation changes or stressful situations.

KEYWORDS: Khindivi, Hydrocortisone, Cortical replacement therapy, adrenocortical insufficiency, Pediatric endocrinology, gastrointestinal perforation, congenital adrenal hyperplasia.

INTRODUCTION

For children aged 5 and up with adrenocortical insufficiency, including Addison's disease, the FDA has approved Khindivi, an oral hydrocortisone solution (1 mg/ml). It is the first liquid formulation designed specifically for children and was approved in May 2025, providing a tablet substitute. Propylene glycol and PEG-

400, which are not recommended for use in children under five, can have negative effects like metabolic acidosis and central nervous system toxicity. It needs to be carefully dosed and monitored when used as a hormone replacement. The medication must be thrown out 120 days after opening, has a 12-hour half-life, and tastes like berries. Keep between 2 and 25°C.^[1]



Figure 1: Khindivi.

Mechanism of Action

Khindivi (oral hydrocortisone) is taken up by the GI tract and reaches its highest levels in the blood in about 0.5 hours. Over 90% binds to plasma proteins (CBG and albumin). It enters target cells, binds cytoplasm glucocorticoid receptors, and the complex moves to the nucleus to regulate gene expression. This results in key physiological effects: increased blood glucose, altered fat/protein metabolism, reduced inflammation, immune suppression, sodium retention, and potassium excretion. It replaces cortisol in patients with deficiency, aiding stress response and metabolism.^[2]

Dosing and administration

Khindivi's recommended starting dose is 8–10 mg/m²/day, divided into 2–3 doses depending on age. If some cortisol production is still present, lower dosages might be used. It is not authorized for stress dosage; in these situations, use a different hydrocortisone product. PEG 400, propylene glycol, and glycerin are ingredients in Khindivi; stop using it if you experience any negative side effects. For comprehensive dosing instructions, consult the complete prescribing information.^[3]

Drug interaction

When taking Khindivi with other medications, the dosage may need to be changed. While CYP3A4 inducers may need an increase in dosage, CYP3A4 inhibitors may need a decrease. Estrogen-containing products can also necessitate a higher dose. High doses of Khindivi may raise blood glucose, possibly requiring adjustments to anti-diabetic medications. Co-administration with NSAIDs increases the risk of gastrointestinal side effects.^[4]

Pharmacokinetics

Absorption

After a 5 mg oral dose of Khindivi in fasted, dexamethasone suppressed adults, peak plasma hydrocortisone concentration is 152 ng/mL, reached within 0.5 hours.

Distribution

Over 90% of circulating hydrocortisone binds reversibly to plasma proteins, mainly albumin and a glycoprotein. Its mean apparent volume of distribution (Vd/F) is 23 L.

Elimination

Hydrocortisone is mainly metabolized in the liver and tissues into inactive forms like tetra hydrocortisol, excreted in urine as glucuronides. Its mean terminal half-life is approximately 0.95 hours.^[5]

Pharmacodynamics

Khindivi mimics natural cortisol with key effects including metabolic regulation of carbohydrates, proteins, and fats; modulation of immune responses; and salt-retaining properties similar to endogenous glucocorticoids.^[6]

Adverse reaction

Growth Retardation

Long-term excessive corticosteroid use can cause growth retardation in children, as seen in past congenital adrenal hyperplasia treatments. With replacement therapy like Khindivi, growth effects are less likely. Use the lowest effective dose and monitor the child's growth closely.

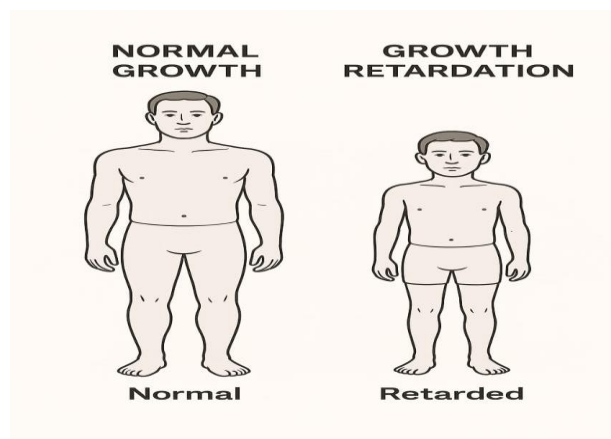


Figure: Growth Retardation.

Cushing's syndrome

Long-term overdosing of corticosteroids like Khindivi can cause Cushing's syndrome, characterized by weight gain, slowed growth, high blood sugar, hypertension, edema, bruising, muscle weakness, round face, and mood changes. Monitor patients closely for these symptoms.

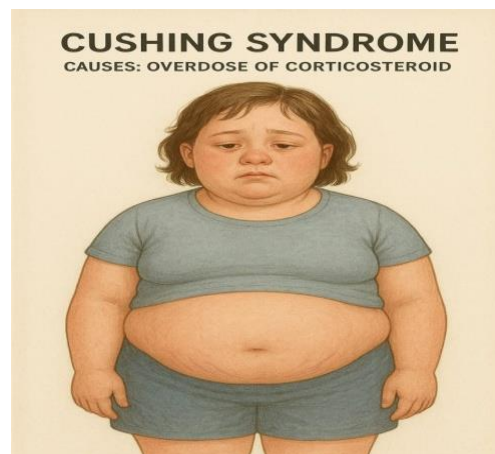


Figure: Cushing's syndrome

Decrease in Bone marrow Density

Corticosteroids like Khindivi can cause osteoporosis by increasing bone resorption and reducing bone formation. Past patients treated from childhood showed decreased bone density and higher fracture risk. Use the lowest effective dose to minimize these effects.

Psychiatric Adverse Reaction

Corticosteroids like Khindivi can cause serious mental effects such as euphoria, mania, psychosis, delirium, or depression, often appearing within weeks of starting treatment. Symptoms may worsen with higher doses but

usually improve with dose reduction or stopping the drug. Monitor patients for behavioral changes and advise them or caregivers to seek medical help if psychiatric symptoms occur.



Figure: Delirium

Gastro intentional Perforation

Patients with certain gastrointestinal conditions are at higher risk of perforation when taking corticosteroids like Khindivi. Symptoms may be masked, so use caution if there's risk of perforation, abscess, infection, diverticulitis, recent intestinal surgery, or active/latent peptic ulcer.

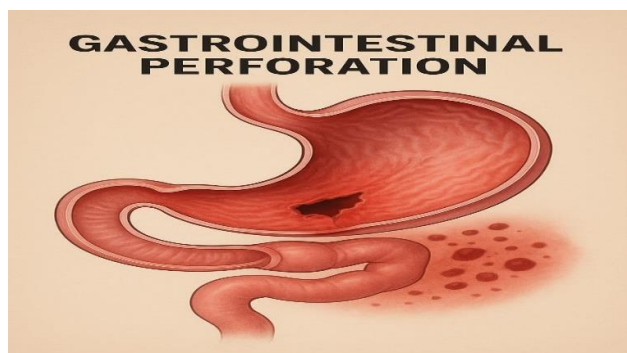


Figure: Gastrointestinal Perforation.

Side effects^[5]

The most frequently reported side effects of KHINDIVI include

- Aggression
- Anxiety
- Blurred Vision
- Burning, dry, or itching eyes
- Decrease in the amount of urine
- Discharge, excessive tearing
- Dizziness
- Dry mouth
- Ear congestion
- Fast, slow, pounding or irregular heartbeat or pulse
- Fever
- Headache
- Irregular heartbeats
- Irritability
- Mental depression
- Mood changes

- Noisy, rattling breathing
- Numbness or tingling in the arms or legs
- Pounding in the ears
- Redness, pain, swelling of eye, eyelid or inner lining of the eyelid
- Restlessness
- Runny or stuffy nose
- Sore throat
- Swelling of the fingers, hands, feet or lower legs
- Trouble breathing
- Trouble sleeping
- Trouble thinking, speaking, or walking
- Unusual tiredness or weakness

Contraindication

Possess an allergy to hydrocortisone or any of the other ingredients in Khindivi. experience any side effects from taking Khindivi, such as swelling or dyspnea. These could be signs of allergic reactions. Get medical help right away, and let your doctor know as soon as you can. One of the contraindications is hypersensitivity to hydrocortisone or any of the ingredients in the formulation. Care should be taken when switching from other hydrocortisone medications as a poor transition may result in an adrenal crisis. Parenteral corticosteroids should be used in stressful situations for patients who are unable to take oral medications.^[5]

Vaccination

Advise patients and/or caregivers that live vaccination administration might be acceptable.

Limitations

Importantly, higher dosages of khindivi are not permitted during stressful or acute situations. During acute febrile illness, gastroenteritis, surgery, or severe trauma, patients require higher dosages of corticosteroids, which must be given using different prescription formulations that contain hydrocortisone. This limitation stems from the distinct inactive chemical profile of khindivi, which increases the risk of adverse reactions when taken in excess of replacement dosages.

Medical Uses

Condition	Purpose
Adrenocortical Insufficiency	Restoring cortisol levels in kids five years old
Congenital Adrenal Insufficiency	Controlling hormone imbalances brought on by enzyme deficiencies
Secondary Adrenal Insufficiency	When the pituitary glands are unable to stimulate the adrenal glands, cortisol production is maintained.

CONCLUSION

The oral solution of khindivi (hydrocortisone), a significant advancement in the treatment of juvenile adrenocortical insufficiency, resolves long-standing problems with precisely dosing children for hormone replacement. The first and only FDA-approved hydrocortisone liquid formulation, khindivi, offers families and medical professionals a practical tool for improving clinical outcomes and expediting medication administration. The drug's approval shows how pharmaceutical innovation, regulatory science, and clinical knowledge may successfully work together to solve unmet medical needs in rare disorders. Although khindivi's distinct inactive component composition and particular safety concerns necessitate close monitoring, its availability closes a significant gap in pediatric endocrinology treatments. The availability of age-appropriate formulations for additional disorders needing precision dosing may be accelerated by the commercial success and clinical adoption of khindivi, which is expected to impact future. The availability of khindivi fills a major gap in pediatric endocrinology treatments, despite the fact that its unique inactive component composition and unique safety concerns call for careful monitoring. The commercial and clinical success of khindivi is anticipated to influence future development priorities in pediatric rare diseases and may expedite the availability of age-appropriate formulations for other disorders requiring precision dosing. As practical experience grows, Khindivi is poised to become a standard component of comprehensive therapy for children with adrenocortical insufficiency, improving clinical outcomes and the quality of life for this vulnerable patient population.

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