

PRODUCT MONOGRAPH

Pr JAMP Fludrocortisone

Fludrocortisone Acetate Tablets

0.1 mg

House Standard

Mineralocorticoid for adrenal insufficiency

JAMP Pharma Corporation
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Boucherville, Quebec
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0.1 mg

Therapeutic class

Mineralocorticoid for adrenal insufficiency

ACTIONS AND CLINICAL PHARMACOLOGY

The physiologic action of fludrocortisone is similar to that of hydrocortisone. However, the effects of fludrocortisone, particularly on electrolyte balance, but also on carbohydrate metabolism, are considerably heightened and prolonged. In small oral doses, fludrocortisone produces marked sodium retention and increased urinary potassium excretion. It also causes a rise in blood pressure, apparently because of these effects on electrolyte levels. In larger doses, fludrocortisone inhibits endogenous adrenal cortical secretion, thymic activity, and pituitary corticotropin excretion: promotes the deposition of liver glycogen; and, unless protein intake is adequate, induces negative nitrogen balance.

INDICATIONS AND CLINICAL USE

Partial replacement therapy for primary and secondary adrenocortical insufficiency in Addison's disease and for the treatment of salt losing adrenogenital syndrome.

CONTRAINDICATIONS

Corticosteroids are contraindicated in patients with systemic fungal infections.

PRECAUTIONS

Because of its marked effect on sodium retention, the use of fludrocortisone in the treatment of conditions other than those indicated herein is not advised.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used. If an infection occurs during fludrocortisone therapy, it should be promptly controlled by suitable antimicrobial therapy.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure,

salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. However, since fludrocortisone is a potent mineralocorticoid, both the dosage and salt intake should be carefully monitored in order to avoid the development of hypertension, edema, or weight gain. Periodic checking of serum electrolyte levels is advisable during prolonged therapy; dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Patients should not be vaccinated against smallpox while on corticosteroid therapy. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

The use of fludrocortisone in patients with active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary since reactivation of the disease may occur. During prolonged corticosteroid therapy these patients should receive chemoprophylaxis.

Pregnancy and Lactation: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers, or women of childbearing potential requires that the possible benefits of the drug be weighted against the potential hazards to the mother, embryo, fetus or nursing infant. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Adverse reactions to corticosteroids may be produced by too rapid withdrawal or by continued use of large doses.

To avoid drug induced adrenal insufficiency, supportive dosage may be required in times of stress (such as trauma, surgery, or severe illness) both during treatment with fludrocortisone and for a year afterwards.

There is an enhanced corticosteroid effect in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

The lowest possible dose of corticosteroid should be used to control the condition being treated. A gradual reduction in dosage should be made when possible.

Psychic derangements may appear when corticosteroids are used. These may range from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Existing emotional instability or psychotic tendencies may also be aggravated by corticosteroids.

ASA should be used cautiously in conjunction with corticosteroids in patients with hypoprothrombinemia

Corticosteroids should be used with caution in patients with non-specific ulcerative colitis if there is a probability of impending perforation, abscess, or other pyogenic infection.

Corticosteroids should also be used cautiously in patients with diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, acute glomerulonephritis, vaccinia, varicella, exanthema, Cushing's syndrome, antibiotic resistant infections, diabetes mellitus, congestive heart failure, chronic nephritis, thromboembolic tendencies, thrombophlebitis, convulsive disorders, metastatic carcinoma, and myasthenia gravis.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

ADVERSE REACTIONS

In the recommended small dosages, the side effects seen with cortisone and its derivatives are not usually a problem with fludrocortisone. However, the following untoward effects should be kept in mind, particularly when this agent is used over a prolonged period of time or in conjunction with cortisone or a similar glucocorticoid:

Fluid and electrolyte disturbances: sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalemic alkalosis, and hypertension.

Musculoskeletal: muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathologic fracture of long bones, and spontaneous fractures.

Gastrointestinal: peptic ulcer with possible perforation and hemorrhage, pancreatitis, abdominal distention, and ulcerative esophagitis.

Dermatologic: impaired wound healing, thin fragile skin, bruising, petechiae and ecchymoses, facial erythema, increased sweating, subcutaneous fat atrophy, purpura, striae, hyperpigmentation of the skin and nails, hirsutism, and acneiform eruptions; reactions to skin tests may be suppressed.

Neurological: convulsions, increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment, vertigo, headache, and severe mental disturbances.

Endocrine: menstrual irregularities; development of the Cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress (e.g., trauma, surgery, or illness); decreased carbohydrate tolerance; manifestations of latent diabetes mellitus; and increased requirements for insulin or oral hypoglycemic agents in diabetics.

Ophthalmic: posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and exophthalmos.

Metabolic: hyperglycemia, glycosuria, and negative nitrogen balance due to protein catabolism.

Other adverse reactions that may occur following the administration of a corticosteroid are necrotizing angitis, thrombophlebitis, aggravation or masking of infections, insomnia, syncopal episodes, and anaphylactoid reactions.

DOSAGE AND ADMINISTRATION

Addison's disease: Usual dose is 0.1 mg daily, although dosage ranging from 0.1 mg 3 times a week to 0.2 mg daily has been employed. In the event transient hypertension develops as a consequence of therapy, the dose should be reduced to 0.05 mg daily. Fludrocortisone is preferably administered in conjunction with cortisone (10 to 37.5 mg daily in divided doses) or hydrocortisone (10 to 20 mg daily in divided doses).

Salt losing adrenogenital syndrome: 0.1 to 0.2 mg daily.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional poison control centre.

COMPARATIVE BIOAVAILABILITY STUDY

A randomized, double blinded, two-treatment, two-period, two-sequence, crossover, bioequivalence study of ^{Pr}JAMP Fludrocortisone (fludrocortisone acetate) tablets (JAMP Pharma Corporation) and ^{Pr}FLORINEF[®] (fludrocortisone acetate) tablets (Paladin Labs Inc.) was conducted in healthy, adult male subjects under fasting conditions. The test and reference products were administered as single oral doses of 1 x 0.1 mg fludrocortisone acetate. A summary of the bioavailability data from the 23 subjects who completed the study is presented in the following table.

SUMMARY TABLE OF THE COMPARATIVE BIOAVAILABILITY DATA

| Fludrocortisone (1 x 0.1 mg fludrocortisone acetate) Geometric Mean Arithmetic Mean (CV%) | | | | |
|--|----------------------------|----------------------------|-------------------------------|----------------------------|
| Parameter | Test ¹ | Reference ² | % Ratio of Geometric Means | 90% Confidence Interval |
| AUC _T (pg·h/mL) | 3820.56 3947.70 (24.91) | 4069.40 4159.24 (20.02) | 93.9 | 90.7 – 97.2 |
| AUC _I (pg·h/mL) | 4018.49 4124.78 (23.85) | 4252.01 4331.89 (19.62) | 94.3 | 91.5 – 97.3 |
| C _{max} (pg/mL) | 1046.61 1116.33 (38.35) | 1285.65 1314.05 (22.62) | 81.4 | 73.3 – 90.4 |
| T _{max} ³ (h) | 0.83 (0.50 - 1.50) | 0.67 (0.33 - 1.50) | | |
| T _{1/2} ⁴ (h) | 2.93 (11.49) | 3.01 (10.64) | | |

¹ JAMP Fludrocortisone (fludrocortisone acetate) 0.1 mg tablets (JAMP Pharma Corporation)

² ^{Pr}FLORINEF[®] (fludrocortisone acetate) 0.1 mg tablets (Paladin Labs Inc.)

³ Expressed as the median (range) only

⁴ Expressed as the arithmetic mean (CV%) only

DOSAGE FORMS, COMPOSITION AND PACKAGING

Each JAMP Fludrocortisone tablet contains 0.1 mg of fludrocortisone acetate. Non-medical ingredients are calcium hydrogen phosphate anhydrous, lactose anhydrous, lactose monohydrate, magnesium stearate, sodium benzoate, starch-maize and talc.

JAMP Fludrocortisone tablets are white to off-white, round shaped tablet with score line on one side.

JAMP Fludrocortisone tablets are available in bottle of 100 tablets.

STORAGE AND STABILITY

Store between 2-8°C. Protect from moisture.

REFERENCES

FLORINEF® (fludrocortisone acetate tablets; 0.1 mg), submission control 129527, Product Monograph, Paladin Labs Inc. (February 27, 2019)

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

If you want more information about JAMP Fludrocortisone:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (www.jamppharma.com), or by calling 1-866-399-9091.

This leaflet was prepared by JAMP Pharma Corporation.

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