Fludrocortisone Acetate

- **(flue-droe-kor-ti-sone)**
- ***Florinef*®**
- **Mineralocorticoid**

PRESCRIBER HIGHLIGHTS

- Oral mineralocorticoid alternative to DOCP used to treat adrenal insufficiency in small animals; may be useful to treat hyperkalemia as well.
- Also has some glucocorticoid effect that could cause adverse effects.
- Adverse Effects: Dosage related; PU/PD, hypertension, edema, & hypokalemia possible.
- May be excreted in significant quantities in milk.
- Patients may require supplemental glucocorticoids.
- Expense may be an issue, especially in larger dogs.

USES/INDICATIONS

Fludrocortisone is used in small animal medicine for the treatment of adrenocortical insufficiency (Addison's disease). It can also be used as adjunctive therapy in hyperkalemia.

In humans, fludrocortisone has also been used for severe postural hypotension, and salt-losing, congenital adrenogenital syndrome.

PHARMACOLOGY/ACTIONS

Fludrocortisone acetate is a potent corticosteroid that possesses both glucocorticoid and mineralocorticoid activity. It is approximately 10-15X as potent a glucocorticoid agent as hydrocortisone, but is a much more potent mineralocorticoid (125X that of hydrocortisone). It is only used clinically for its mineralocorticoid effects.

The site of action of mineralocorticoids is at the renal distal tubule where they increase the absorption of sodium. Mineralocorticoids also enhance potassium and hydrogen ion excretion.

PHARMACOKINETICS

In humans, fludrocortisone is well absorbed from the GI with peak levels occurring in approximately 1.7 hours; plasma half-life is about 3.5 hours, but biologic activity persists for 18-36 hours.

CONTRAINDICATIONS/PRECAUTIONS/WARNINGS

Fludrocortisone is contraindicated in patients known to be hypersensitive to it.

Some dogs or cats may require additional supplementation with a glucocorticoid agent on an ongoing basis. All animals with hypoadrenocorticism should receive additional glucocorticoids (at least 2X basal) during periods of stress or acute illness.

ADVERSE EFFECTS

Adverse effects of fludrocortisone are generally a result of chronic, excessive dosage (see Overdosage section below) or if withdrawal is too rapid. Since fludrocortisone also possesses glucocorticoid activity, it theoretically could cause the adverse effects associated with those compounds such as polyuria/polydipsia, which could be a problem for some dogs. (See the monograph on glucocorticoids for more information.)

REPRODUCTIVE/NURSING SAFETY

In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans*.)

Fludrocortisone may be excreted in clinically significant quantities in milk. Puppies or kittens of mothers receiving fludrocortisone should receive milk replacer after colostrum is consumed.

OVERDOSAGE/ACUTE TOXICITY

Overdosage may cause hypertension, edema, and hypokalemia. Electrolytes should be aggressively monitored and potassium may need to be supplemented. Patients should have the drug discontinued until clinical signs associated with overdosage have resolved; then restart the drug at a lower dosage.

DRUG INTERACTIONS

The following drug interactions have either been reported or are theoretical in humans or animals receiving fludrocortisone and may be of significance in veterinary patients. Unless otherwise noted, use together is not necessarily contraindicated, but weigh the potential risks and perform additional monitoring when appropriate.

- **Amphotericin B**: Patients may develop hypokalemia if fludrocortisone is administered concomitantly with amphotericin B.
- **Aspirin**: Fludrocortisone may reduce salicylate levels.

- **Diuretics, Potassium-depleting** (*e.g.*, **thiazides**, **furosemide**): Patients may develop hypokalemia if fludrocortisone is administered concomitantly with diuretics; diuretics can cause a loss of sodium, and may counteract the effects of fludrocortisone.
- **Insulin**: Potentially, fludrocortisone could increase the insulin requirements of diabetic patients.

DOSES

Dogs:

- **For maintenance therapy of hypoadrenocorticism** (extra-label): Initial dosage recommendations vary somewhat but most recommend 0.01 mg/kg PO q12h. Dosages are adjusted in 0.05 – 0.1 mg increments (1/2 to one 0.1 mg tablet) based on monitoring serum electrolyte concentrations every 1-2 weeks until stable; many dogs can be transitioned to once daily dosing. Once stable, recheck every 3-4 months. Most dogs will eventually require 0.02 – 0.03 mg/kg per day. Approximately 50% of dogs will not require supplemental prednisone, but owners should have supplemental prednisone on hand and instructed to use it when animal undergoes stress or illness (*e.g.* veterinary visits, boarding etc.). In dogs that develop signs associated with Cushing's (*e.g.,* polyuria/polydipsia) even when hyponatremia and, less frequently, hyperkalemia persist, the addition of NaCl (0.1 g/kg/day) may be useful to reduce the dose of fludrocortisone, while maintaining normal serum sodium.

Cats:

- **For maintenance therapy of hypoadrenocorticism** (extra-label): 0.02 mg/kg PO once daily with prednisolone. Practically, one 0.1 mg tablet PO once daily with prednisolone (at 1.25 mg per cat PO once daily; ¼ of a 5 mg tablet).

Ferrets:

- **For hypoadrenocorticism** (extra-label): For those animals that still exhibit Addisonian signs even with prednisone therapy: 0.05 – 0.1 mg/kg PO q24h or divided q12h. (Johnson 2006)

MONITORING

- Serum electrolytes, BUN, creatinine; initially every 1-2 weeks, then every 3-4 months once stabilized.
- Weight, PE for edema.

CLIENT INFORMATION

- May give with or without food. If your animal vomits or acts sick after getting it on an empty stomach, give with food or small treat to see if this helps. If vomiting continues, contact your veterinarian.
- Side effects not likely, but if dose is too high (long-term) "Cushingoid" effects (change in coat, swelling abdomen, etc.) could occur; if too low, Addison's effects (*e.g.*, weakness, depression, lack of appetite, vomiting, diarrhea, etc.) could occur.
- Surgery or stress (*e.g.,* trauma, illness) may require additional glucocorticoids (*e.g.,* prednisolone, etc.).
- Do not stop the drug abruptly ('cold turkey') or serious side effects could occur.

CHEMISTRY/SYNONYMS

A synthetic glucocorticoid with significant mineralocorticoid activity, fludrocortisone acetate occurs as hygroscopic, fine, white to pale yellow powder or crystals. It is odorless or practically odorless. Fludrocortisone is insoluble in water and slightly soluble in alcohol.

Fludrocortisone acetate may also be known as: fluohydrisone acetate, fluohydrocortisone acetate, 9alpha-fluorohydrocortisone acetate, fludrocortisoni acetas, 9alpha-fluorohydrocortisone 21-acetate, *Astonin®, Astonin H®, Florinef®, Florinefe*®, and *Lonikan*®.

STORAGE/STABILITY

Fludrocortisone acetate tablets should be stored at room temperature (15-30°C) in well-closed containers; avoid excessive heat. The drug is relatively stable in light and air.

COMPATIBILITY/COMPOUNDING CONSIDERATIONS

No specific information noted.

DOSAGE FORMS/REGULATORY STATUS

Veterinary-Labeled Products: None.

Human-Labeled Products:

Fludrocortisone Acetate Tablets: 0.1 mg; generic; (Rx)