



Fludrocortisone (Florinef®) Shortage

Suppliers of fludrocortisone¹

Product	Strength	DIN	MFR
Florinef	0.1 mg	02086026	PAL

Health Canada approved indications of fludrocortisone²:

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

Off-label uses of fludrocortisone³:

- increase blood pressure in patients with orthostatic hypotension

Fludrocortisone acetate 0.1 mg tablets may become shorted due to shipping delays. The estimated end date is mid-May 2022.⁴ **Consider giving priority of existing inventory to infants and children** (see PEDIATRICS below) until stable supply is re-established.

Management Options in the Event of Manufacturer Shortage

Pharmaceutical Alternatives

- Compounding
 - Compounding pharmacies are able to compound capsules.
 - Medisca has a limited supply of bulk fludrocortisone acetate (CAS RN 514-36-3) in smaller package sizes (1 g, 5 g). There is adequate inventory of 25 g packages, which are expensive.⁵
 - The Saskatchewan Drug Plan needs to be contacted in advance for approval of the compounded products, which are only covered when no manufactured product is available.⁶
 - Bill NIHB claims with the pseudoDIN 99505004, the extemporaneous DIN for backordered products; document the reason for the claim for auditing purposes.⁷

Therapeutic Alternatives

Chronic adrenocortical insufficiency (e.g., Addison's Disease) and Congenital Adrenal Hyperplasia (Salt Losing Adrenogenital Syndrome)

Fludrocortisone is a potent mineralocorticoid agent for which there are no alternatives with the same therapeutic effects. Individualized treatment will be necessary. **Patients, especially pediatric patients, should seek consultation with their endocrinologist (either directly or via their primary care provider).**

Background⁸⁻¹⁰

- Patients with primary chronic adrenocortical insufficiency (e.g., Addison's disease, post-operative adrenalectomy, other) need supplementation with corticosteroids for glucocorticoid and/or mineralocorticoid activity.
- Congenital adrenal hyperplasia (CAH) is a genetic enzyme deficiency disorder that most often presents in infancy; the classic salt-losing type is associated with mineralocorticoid deficiency.¹¹
- Fludrocortisone is a potent mineralocorticoid corticosteroid that is sometimes added to glucocorticoid-dominant corticosteroids such as prednisone, dexamethasone, or hydrocortisone to prevent hyponatremia, hypotension,

and hyperkalemia. Requirements for aldosterone/fludrocortisone vary individually and some patients do not require daily or any supplementation.

- The most common doses of fludrocortisone are 0.05 mg to 0.1 mg once daily, although doses vary depending on patient response.
- IV glucocorticoids given at stress doses (i.e., hydrocortisone 100 mg IV q 6-8 hrs) provide mineralocorticoid and additional overlapping with oral fludrocortisone is not required.
- Glucocorticoid-dominant corticosteroids may have some mineralocorticoid activity, though considerably less than that provided by fludrocortisone.
 - Relative mineralocorticoid potency: fludrocortisone >>>> hydrocortisone > prednisone > dexamethasone (no mineralocorticoid activity)
 - Estimates of doses resulting in equivalent mineralocorticoid activity among the corticosteroids vary as they are not well-established. The table below is intended to give an indication of the *relative* activity.

Table 1: Approximate doses resulting in equivalent MINERALOCORTICOID activity

Corticosteroid	Approximate Equivalent Dose
Fludrocortisone	0.1 mg
Hydrocortisone	20 mg ^{8,12,13} to 40 mg ¹⁰
Prednisone	50 mg ^{8,12,13}
Dexamethasone	No mineralocorticoid activity at replacement doses
Note: Fludrocortisone also has some glucocorticoid activity; 0.1 mg of fludrocortisone has the glucocorticoid potency of 1 mg of hydrocortisone. ¹³	

Therapeutic Management

PEDIATRICS

- Consult pediatric endocrinologist – the strategies used in adults may be ineffective or unsafe in infants and children.

ADULTS (potentially adolescents)

- **Consider reducing dose to conserve tablets;** adults often do well on twice weekly dosing. **Patients on prednisone or dexamethasone** can be switched to hydrocortisone for maximal mineralocorticoid activity (see Table 1). Hydrocortisone is usually given in 2 or 3 divided doses with a larger dose in the morning.^{8,14} Note that there have also been supply disruptions with [hydrocortisone tablets](#) and conservation efforts are recommended during the disruption to keep the medication available for those most in need, such as pediatric patients with CAH.
- **For patients already taking hydrocortisone,** emphasize increased sodium and fluid intake and close monitoring.
- Pickles are a good source of sodium.
- **Monitoring parameters** include symptoms of pre-syncope, syncope, salt cravings and postural hypotension. Measurement of serum electrolytes and plasma renin levels may be necessary in some patients.

Orthostatic Hypotension (OH)¹⁵⁻¹⁷

- Remind/encourage patients to adopt non-pharmacological practices such as:
 - getting up gradually
 - avoiding: large meals; alcohol intake; warm environments/hot baths; and heavy exertion
 - raising the head of the bed using blocks or bricks, if tolerated
 - increasing salt and fluid intake if appropriate
 - physical maneuvers such as leg crossing when standing, bending forward, squatting
 - compression stockings (waist-high) or abdominal binders
- Check profile for exacerbating medications and discontinue/reduce dose if possible.

Therapeutic alternatives

- All pharmacological agents used for OH have limitations.
- Most commonly used agents in Canada are fludrocortisone and midodrine.
 - midodrine 2.5 mg TID, increasing to effect up to 10 mg TID
- Other agents with less evidence and/or specific situations:
 - caffeine, desmopressin acetate, epoetin alfa, NSAIDs, octreotide, pyridostigmine
- See the RxFiles [Orthostatic hypotension \(OH\): considerations for management](#) for more details.

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