

# Fludrocortisone (Florinef®) Shortage

## Suppliers of fludrocortisone<sup>1</sup>

Product	Strength	DIN	Manufacturer
Florinef	0.1 mg	02086026	PAL

## Health Canada approved indications of fludrocortisone<sup>2</sup>:

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

## Off-label uses of fludrocortisone<sup>3</sup>:

- increase blood pressure in patients with orthostatic hypotension

Fludrocortisone acetate 0.1 mg tablets may become shorted due to shipping delays. As of June 2022, the product is on allocation based on historical demand until end of September, 2022.<sup>4</sup> **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.<sup>5</sup>
- 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.<sup>6</sup>
- Bill NIHB claims with the pseudoDIN 99505004, the extemporaneous DIN for backordered products; document the reason for the claim for auditing purposes.<sup>7</sup>

### 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).**

#### Background<sup>8-10</sup>

- 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.<sup>11</sup>
- 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 <sup>8,12,13</sup> to 40 mg <sup>10</sup>
Prednisone	50 mg <sup>8,12,13</sup>
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.<sup>13</sup>

## 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.<sup>8,14</sup>  
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)<sup>15-17</sup>

- 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 Management

- 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 (subscription required).

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