Fludrocortisone (Florinef®) Shortage

05 Jul 2019

Fludrocortisone 0.1 mg tablets are currently in short supply and may become shorted.

Suppliers of fludrocortisone:

<table>
<thead>
<tr>
<th>Product</th>
<th>Strength</th>
<th>DIN</th>
<th>MFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florinef</td>
<td>0.1 mg</td>
<td>02086026</td>
<td>PAL</td>
</tr>
</tbody>
</table>

Health Canada approved indications of fludrocortisone:
- partial replacement therapy for primary and secondary adrenocortical insufficiency in Addison’s disease
- treatment of salt losing adrenogenital syndrome.

Off-label uses of fludrocortisone:
- increase blood pressure in patients with orthostatic hypotension

Status as of 05 Jul 2019:
- Allocation
  - Paladin has limited stock available that is being placed on allocation and distributed to requesting wholesalers, who will then be responsible for allocation among their customers. **Be sure to inform your wholesaler of fludrocortisone needs as soon as possible.** Paladin anticipates supply to be re-established in September, 2019.
  - **Consider giving priority to infants and children** (see PEDIATRICS below).

Management Options in the Event of Manufacturer Shortage

Pharmaceutical Alternatives
- Compounding
  - Compounding pharmacies currently have access to fludrocortisone to compound.
  - Medisca has a limited supply of bulk fludrocortisone that pharmacies can order.
    - Acquisition cost of the powder may be quite expensive (>$150 per gram)
  - 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.
  - Bill NIHB claims with the pDIN 99505004, the extemporaneous DIN for backorder products; document the reason for the claim for auditing purposes.

Therapeutic Alternatives

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

**Fludrocortisone is a potent mineralocorticoid agent and 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:
- Patients with primary chronic adrenocortical insufficiency (i.e. Addison’s disease, post-operative adrenalectomy, other) need supplementation with corticosteroids for glucocorticoid and mineralocorticoid activity.
Congenital adrenal hyperplasia (CAH) is a genetic enzyme deficiency disorder that most often presents in infancy; more than 75% of those with CAH have mineralocorticoid deficiency.²

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 0.05-0.1 mg once daily, although doses vary depending on patient response.

IV glucocorticoids given at stress doses (i.e. hydrocortisone 100 mg IV q6-8 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

<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Approximate Equivalent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fludrocortisone</td>
<td>0.1 mg</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>20 mg⁶,¹⁰,¹¹ to 40 mg⁸</td>
</tr>
<tr>
<td>Prednisone</td>
<td>50 mg⁶,¹⁰,¹¹</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>No mineralocorticoid activity at replacement doses</td>
</tr>
</tbody>
</table>

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. Hydrocortisone is given in 2 or 3 divided doses with a larger dose in the morning.⁶,¹² Use Table 2 below to find the dose that provides approximately equivalent glucocorticoid activity. This may be sufficient but patients may need to increase fluid/sodium and will need to be monitored.

### Table 2: Approximate doses resulting in equivalent GLUCOCORTICOID activity

<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Approximate Equivalent Dose¹⁰</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>20 mg</td>
</tr>
<tr>
<td>Prednisone</td>
<td>5 mg</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.75 mg</td>
</tr>
<tr>
<td>Cortisone</td>
<td>25 mg</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>4 mg</td>
</tr>
</tbody>
</table>

- **For patients already taking hydrocortisone,** emphasize increased sodium and fluid intake and close monitoring.
- Pickles are a good source of sodium.
- **Monitoring parameters** include salt cravings and postural hypotension; electrolytes may be necessary in some patients.
Orthostatic Hypotension (OH)\textsuperscript{13-15}

- 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, clonidine, desmopressin acetate, erythropoietin, NSAIDs, octreotide, pyridostigmine
- See the RxFiles Chart Orthostatic hypotension (OH): considerations for management for more details.

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References:
5. Personal phone communication with Medisca Canada, 1.800.665.6334; 24 Jun 2019

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