

# Hydrocortisone (Cortef) 10 mg Tablet Shortage

Suppliers of hydrocortisone oral tablets in Canada<sup>1</sup>

Product	Strength	DIN (NDC U.S.)	Manufacturer
Cortef	10 mg	00030910	PFI
	20 mg	00030929	
	5 mg	NDC 0009-0012-01 [Available only through the <a href="#">Special Access Programme</a> for patients requiring low doses. <sup>2</sup> ]	

## Health Canada approved indications of hydrocortisone oral tablets<sup>3</sup>:

There are several indications for inflammatory, autoimmune and other conditions\*. The focus of this document is conditions requiring glucocorticoid (a type of corticosteroid) replacement:

- primary or secondary adrenocortical insufficiency
- congenital adrenal hyperplasia

\*Depending on the dose and duration, patients who use glucocorticoid therapy may be at risk of adrenal insufficiency during times of physiological stress (e.g., acute illness, surgery) and require hydrocortisone during these times.<sup>4,5</sup>

## Background

- Cortef 10 mg tablets are currently [shorted](#) in Canada,<sup>6</sup> with an end date of Sept 30, 2022,<sup>6</sup> though have not been added to the Quebec [RAMQ](#) as of April 21, 2022.
- For many indications in which glucocorticoids are used, other glucocorticoids may be used interchangeably.
- For adrenocortical insufficiency and congenital adrenal hyperplasia, hydrocortisone or cortisone are generally the preferred glucocorticoids though other glucocorticoids, especially prednisone, may be used.<sup>7-10</sup>
  - Different glucocorticoids have different mineralocorticoid activity.<sup>10</sup> Therefore, when used for glucocorticoid replacement, switching is not as simple as switching to a different glucocorticoid at the usual equivalent dose because mineralocorticoid activity needs to be considered. **The goal is to keep patients on their original glucocorticoid.**<sup>7</sup>
- As of April 21, 2022, there are no reports of Cortef 20 mg tablet shortage<sup>11</sup>, though efforts must be made to protect this supply (see strategies below).

## MESSAGE FROM THE CANADIAN SOCIETY OF ENDOCRINOLOGY AND METABOLISM:

Thousands of Canadians, adult and pediatric, use hydrocortisone (Cortef) for treatment of adrenal insufficiency (e.g., Addison's Disease). For these patients, hydrocortisone is a critical, life-saving medication that must be taken every day. Missing this glucocorticoid medication can result in major health issues, hospitalizations and even death. Substitution with other medications can be very complicated and onerous, and in some patients may not work at all. Thus, the goal is to keep patients on their original glucocorticoid.

## Conservation Strategies

- Patients should have adequate supply on hand at all times but encourage to **limit to no more than 30-60 days'** supply of any strength.
- Should hydrocortisone 10 mg tablets be available in limited quantities:
  - Reserve for patients (especially young children) who require low doses in which 20 mg tablets are unsuitable.
  - Use 20 mg tablets for compounding oral suspensions.
  - Use 20 mg tablets instead of 2x10 mg tablets for **stress dosing** if appropriate.

## Pharmaceutical Alternatives

### • Cortef 5 mg Tablets

- o Available through the Special Access Programme for patients requiring low doses.<sup>2</sup>
- o Only prescribers may apply on behalf of the patient. Application information [here](#).
- o Some hospital pharmacies are able to help facilitate applications.

### Cortef 20 mg Tablets

- Cortef 20 mg tablets are not scored; the manufacturer has no stability studies on the use of cut 20 mg tablets and cannot recommend this practice. However, when necessary, consider splitting 20 mg tablets so long as <sup>12-14</sup>:
  - o The patient's dose is stable.
    - This is under ideal conditions; using cut 20 mg tablets is preferable to switching to a different glucocorticoid even if dose has not been stabilized.
  - o The patient/caregiver has necessary physical (e.g., dexterity, vision, strength) and cognitive abilities and is motivated to split tablets. If not, consider compounded suspension using 20 mg tablets.
  - o A tablet-splitting device is used.
  - o One tablet is split at a time; each half is taken before splitting the next tablet.
    - The dose in each half may not be uniform, which will be evened out by taking both halves of the same tablet.
  - o The patient is monitored for therapeutic effect.

## A Note About Pediatrics

- [ISMP Canada has highlighted](#) the lack of pediatric formulations (in general) in Canada as a concern requiring action.
- Regarding hydrocortisone, there are no commercially available formulations palatable to children and appropriate strengths are not available.<sup>1</sup>
  - o Children may require doses of 2.5 mg or lower, which are not easily or accurately obtained by 10 mg and 20 mg tablets. As mentioned, hydrocortisone 5 mg tablets are available through the Special Access Programme, which requires application by the prescriber.<sup>2</sup>
  - o Hydrocortisone suspension can be compounded by some pharmacies. A study that compared pharmacokinetic and pharmacodynamic outcomes between children treated with compounded suspension to those treated with tablets found no significant differences in most outcomes.<sup>15</sup> Commercially available tablets are preferred but when these are not feasible (especially in young children), compounded suspension can be considered. SickKids has a [formula](#).
  - o Manipulation of dosage forms (e.g., splitting tablets, compounding suspensions) is necessary for some patients; however, it introduces additional risk of dosing inaccuracy<sup>16,17</sup>, which caregivers and health care providers should keep in mind.
  - o Hydrocortisone oral granules (ALKINDI SPRINKLE®) in pediatric strengths (0.5 mg, 1 mg, 2 mg, 5 mg) are available in other jurisdictions (e.g., USA, Europe).<sup>18</sup> Advocacy work is underway to make the product available in Canada.

## Other Important Information

### Stress Dosing and COVID-19

- Patients with adrenal insufficiency may be at higher risk of contracting infections, including COVID-19.<sup>19</sup> It is important that [measures](#) – as recommended for the general population – are taken to prevent infection including vaccination, masking, hand hygiene, and physical distancing.
  - o In the event of COVID-19 infection it is of even greater importance to ensure:
    - daily glucocorticoid replacement, or
    - the more likely scenario of stress glucocorticoid dosing during symptomatic illness, and
    - emergency use of parenteral hydrocortisone for those with suspected adrenal crisis
- A UK research group recommends the following at onset of signs and symptoms suggestive of COVID-19 (fever >38°C, a new or continuous dry cough, sore throat, loss of sense of smell or taste, aches and pains, fatigue)<sup>19</sup>:
  - adults and adolescents: 20 mg hydrocortisone orally every 6 hours
  - children: triple the usual daily dose and administer in four equal doses every 6 hours

**Note:** the above is a general guideline. Patients should consult with their medical team to determine their stress dosing plan.

- In general, patients requiring the COVID-19 antiviral Paxlovid™ (nirmatrelvir/ritonavir) should take hydrocortisone stress doses as per their regular sick day rules.
  - Hydrocortisone is a minor substrate of CYP3A4, the metabolism of which is inhibited by ritonavir.<sup>20</sup> Hydrocortisone concentrations are potentially increased in the presence of ritonavir, though the clinical significance of this interaction is unknown.
  - Several Paxlovid™ resources do not include hydrocortisone in the list of interacting agents.<sup>21-23</sup> The Liverpool COVID-19 Drug Interaction Checker states “No Interaction Expected” between Paxlovid™ and hydrocortisone.<sup>24</sup>
  - Given the short duration of Paxlovid™ treatment (5 days) and the importance of hydrocortisone stress dosing during illness, patients should follow their regular sick day rules. **It is important that clinicians gauge symptoms (nausea, blood pressure, fever, O<sub>2</sub> sat, etc.) when determining dose requirements. Individual prescriber discretion is advised.**

## Emergency Preparedness

- Ensure patients always have an [emergency injection kit](#) on hand, know how to use it, and have a hospital emergency care [plan](#). A hospital emergency care plan will help ensure that lifesaving hydrocortisone is administered without delay.
  - o Ensure patients and caregivers have been given training on intramuscular/subcutaneous administration (see resources below).
  - o Patients may want to have a [notice](#) available to provide to emergency personnel.
- Encourage patients to have an emergency card, bracelet or necklace stating the diagnosis and/or that in an emergency, intravenous hydrocortisone (e.g. [Solu-Cortef®](#)) is required.
  - o Acceptable formulations are hydrocortisone sodium succinate and hydrocortisone sodium phosphate (sodium phosphate formulation is not available in Canada<sup>1</sup>).
  - o Hydrocortisone acetate (not available in Canada in injectable form<sup>1</sup>) is a slow-onset product and is not suitable for emergency use.<sup>25</sup>
- Be alert to the possibility that emergency attention may be required when communicating with patients or their caregivers.
  - o Some of the signs and symptoms that may be apparent in adrenal crisis may include, but are not limited to<sup>26</sup>:
    - vomiting, diarrhea, headache, dizziness, low back pain, low blood pressure, shock-like symptoms, confusion, low blood sugar, loss of appetite
- Stress to patients the importance of continuing glucocorticoid therapy unless directed otherwise by their medical professional. Interruption of or fast withdrawal of glucocorticoid therapy may result in an adrenal crisis.<sup>3,4</sup>
- Remind patients to keep a [list of current medications](#), ensure they [understand their medications](#) and are taking correctly – especially to double check the tablet strength before taking if more than one strength is on hand. Report medication incidents to [ISMP Canada](#).

## Emergency resources for patients with adrenal insufficiency:

- o Emergency [medical information card](#) (Canadian Society of Endocrinology and Metabolism) - copies to distribute to patients can be obtained by [contacting](#) CSEM.
- o Emergency [hydrocortisone dosing sample wallet card](#) (Canadian Paediatric Society)
- o Emergency injection instructions [wallet card](#)
- o Emergency Injection instructions [video](#). Instructions for pediatric emergency injection are provided [here](#).
- o Emergency injection instructions [written/infographic](#)

## Taking With Food

- Glucocorticoids are often recommended to be taken with food<sup>20</sup> though this is not always necessary for patients requiring replacement glucocorticoids and may delay absorption.
  - o Studies assessing the effects of food on time to peak concentration of oral hydrocortisone have found variable results.<sup>27-29</sup> However:
    - Doses used for physiological replacement are unlikely to cause gastrointestinal distress. If gastrointestinal distress (e.g., indigestion) occurs when taken only with water, taking with milk or a milk substitute usually helps.
    - Patients may notice quicker onset if hydrocortisone tablets are taken in the fasted state.

## Sources of More Information

- o [Canadian Addison Society](#)
- o [Canadian Society of Endocrinology and Metabolism](#)
- o [Society for Endocrinology](#) – document regarding COVID-19 for patients taking replacement steroids
- o [CARES Foundation](#)

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