

## Solu-Cortef® Shortage

There is only one supplier of hydrocortisone sodium succinate for injection in Canada<sup>1</sup>:

**Table 1: Solu-Cortef® Act-O-Vials, Pfizer Canada ULC<sup>1</sup>**

Strength per Vial	DIN
100 mg	0030600
250 mg	0030619
500 mg	0030627
1000 mg	0030635

### Health Canada approved indications of hydrocortisone sodium succinate for injection<sup>2</sup>:

- Solu-Cortef® is indicated for several conditions. The focus of this document is emergency use in pre-hospital/emergent settings for conditions in which no other treatments (including other corticosteroids) are as effective, specifically:
  - in primary, secondary, and acute adrenal insufficiency
- Note that other conditions, generally treated in a medical facility, may also warrant preferential use of Solu-Cortef®.

### Solu-Cortef® Availability

- There have been intermittent shortages of various Solu-Cortef® vial sizes in Canada.<sup>3</sup>
  - The concentrations differ among the vial strengths of Solu-Cortef® and, therefore, volumes differ to deliver the same dose.<sup>2</sup> **Patients need to be educated on the correct volume for required dose.** See Table 2.
  - Depending on the duration of shortage of any one vial size, demand for the other vial sizes may increase. **The goal is to conserve available Solu-Cortef® and ensure availability to those who need rescue corticosteroids for emergency purposes.**
- Solu-Cortef® is stable for three days following reconstitution (i.e. Act-O-Vial activation) *before vial puncture* when stored at 15-30°C.<sup>2</sup>
  - If the hydrocortisone is reconstituted, but the vial is not punctured, keep on hand for up to three days.
- Solu-Cortef® is preservative-free.<sup>2</sup> Once the vial is punctured, any contents not used within 1 hour should be discarded.<sup>4</sup>
  - The risks and benefits of using remaining reconstituted hydrocortisone after an Act-O-Vial or other single-use vial has been punctured must be weighed and determined: Consultation with a healthcare provider as per individual cases and/or organization policies and procedures is recommended.

**Table 2: Comparison of Concentrations and Volumes of Solu-Cortef® Vial Sizes<sup>2</sup>**

Vial Strength	Concentration	Total Volume After Reconstitution	Volume Required for 25 mg	Volume Required for 50 mg	Volume Required for 100 mg
100 mg	50 mg/mL	2 mL	0.5 mL	1 mL	2 mL
250 mg	125 mg/mL	2 mL	0.2 mL	0.4 mL	0.8 mL
500 mg	125 mg/mL	4 mL	0.2 mL	0.4 mL	0.8 mL
1000 mg	125 mg/mL	8 mL	0.2 mL	0.4 mL	0.8 mL

## Conservation Strategies

- Ensure patients have Solu-Cortef® on hand, but not to purchase more than necessary (generally keep three to five 100 mg vials per patient on hand). Multiple vials may be necessary if vials break and/or signs/symptoms worsen in the pre-hospital or hospital setting. Always carry additional vials in the event emergency medical services (EMS) and/or the hospital lack supply.
- Prevent acute adrenal insufficiency through patient education. See Table 3.
- Consider off-label use of expired Solu-Cortef® **if it is the only product available**.
  - Discuss with endocrinology care team to determine benefit versus risk for specific patients.
  - Precedence has been set during the auto-injector epinephrine shortage in 2018, a somewhat similar situation, when [Health Canada advised use of expired epinephrine during the shortage](#).
  - Hydrocortisone sodium succinate injection solution was included in the US FDA & Department of Defense Shelf-Life Extension Program (SLEP). Only three samples were available, but SLEP was able to extend the expiration date beyond the original labelled expiration.<sup>5</sup>
  - Examples of use of expired medication policies are available from EM agencies in [Wisconsin, USA](#) and [Pennsylvania, USA](#).

## Pharmacological Alternatives

- If Solu-Cortef® is not available, consider use of an alternative parenteral corticosteroid: dexamethasone sodium phosphate or methylprednisolone sodium succinate (Solu-Medrol®).
- The most important disadvantage of these agents is their negligible/minimal mineralocorticoid activity<sup>6,7</sup>, which may need to be supplemented with fludrocortisone for patients with primary adrenal insufficiency, especially infants.
- Hydrocortisone has a shorter biological half-life (8-12 hours) than dexamethasone (36-72 hours) and methylprednisolone (12-36 hours).<sup>6</sup>
- **Dexamethasone sodium phosphate** (generic, Decadron)
  - *Considerations:*
    - same routes of administration as Solu-Cortef® (intramuscular (IM) or intravenous (IV))<sup>8</sup>
    - not available as an Act-O-Vial<sup>1</sup> and other vial format availability varies<sup>9</sup>
      - single-use vials: may be available in 10 mg/mL (1 mL vials)
      - multiuse vials: may be available in 4 mg/mL (5 mL vials) and 10 mg/mL (10 mL vials)
  - **4 mg dexamethasone sodium phosphate** = ~ 100 mg hydrocortisone sodium succinate (glucocorticoid equivalency)<sup>6,10</sup>
  - Dose less frequently than hydrocortisone (e.g. every 12-24 hours<sup>11</sup> vs. every 6-8 hours with hydrocortisone).
- **Methylprednisolone sodium succinate** (Solu-Medrol®)
  - *Considerations:*
    - same routes of administration as Solu-Cortef® (IM or IV)
    - available in same vial format as Solu-Cortef® (Act-O-Vial) (40 mg, 125 mg, 500 mg, 1000 mg vials)<sup>12</sup>
    - similar to Solu-Cortef®, some vial sizes have been shorted<sup>3</sup>
    - DO NOT use methylprednisolone acetate (Depo-Medrol®) because of delayed absorption (peak plasma concentrations ~ 7 hours).<sup>13</sup>
  - **20 mg methylprednisolone sodium succinate** = ~ 100 mg hydrocortisone sodium succinate (glucocorticoid equivalency)<sup>6,10</sup>
  - Dose less frequently than hydrocortisone (e.g. every 8-12 hours vs. every 6-8 hours with hydrocortisone).

## Pharmaceutical Alternatives

- Due to the need for quick onset and reliable achievement of a minimum plasma concentration, other dosage forms of hydrocortisone are generally not suitable for acute adrenal insufficiency.
  - Hydrocortisone rectal suppositories have been investigated as an alternative to parenteral hydrocortisone in children for *stress dosing* when oral administration is not possible.<sup>14,15</sup>
    - Adequate concentrations may not be achieved in all children.<sup>14</sup>
    - Rectal hydrocortisone suppositories are not available commercially and need to be compounded. Absorption will depend on the suppository base such that it may not be possible to apply results of the studies to available compounded products.

## Adrenal Insufficiency Background Information

- Cortisol and aldosterone are important hormones secreted by the adrenal cortex. Cortisol is involved in protein, fat, and carbohydrate metabolism and, importantly, is secreted in higher amounts during times of physiological and/or psychological stress. Aldosterone controls volume and electrolyte balance.<sup>16</sup>
- Adrenal insufficiency (AI), in which there is inadequate or no secretion of cortisol and, in some, aldosterone, may be primary or secondary.
  - **Primary AI (also called Addison disease)** is a result of damage to the adrenal cortex and, in developed countries, is most commonly caused by autoimmune dysfunction. Those with primary AI require daily glucocorticoid (usually hydrocortisone, e.g. [Cortef®](#)) and mineralocorticoid (fludrocortisone, e.g. [Florinef®](#)) supplementation; mineralocorticoid needs may be met by the glucocorticoid in some such that fludrocortisone may not be necessary. During times of physiological and/or psychological stress, the corticosteroid dose needs to be increased to avoid acute adrenal insufficiency (adrenal crisis).<sup>16-18</sup> Consider [Cortef®](#) and/or [Florinef®](#) drug shortage information.
  - **Secondary AI** is a result of suppression of the hypothalamic-pituitary-adrenal (HPA) axis.<sup>16,19,20</sup> The most common cause of secondary AI is use of supraphysiological doses of exogenous corticosteroid.<sup>16,20</sup> After prolonged use and/or high doses of corticosteroids, the negative feedback system of the HPA axis may be disrupted, which ultimately leads to lower or no cortisol secretion.<sup>21</sup> If the corticosteroid dose is reduced to lower than physiological levels or additional corticosteroid is not provided during times of stress, acute adrenal insufficiency may ensue.<sup>6,22</sup> Other causes of secondary AI include:
    - conditions that interfere with adrenocorticotrophic hormone (ACTH) secretion (e.g. tumours, stroke)<sup>16,23</sup>
    - procedures that interfere with ACTH secretion (e.g. pituitary surgery or pituitary radiation)<sup>16,23</sup>
    - drug-induced (other than glucocorticoids) such as high-dose progestins, opioids, monoclonal antibodies (most commonly checkpoint inhibitors for immunotherapy)<sup>16,23-25</sup>
- **Acute adrenal insufficiency (AAI) is a medical emergency** associated with hypotension and shock.<sup>16,26</sup>
  - Symptoms include, but are not limited to: vomiting, diarrhea, headache, dizziness, low back pain, low blood pressure, shock-like symptoms, confusion, low blood sugar, and loss of appetite.<sup>16,17,27</sup>
  - Prompt treatment is required with parenteral corticosteroid therapy, preferably IV hydrocortisone sodium succinate (e.g. Solu-Cortef®) because of its glucocorticoid and mineralocorticoid activity, and fluids.<sup>16,28</sup>
  - Ideally, patients have Solu-Cortef® on hand for IM administration to provide some treatment until IV hydrocortisone and normal saline, with or without dextrose, can be administered in the pre-hospital or hospital settings. The following are suggested for anyone at risk of AAI:
    - know how to prevent AAI (see Table 3)
    - know what to do in an emergency (see Sidebar 1 for more resources)
      - have a stress dose/emergency plan, developed in consultation with the endocrinology care team
      - have an [emergency injection kit](#) on hand and know how to use it
        - ensure adequate training on IM / subcutaneous (SC) administration (see Sidebar 2 regarding SC administration)
        - if Solu-Cortef® is not available, education regarding use – including appropriate dose, preparation/ administration, and storage – of an alternative corticosteroid (e.g. dexamethasone sodium phosphate, methylprednisolone sodium succinate) is of utmost importance
      - have a [hospital emergency protocol](#) and consider carrying a [notice](#) to provide to emergency personnel
      - have an emergency card, bracelet, or necklace stating the diagnosis and/or that in an emergency, IV hydrocortisone (e.g. Solu-Cortef®) is required

## Sidebar 1: Sample Emergency Resources for Patients with Adrenal Insufficiency

- [Emergency injection kit](#) contents and instructions for use
- [Pediatric hydrocortisone stress dosing sample wallet card](#)
- [Pediatric hydrocortisone stress dosing, emergency dosing, and emergency care plan](#) document
- Pediatric [adrenal insufficiency action plan](#)
- [Daycare or school preparation](#)
- Emergency intramuscular injection instructions [wallet card](#)
- Emergency intramuscular injection instructions videos for [adults](#) (UK source) and [children](#) (US source)
- Emergency subcutaneous injection instructions [video](#) (French source)
- [Subcutaneous injection instructions](#) video
- Emergency injection instructions [written/infographic](#)
- [EMS notice](#)
- Emergency [medical information card](#) (copies to distribute to patients can be obtained by [contacting Canadian Society of Endocrinology and Metabolism](#))
- [Hospital emergency protocol](#)

**Table 3: Potential Causes of Inadequate Corticosteroid Levels in Patients with Adrenal Insufficiency (AI)**

Potential Causes	Mitigation Strategies
Increased requirements during times of physical <b>stress</b> (e.g. moderate to severe illness/infection, trauma, surgery) and/or psychological stress	<ul style="list-style-type: none"> <li>• Patients with AI should have a stress dosing plan, developed through consultation with their endocrinology care team. Be sure to discuss COVID-19. The UK Addison's Self-Help Group has some <a href="#">suggested clinical management</a>. Information about the benefits of care plans is available for <a href="#">patients</a> and healthcare providers.</li> <li>• Note, <b>gastroenteritis</b> may also reduce absorption of oral corticosteroids<sup>10,29</sup> in which parenteral treatment may be required (e.g. severe diarrhea, vomiting within ½ hour of two oral stress doses).<sup>30</sup></li> </ul>
<b>Non-adherence</b> to or insufficient dose of daily glucocorticoid therapy	<ul style="list-style-type: none"> <li>• If patient is non-adherent, determine underlying cause of non-adherence and work with patient for solutions (e.g. setting alarms, compliance packaging, education on importance of taking all doses).</li> <li>• If adherence is not a problem, re-evaluate current doses.</li> </ul>
<b>Abrupt cessation of or too rapid of a reduction</b> in dose of chronic and/or high doses of exogenous corticosteroids to below physiological levels (especially oral and high-dose inhaled corticosteroids) <sup>6,18,31</sup>	<ul style="list-style-type: none"> <li>• Ensure all patients taking chronic and/or high doses of corticosteroids understand the importance of maintaining adherence to dosing recommendations (including tapering).</li> <li>• Taper long-term/high-dose corticosteroids → the taper can be relatively quick until physiological doses are reached (e.g. equivalent to 5–7.5 mg prednisone daily) after which tapering should take weeks to months, depending on duration of corticosteroid use, and adjusted according to patient's response.<sup>6,22</sup></li> <li>• <b>Tapering can be complex and prone to errors</b>, as discussed in this <a href="#">ISMP Canada report</a>. Among other strategies: prescribers can consider standardized, pre-printed order forms; pharmacy professionals can undertake independent double checks during order entry and dispensing; health care providers can communicate and ensure the patient understands the regimen and provide tools (e.g. calendar).<sup>32</sup></li> </ul>
<b>Addition of CYP3A4 enzyme-inducing</b> medications resulting in reduced serum glucocorticoid levels <sup>11,18,33,34</sup>	<ul style="list-style-type: none"> <li>• Monitor closely for signs of insufficient corticosteroid replacement with a plan to increase corticosteroid dose upon emergence of symptoms/signs.<sup>33</sup></li> </ul>
<b>Discontinuation of moderate to strong CYP3A4 enzyme-inhibiting</b> medications resulting in reduced serum glucocorticoid levels <sup>33</sup>	<ul style="list-style-type: none"> <li>• Monitor closely for signs of insufficient corticosteroid replacement with a plan to increase corticosteroid dose upon emergence of symptoms/signs.</li> <li>• If corticosteroid dose had been reduced at time of addition of the interacting medication, consider returning to original corticosteroid dose. Monitoring is still required as corticosteroid requirements may have changed (e.g. children).</li> </ul>

## Sidebar 2: Subcutaneous vs. IV/IM Administration of Solu-Cortef®

The therapeutic effects of hydrocortisone are evident within a few minutes following IV injection. It is absorbed rapidly when administered intramuscularly.<sup>2</sup> Solu-Cortef® is not approved for SC administration<sup>2</sup>; however, this route<sup>‡</sup> may be more feasible in some emergency situations. A small pharmacokinetic study suggests that SC hydrocortisone sodium succinate may be a possible alternative route of administration to IM.<sup>35</sup> While serum concentrations were comparable between IM and SC, Hahner, et al found a delayed onset following SC compared to IM.

**‡ Because of the potentially delayed onset and lack of clinical data, IV/IM are preferred. If SC is considered, it should be discussed with the endocrinology care team.** SC administration is endorsed as an acceptable alternate route of administration by the Canadian Society of Endocrinology and Metabolism, the Canadian Pediatric Endocrine Group, and the Canadian Association of Emergency Physicians.<sup>36,37</sup>

## Summary

Solu-Cortef® can be a life-saving medication for those with adrenal insufficiency (whether primary or secondary). During times of shortage of some vial sizes, the goal is to conserve available inventory so that medication is available to those who are at risk of acute adrenal insufficiency. In the event of a complete shortage of Solu-Cortef®, other less well-suited corticosteroids such as dexamethasone and methylprednisolone may be used.

## Additional Resources

- [The Canadian Addison Society](#)
- [Canadian Society of Endocrinology and Metabolism](#)
- [CARES Foundation](#)
- Reporting medication errors
  - o Report actual and potential medication errors to ISMP Canada at [www.mederror.ca](http://www.mederror.ca) (consumers) or [https://www.ismp-canada.org/err\\_report.htm](https://www.ismp-canada.org/err_report.htm) (health care providers) or by calling 1-866-54-ISMP.

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### References:

1. Health Canada. Drug Product Database Online Query. Ottawa (ON): Health Canada; 2022 [cited 22 Aug 2022]. Available from: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>.
2. Solu-Cortef [product monograph]. Kirkland (QC): Pfizer Canada ULC; 04 Mar 2022. Available from: [https://pdf.hres.ca/dpd\\_pm/00064949.PDF](https://pdf.hres.ca/dpd_pm/00064949.PDF)
3. Drug Shortages Canada. Search Products. [cited 22 Aug 2022]. Available from: <https://www.drugshortagescanada.ca/drugsearch?perform=0>
4. National Association of Pharmacy Regulatory Authorities (NAPRA). Model standards for pharmacy compounding of non-hazardous sterile preparations. Ottawa, ON: NAPRA; 2016 [cited 06 2022]. Available from: [https://napra.ca/sites/default/files/2017-09/Mdl\\_Stnds\\_Pharmacy\\_Compounding\\_NonHazardous\\_Sterile\\_Preparations\\_Nov2016\\_Revised\\_b.pdf](https://napra.ca/sites/default/files/2017-09/Mdl_Stnds_Pharmacy_Compounding_NonHazardous_Sterile_Preparations_Nov2016_Revised_b.pdf)

5. Lyon RC, Taylor JS, Porter DA, et al. Stability profiles of drug products extended beyond labeled expiration dates. *J Pharm Sci.* 2006 Jul;95(7):1549-60. doi: 10.1002/jps.20636. PMID: 16721796.
6. Liu D, Ahmet A, Ward L, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy Asthma Clin Immunol.* 2013 Aug 15;9(1):30. doi: 10.1186/1710-1492-9-30.
7. Miller BS, Spencer SP, Geffner ME, et al. Emergency management of adrenal insufficiency in children: advocating for treatment options in outpatient and field settings. *J Investig Med.* 2020 Jan;68(1):16-25. doi: 10.1136/jim-2019-000999.
8. Dexamethasone Omega Unidose [product monograph]. Montreal (QC): Omega Laboratories Limited; 12 Jun 2012 [cited 19 Jun 2022]. Available from: [https://pdf.hres.ca/dpd\\_pm/00020491.PDF](https://pdf.hres.ca/dpd_pm/00020491.PDF)
9. McKesson Canada. PharmaClik [Internet]. 2022 [cited 22 Aug 2022]. Available from <http://clients.mckesson.ca>. Account required.
10. Nieman L. Treatment of adrenal insufficiency in adults. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc; 2022 [updated 02 Feb 2022; cited 15 Jun 2022]. Available from: <https://www.uptodate.com> Subscription required.
11. Lexi-Comp Online Database [database on the Internet]. Hudson (OH): Lexi-Comp, Inc.; 2022 [cited 08 Aug 2022]. Available from: <http://online.lexi.com>. Subscription required.
12. Solu-Medrol [product monograph]. Kirkland (QC): Pfizer Canada ULC; 07 Feb 2022. Available from: [https://pdf.hres.ca/dpd\\_pm/00064686.PDF](https://pdf.hres.ca/dpd_pm/00064686.PDF)
13. Depo-Medrol [product monograph]. Kirkland (QC): Pfizer Canada ULC; 04 Feb 2021. Available from: [https://pdf.hres.ca/dpd\\_pm/00059909.PDF](https://pdf.hres.ca/dpd_pm/00059909.PDF)
14. De Vroede M, Beukering R, Spit M, et al. Rectal hydrocortisone during stress in patients with adrenal insufficiency. *Arch Dis Child.* 1998 Jun;78(6):544-7. doi: 10.1136/adc.78.6.544.
15. Newrick PG, Braatvedt G, Hancock J, et al. Self-management of adrenal insufficiency by rectal hydrocortisone. *Lancet.* 1990 Jan 27;335(8683):212-3. doi: 10.1016/0140-6736(90)90289-h.
16. Smith SM, Piszczatoski C, Gums JG. Adrenal Gland Disorders. In: DiPiro JT, Yee GC, Michael Posey LL, Haines ST, Nolin TD, Ellingrod VL. eds. *DiPiro: Pharmacotherapy A Pathophysiologic Approach*, 12e. McGraw Hill; 2021. Accessed June 24, 2022. <https://accesspharmacy.mhmedical.com/content.aspx?bookid=3097&sectionid=264604996>
17. Schimmer BP, Funder W. Adrenocorticotrophic Hormone, Adrenal Steroids, and the Adrenal Cortex. In: Brunton LL, Hilal-Dandan R, Knollmann BC. eds. *Goodman & Gilman's: The Pharmacological Basis of Therapeutics*, 13e. McGraw Hill; 2017. Accessed June 24, 2022. <https://accesspharmacy.mhmedical.com/content.aspx?bookid=2189&sectionid=172482605>
18. Dineen R, Thompson CJ, Sherlock M. Adrenal crisis: prevention and management in adult patients. *Ther Adv Endocrinol Metab.* 2019 Jun 13;10:2042018819848218. doi: 10.1177/2042018819848218.
19. Munir S, Quintanilla Rodriguez BS, Waseem M. Addison Disease. 2022 May 15. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. PMID: 28723023.
20. Arlt W. Disorders of the Adrenal Cortex. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. eds. *Harrison's Principles of Internal Medicine*, 20e. McGraw Hill; 2018. Accessed August 18, 2022. <https://accessmedicine.mhmedical.com/content.aspx?bookid=2129&sectionid=192287137>
21. Gjerstad JK, Lightman SL, Spiga F. Role of glucocorticoid negative feedback in the regulation of HPA axis pulsatility. *Stress.* 2018 Sep;21(5):403-416. doi: 10.1080/10253890.2018.1470238.
22. Ahmet A, Rowan-Legg A, Pancer L. Adrenal suppression from exogenous glucocorticoids: Recognizing risk factors and preventing morbidity. *Paediatr Child Health.* 2021 Jun 11;26(4):242-254. doi: 10.1093/pch/pxab015.
23. Nieman L. Causes of secondary and tertiary adrenal insufficiency in adults. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc; [updated 25 Feb 2021; cited 17 Aug 2022]. Available from: <https://www.uptodate.com> Subscription required.
24. He X, Findling JW, Auchus RJ. diagnosis and management of adrenal insufficiency. In: Levine, A. (eds) *Adrenal Disorders. Contemporary Endocrinology*. 2018. Humana Press, Cham. Available from: [https://doi.org/10.1007/978-3-319-62470-9\\_9](https://doi.org/10.1007/978-3-319-62470-9_9)
25. Raschi E, Fusaroli M, Massari F, et al. The changing face of drug-induced adrenal insufficiency in the Food and Drug Administration Adverse Event Reporting System. *J Clin Endocrinol Metab.* 2022 Jul 14;107(8):e3107-e3114. doi: 10.1210/clinem/dgac359.
26. Donohue P. Treatment of adrenal insufficiency in children. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc; [updated 01 Dec 2021; cited 15 Jun 2022]. Available from: <https://www.uptodate.com> Subscription required.
27. The Canadian Addison Society. Addison's Disease. Etobicoke, ON. [cited 19 Aug 2022]. Available from: <http://www.addisonsociety.ca/pdfs/cas-brochure.pdf>
28. Bornstein SR, Allolio B, Arlt W, et al. diagnosis and treatment of primary adrenal insufficiency: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2016 Feb;101(2):364-89. doi: 10.1210/jc.2015-1710.
29. Johannsson G, Skrtic S, Lennernäs H, et al. Improving outcomes in patients with adrenal insufficiency: a review of current and future treatments. *Curr Med Res Opin.* 2014 Sep;30(9):1833-47. doi: 10.1185/03007995.2014.925865.
30. SickKids. Your child's cortisol replacement instructions. Toronto (ON): SickKids; [18 Jun 2022] <https://www.sickkids.ca/siteassets/care--services/clinical-departments/endocrinology/stress-dosing-illness-dosing.pdf?hub=endocrinology>
31. Canadian Paediatric Society. Adrenal suppression from exogenous glucocorticoids: Recognizing risk factors and preventing morbidity. Ottawa (ON): CPS; [15 Jun 2021; cited 24 Jun 2022]. Available from: <https://cps.ca/documents/position/adrenal-suppression>.

32. ISMP Canada. Medication incidents involving drug tapering in community pharmacy. ISMP Canada Safety Bulletin; 2014 [cited 23 Aug 2022]. Available from: [https://www.ismp-canada.org/download/PharmacyConnection/PC2014-Fall\\_DrugTapering.pdf](https://www.ismp-canada.org/download/PharmacyConnection/PC2014-Fall_DrugTapering.pdf).
33. Preston CL (ed), Stockley's Drug Interactions. [online] London: Pharmaceutical Press; 2022 [cited 24 Jun 2022]. Available from: <http://www.medicinescomplete.com>.
34. Yanase T, Tajima T, Katabami T, et al. Diagnosis and treatment of adrenal insufficiency including adrenal crisis: a Japan Endocrine Society clinical practice guideline [Opinion]. Endocr J. 2016 Sep 30;63(9):765-784. doi: 10.1507/endocrj.EJ16-0242.
35. Hahner S, Burger-Stritt S, Allolio B. Subcutaneous hydrocortisone administration for emergency use in adrenal insufficiency. Eur J Endocrinol. 2013 Jun 29;169(2):147-54. doi: 10.1530/EJE-12-1057.
36. The Canadian Addison Society. Emergency medical information card. Etobicoke, ON; [cited 20 Aug 2022]. Available from: <https://addisonsociety.ca/pdfs/medical-information-card.pdf>
37. CARES Foundation. Medication safety alert: EMS protocols for adrenal crisis. Union (NJ); [cited 20 Aug 2022]. Available from: <https://caep.ca/wp-content/uploads/2019/12/EMSAdvisoryFINALGIEDIT.pdf>