Health Canada Santé Canada

Canada

Health Product InfoWatch

August 2024

Contents

REPORTING ADVERSE REACTIONS

Canada Vigilance Program
Online: Adverse Reaction and Medical Device Problem Reporting
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To receive the Health Product InfoWatch and notifications of health product advisories electronically, subscribe to MedEffect™ e-Notice or to MedEffect™ Canada RSS feeds.

This monthly publication is intended primarily for healthcare professionals and includes information on pharmaceuticals, biologics, medical devices and natural health products. It provides a summary of key health product safety information published in the previous month by Health Canada, as well as a selection of new health product safety information meant to raise awareness. New information contained in this issue is not comprehensive but rather represents a selection of clinically relevant items warranting enhanced dissemination.

MONTHLY RECAP OF HEALTH PRODUCT SAFETY INFORMATION

The following is a list of health product advisories, type I drug recalls and summaries of completed safety reviews published in July 2024 by Health Canada.

CPAP and BiLevel PAP machines and mechanical ventilators

Since 2021, Philips Respironics has established a registration portal for affected CPAP and BiLevel PAP machines and mechanical ventilators in Canada. Philips Respironics plans to close its registration portal at the end of December 2024, with the goal of completing its repair and replacement program by the end of June 2025. The company has asked that all customers who have not yet registered their devices do so as soon as possible.

Advisory: CPAP and BiLevel PAP machines and mechanical ventilators

Homemade sunscreens

Health Canada warned the public about the potential risks of making and using homemade sunscreens as they are unlikely to provide effective protection from the sun's harmful UV rays. Health Canada recommends using only authorized sunscreen products. All sunscreens approved for sale in Canada must have a Drug Identification Number (DIN) or Natural Product Number (NPN).

Advisory: Homemade sunscreens

Mega 2000 and Mega Soft Patient Return Electrodes

Megadyne received reports of patient and healthcare professional burns during or after surgical procedures in which Mega 2000 and Mega Soft Patient Return Electrode pads were used. Corrective actions have been taken to mitigate the potential health risk to healthcare professionals and patients, particularly focusing on children under 12 years of age. Health Canada is working with Megadyne to update the instructions for use for all affected product codes.

Health Professional Risk Communication: Mega 2000 and Mega Soft Patient Return Electrodes

Naloxone Take Home Kits by Canadian Hospital Specialties Ltd.

Naloxone Take Home Kits by Canadian Hospital Specialties Ltd. may contain incorrect naloxone dosing information on the "SAVE ME" instructional card, which could impact the efficacy of the treatment. The product labelling for naloxone indicates that, if necessary, a second dose of the product can be administered 2 to 3 minutes after the first dose. The "SAVE ME" instructional card provided in the kit may recommend re-administration after 3 to 5 minutes. This is an error. A recall was also posted.

Advisory: Naloxone Take Home Kit by Canadian Hospital Specialties Ltd.

Unauthorized health products

Health Canada advised Canadians about various unauthorized health products being sold at retail locations across Canada or online that may pose serious health risks.

Advisory: Unauthorized drug products sold illegally on Quadragen and Advanced Research websites

Advisory: Unauthorized sexual enhancement products

Various multivitamins and supplements

Factors Group of Nutritional Companies Inc. recalled various multivitamins and supplements sold under the following brands: Kirkland Signature, Life, Option+, Webber Naturals, Wellness by London Drugs, Equate, Wellquest, VegiDay, and Natural Factors. The affected products may contain metal fibres which, if ingested, may cause injury to the digestive system.

Advisory: Various multivitamins and supplements

NEW HEALTH PRODUCT SAFETY INFORMATION

The following topics have been selected to raise awareness and encourage reporting of adverse reactions.

Safety brief

Calcium carbonate antacids and milk-alkali syndrome in pregnancy

Calcium carbonate is a calcium salt that can be found in various antacid formulations. In Canada, calcium carbonate antacids are authorized for the symptomatic management of gastroesophageal reflux disorder (GERD).[1,2] The symptoms of GERD are common during pregnancy. Hormonal changes can cause the valve at the entrance to the stomach to relax, allowing some acid to pass through and cause symptoms.[3,4]

Milk-alkali syndrome (MAS) is a rare condition characterized by a triad of hypercalcemia, metabolic alkalosis, and acute kidney injury that typically occurs due to excessive ingestion of calcium in combination with absorbable alkali (such as calcium carbonate antacids). If left untreated, MAS can cause renal failure and systemic calcification.[5] Hormonal changes during pregnancy, which favor increased gastrointestinal calcium absorption, are likely to contribute to an elevated risk of MAS in the setting of high calcium intake.[4]

As of February 14th, 2024, Health Canada has received 2 Canadian adverse reaction reports and has identified 8 literature reports (including 1 Canadian) involving MAS in pregnancy associated with calcium carbonate antacid exposure. In all reports, MAS in pregnant individuals was associated with excessive intake of a calcium carbonate antacid product. When reported, dosing varied substantially between cases. However, in all cases, the dose and/or duration of consumption of calcium carbonate antacids exceeded labelled recommendations. In one case, a patient who developed MAS was reported to have taken upwards of 10 tablets per day (2000 mg elemental calcium per day), while in another case, the patient was consuming approximately 24 tablets per day paired with about 4 pints (approximately 2L) of milk. Commonly reported signs and symptoms of MAS observed in pregnant individuals included hypercalcemia, acute kidney injury, hypertension, nausea and vomiting, and lethargy/altered level of consciousness. Three case reports described

reduced/impaired fetal heart rate variability. All reported birth outcomes were considered favorable, with proper medical management of MAS. No fatal cases were identified for either the pregnant individual and/or the fetus or baby. In most cases, there was limited information as well as possible confounding factors (e.g., concomitant medications, medical history, other calcium carbonate sources, etc.) which prevented definitive causal associations from being determined.

Key messages for healthcare professionals:

- Healthcare providers are encouraged to inquire about proper use of calcium carbonate antacids in pregnant individuals.
- It is important to communicate the potential risk of MAS associated with excessive use of calcium carbonate antacids beyond labelled recommended amounts and duration while pregnant.
- Healthcare providers are encouraged to report any adverse reactions suspected of being associated with calcium carbonate antacid use to Health Canada.

Health Canada will also be communicating this issue through various social media channels to raise public awareness and promote proper product use.

Health Canada will continue to monitor the safety of calcium carbonate antacids, as it does for all health products on the Canadian market, to identify and assess potential harms. Health Canada will take appropriate and timely action should new health risks be identified.

References

1. Salisbury BH, Terrell JM. Antacids. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526049/
2. Health Canada. ANTACID LABELLING STANDARD. Published September 27th, 1994. Updated July 24th, 1996. Accessed June 24th, 2024. antacid_antiacid-eng.pdf (canada.ca)
3. Gastroesophageal Reflux Disease (GERD). Canadian Pharmacists Association (CPhA) Monograph [database online]. Updated April 30, 2021. Accessed July 6, 2024. https://www.e-therapeutics.ca/search
4. Kolnick L, Harris BD, Choma DP, Choma NN. Hypercalcemia in pregnancy: a case of milk-alkali syndrome. *J Gen Intern Med.* 2011 Aug;26(8):939-42. doi: 10.1007/s11606-011-1658-0
5. Rout P, Hashmi MF, Patel C. Milk-Alkali Syndrome. [Updated 2024 Jun 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557500/

Product monograph updates

The following safety labelling updates, which were recently made to the Canadian product monographs, have been included for your awareness. A complete list of safety labelling updates for pharmaceuticals is available on Health Canada's Product monograph brand safety updates page. Canadian product monographs can be accessed through Health Canada's Drug Product Database.

Clavulin (amoxicillin and clavulanate potassium) and other amoxicillin-containing products

The *Warnings and Precautions*, *Adverse Reactions* and *Patient Medication Information* sections of the Canadian product monographs for Clavulin and other amoxicillin-containing products* have been or will be updated with the risk of **drug-induced enterocolitis syndrome.**

Key messages for healthcare professionals:[1]

- Drug-induced enterocolitis syndrome, an allergic reaction with the leading symptom of protracted vomiting (1-4 hours after medicinal product administration), in the absence of allergic skin or respiratory symptoms, has been reported mainly in children receiving amoxicillin-containing products. Further symptoms could comprise of abdominal pain, lethargy, diarrhea, hypotension or leucocytosis with neutrophilia. In severe cases, drug-induced enterocolitis syndrome can progress to shock.
- Patients should be advised to stop taking the amoxicillin-containing product and seek immediate medical help if they experience symptoms of drug-induced enterocolitis syndrome, as these can be a sign of a serious allergic reaction.

*At the time of publication, the Canadian product monograph update for Clavulin has been completed. Updates for other amoxicillin-containing products are ongoing.

Reference

1. *Clavulin (amoxicillin and clavulanate potassium)* [product monograph]. Mississauga (ON): GlaxoSmithKline Inc.; 2024.

Retevmo (selpercatinib)

The *Warnings and Precautions*, *Adverse Reactions* and *Patient Medication Information* sections of the Canadian product monograph for Retevmo have been updated with the risk of **slipped capital femoral epiphysis/slipped upper femoral epiphysis.**

Key messages for healthcare professionals:[1]

- Slipped capital femoral epiphysis/slipped upper femoral epiphysis (SCFE/SUFE) has been reported in adolescent patients receiving Retevmo.
- Monitor adolescent patients for symptoms indicative of SCFE/SUFE, such as complaints of hip/knee pain or onset of a limp, and treat as medically and surgically appropriate.

Reference

1. *Retevmo (selpercatinib) [product monograph].* Toronto (ON): Eli Lilly Canada Inc; 2024.

Sodium-glucose cotransporter-2 (SGLT2) inhibitors: Invokana (canagliflozin), Invokamet (canagliflozin/metformin), Forxiga (dapagliflozin), Xigduo (dapagliflozin/metformin), Jardiance (empagliflozin) and Synjardy (empagliflozin/metformin)

The *Dosage and Administration* and *Warnings and Precautions* sections of the Canadian product monographs for SGLT2 inhibitors* have been or will be updated with the risk of **prolonged diabetic ketoacidosis (DKA)** despite SGLT2 inhibitor discontinuation and standard treatment of DKA, and with recommendations on **when to interrupt SGLT2 inhibitor treatment prior to major surgical procedures** in patients with type 2 diabetes mellitus (T2DM).

Key messages for healthcare professionals:[1,2]

- DKA associated with SGLT2 inhibitors may be prolonged in some patients. In most post-marketing adverse event reports of suspected or confirmed DKA, ketoacidosis lasted for 3 days or more despite SGLT2 inhibitor discontinuation, as part of standard DKA management.
- Cases of DKA following surgical procedures have also been reported in which SGLT2 inhibitor treatment was withheld for 2 days or less before surgery. SGLT2 inhibitor treatment should be temporarily stopped for at least 3 days, if possible, before major surgery or any other procedures requiring prolonged fasting when, based on the drug's half-life, most of the SGLT2 inhibitor would be expected to be eliminated.
- Monitoring for DKA is recommended in post-operative patients even if SGLT2 inhibitor treatment has been interrupted or discontinued. Ensure risk factors for ketoacidosis are resolved prior to considering SGLT2 inhibitor treatment re-initiation.

*At the time of publication, the Canadian product monograph updates for Invokana and Invokamet have been completed. Updates for other SGLT2 inhibitors are ongoing.

Reference

1. *Invokana (canagliflozin)* [product monograph]. Toronto (ON): Janssen Inc.; 2024.
2. *Invokamet (canagliflozin/metformin)* [product monograph]. Toronto (ON): Janssen Inc.; 2024.

Helpful links

- Recalls and Safety Alerts Database
- New Safety and Effectiveness Reviews
- Canada Vigilance Adverse Reaction Online Database
- Drug Product Database
- Medical Devices Active Licence Listing
- Licensed Natural Health Products Database
- The Drug and Health Product Portal
- Drug Shortages Canada
- Medical device shortages
- COVID-19 vaccines and treatments portal

Contact us

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Adverse reactions (ARs) to health products are considered to be suspicions, as a definite causal association often cannot be determined. Spontaneous reports of ARs cannot be used to estimate the incidence of ARs because ARs remain underreported and patient exposure is unknown.

Due to time constraints relating to the production of this publication, information published may not reflect the most current information.

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