Health Canada Santé Canada

Canada

Health Product InfoWatch

November 2023

CONTENTS

REPORTING ADVERSE REACTIONS

Canada Vigilance Program
Online: Adverse Reaction and Medical Device Problem Reporting
Telephone: 1-866-234-2345
Fax or mail: Form available online

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HEALTH PRODUCTS MENTIONED IN THIS ISSUE

Pharmaceuticals and biologics
- Baxter intravenous solution bags
- Dimethyl Fumarate
- Potassium Chloride for Injection Concentrate
- Vitrakvi (larotrectinib)

Natural and non-prescription health products
- Melatonin

Other
- Unauthorized health products

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 October 2023 by Health Canada.

Baxter intravenous solution bags Health Product Risk Communication **Type 1 drug recalls:** 0.9% Sodium Chloride Injection, USP 5% Dextrose Injection, USP Gentamicin(E) Sulfate Metronidazole Injection, USP	Intravenous bags of Baxter's 0.4% Lidocaine & 5% Dextrose Injection 250 mL; 0.9% Sodium Chloride Injection, USP 100 mL and 250 mL; Lactated Ringer's Injection, USP 250 mL; and Metronidazole Injection, USP 100mL from certain lots have the potential to leak during the process of spiking the administration port. The affected lots are not being recalled at this time in order to prevent a shortage of these medically necessary products. Healthcare professionals are advised to NOT use the product if the defect is observed, follow guidance on the handling and verification of affected products, and ensure preparedness at points of use where affected products are identified. Baxter Corporation recalled certain affected lots of: 0.9% Sodium Chloride Injection, USP; 5% Dextrose Injection, USP; Gentamicin(E) Sulfate; and Metronidazole Injection, USP as the solution bags may be leaking.
Dimethyl Fumarate Summary Safety Review	This safety review evaluated the risk of Fanconi syndrome associated with dimethyl fumarate. Health Canada's review did not find sufficient evidence to support a link. Health Canada will continue to monitor safety information involving dimethyl fumarate.
Potassium Chloride for Injection Concentrate Health Product Risk Communication	Due to a shortage of Potassium Chloride for Injection Concentrate (149 mg/mL) products in Canada and given the medical necessity of this product, Health Canada permitted the exceptional, temporary importation and sale of UK-authorized Potassium Chloride 15% w/v Concentrate for Solution for Infusion with English-only labels. Healthcare professionals are advised that there are significant differences in the packaging formats and related preparation instructions, and inner and outer labels of the UK-authorized product (150 mg/mL) compared to the Canadian-authorized products (149 mg/mL), which may increase the risk for medication errors.

Unauthorized health products Unauthorized health products seized from online retailer "UU Zone" Unauthorized health products sold online Unauthorized sexual enhancement products Unauthorized skin lightening and skin treatment products Various unauthorized health products known as "poppers"	Health Canada advised Canadians about various unauthorized health products being sold at retail locations across Canada or online that may pose serious health risks.

NEW HEALTH PRODUCT SAFETY INFORMATION

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

Safety brief

Melatonin and increased accidental ingestions in children

Melatonin is a natural hormone primarily secreted by the pineal gland that regulates the sleep-wake cycle.[1] In Canada, melatonin is regulated as a natural health product to help promote regular sleep cycles in adults.[2,3] Numerous melatonin health products are available on the Canadian market in various dosage forms including capsules, tablets, gummies, and sublingual tablets. No melatonin products are currently licensed in Canada for use in children and adolescents under the age of 18.

Between January 2016 and April 2022, the number of accidental melatonin ingestions reported to Canadian Poison Control Centres increased compared to previous years. These reports primarily involved children 5 years of age and younger, and the majority of accidental ingestions may have involved a gummy dosage form. The formulation's visual appearance, texture, and taste could have appealed to young children. Health Canada did not find evidence of harm following accidental ingestion in these children. The vast majority of reported accidental melatonin ingestions resulted in either minor or no adverse reactions and no fatal outcome has been reported.

Parents and caregivers should be reminded to keep all health products, including melatonin products, out of the reach and sight of children. Health Canada will also notify consumers of this issue through various social media channels including Facebook, X (formerly known as Twitter), and LinkedIn.

Healthcare professionals are encouraged to report any adverse reactions suspected of being associated with melatonin, including, but not limited to, adverse reactions following accidental ingestion, to the Canada Vigilance Program.

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

References

1. Savage RA, Zafar N, Yohannan S, et al. *Melatonin*. *Nih.gov*. Published October 23, 2019. Accessed September 25, 2023.
2. Health Canada. *Melatonin - Oral* [monograph]. Published August 28, 2018. Accessed September 25, 2023.
3. Health Canada. *Melatonin - Sublingual* [monograph]. Published July 31, 2018. Accessed September 25, 2023.

Product monograph update

The following safety labelling update, which was recently made to the Canadian product monograph, has been selected 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.

Vitrakvi (larotrectinib)

The *Dosage and Administration*, *Warnings and Precautions*, *Adverse Reactions*, and *Drug Interactions* sections of the Canadian product monograph for Vitrakvi have been updated with the risks of **hepatotoxicity and drug interaction involving moderate cytochrome P450 (CYP) 3A4 inducers**.

Key messages for healthcare professionals:[1]

- Cases of hepatotoxicity with increases in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) of Grade 2, 3 or Grade 4 severity and increases in bilirubin ≥ 2 x ULN (upper limit of normal) have been reported in adult patients receiving Vitrakvi.
- Consider baseline assessment of liver function, including transaminase levels, before the first dose. Monitor liver function including ALT, AST, alkaline phosphatase (ALP), and bilirubin during treatment (see Section 7: Warning and Precautions, Hepatic/Biliary/Pancreatic, in the Vitrakvi Canadian product monograph for details on management of liver function test abnormalities).
- In patients with hepatic transaminase elevations, withhold, modify dose, or permanently discontinue Vitrakvi based on the severity (see Section 4: Dosage and Administration, Table 2, in the Vitrakvi Canadian product monograph for details on recommended dose modifications).
- Vitrakvi is a substrate of ***CYP 3A***. Coadministration of Vitrakvi with moderate (or strong) *CYP3A4* inducers may decrease Vitrakvi plasma concentrations.

Reference

1. *Vitrakvi (larotrectinib)* [product monograph]. Mississauga (ON): Bayer Inc; 2023.

Helpful links

- MedEffect™ Canada
- 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: List of shortages and discontinuations
- Stop Illegal Marketing of Drugs and Devices
- List of drugs for exceptional importation and sale
- Coronavirus disease (COVID-19)
- Drug and vaccine authorizations for COVID-19: List of authorized drugs, vaccines and expanded indications
- COVID-19 vaccines and treatments portal
- Reported side effects following COVID-19 vaccination in Canada

Suggestions?

Your comments are important to us. Let us know what you think by reaching us at: infowatch-infovigilance@hc-sc.gc.ca

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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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