Health Canada Santé Canada

Canada

Health Product InfoWatch

April 2023

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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.

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Announcement:

Celebrating the 100th Issue of the Health Product InfoWatch!

Health Canada is publishing it's 100th issue of the Health Product InfoWatch this month, a major milestone! The Health Product InfoWatch was launched in 2015 to replace the Canadian Adverse Reaction Newsletter and over the past 8 years has provided clinically relevant health product safety information to Canadian healthcare professionals. Topics have ranged from safety reminders, important updates to Canadian product monographs, information on medication errors, and, more recently, timely communications concerning COVID-19 vaccines and treatments. The Editorial Team would like to take this opportunity to thank readers for their continued interest.

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.

DRUG AND VACCINE AUTHORIZATIONS AND COMMUNICATIONS FOR COVID-19

New information and recent communications related to authorized COVID-19 vaccines and treatments are highlighted in this section.

Safety brief

Viral vector-based COVID-19 vaccines (Vaxzevria and JCOVDEN) and the risk of thrombosis with thrombocytopenia syndrome

In Canada, authorized viral vector-based COVID-19 vaccines include Vaxzevria* (AstraZeneca COVID-19 Vaccine) and JCOVDEN (Janssen COVID-19 Vaccine). Both vaccines are indicated for active immunization in individuals 18 years of age and older for the prevention of coronavirus disease 2019 (COVID-19).[1,2]

Thrombosis with thrombocytopenia syndrome (TTS) is a very rare adverse event involving blood clots (thrombosis) with low platelets (thrombocytopenia). Reports of TTS following vaccination with viral vector-based COVID-19 vaccines first emerged in Europe in 2021. In response to this potential safety issue, Health Canada notified the public of these reports[3], assessed the available data[4,5] and, after confirming a possible link between the use of viral vector-based COVID-19 vaccines and TTS, communicated these findings.[6-8] Health Canada also worked with the manufacturers of Vaxzevria and JCOVDEN to update the Canadian product monographs for these products with warnings about TTS.[1,2]

In March 2023, Health Canada completed a follow-up review of TTS that took into consideration recent Canadian[9] and international data. This review was triggered by an investigation conducted by the United States Food and Drug Administration that resulted in further restrictions to the authorized use of the Janssen COVID-19 Vaccine in the United States.[10]

Overall, Health Canada's follow-up review did not identify any new safety information; its findings were consistent with information previously published by the Department. As of October 31, 2022, there have been no reports of TTS following vaccination with JCOVDEN in Canada, and the majority of reports associated with Vaxzevria date back to 2021. A precise mechanism by which these vaccines cause TTS is still unknown.

The current Canadian product safety information for Vaxzevria and JCOVDEN remains accurate and accounts for the evolving nature of the data. Health Canada will continue to monitor the safety of viral vector-based COVID-19 vaccines and will take appropriate action should new health risks be identified.

Safety reminders:

- Healthcare professionals should be alert to, and inform vaccine recipients of, the signs and symptoms of thrombosis, thromboembolism, and/or thrombocytopenia following the administration of a viral vector-based COVID-19 vaccine.
- The majority of cases of TTS occurred within 3 weeks following vaccination.

- Clinical information on TTS is described in the Canadian product monographs for Vaxzevria and JCOVDEN.
- Healthcare professionals are encouraged to report adverse reactions suspected of being associated with COVID-19 vaccines.

For information on authorized COVID-19 vaccines and treatments, please visit the COVID-19 vaccines and treatments portal.

References

1. *Vaxzevria (COVID-19 Vaccine (ChAdOx1-S [recombinant])* [product monograph]. Mississauga (ON): AstraZeneca Canada Inc.; 2022.
2. *JCOVDEN (COVID-19 Vaccine (Ad26.COV2-S [recombinant])* [product monograph]. Toronto (ON): Janssen Inc.; 2023.
3. Health Canada. *Adverse events in Europe following immunization with the AstraZeneca COVID-19 vaccine* [Public Advisory]. Published March 11, 2021. Accessed March 14, 2023.
4. Health Canada. *Summary Safety Review - AstraZeneca and COVISHIELD COVID-19 Vaccines - Assessing the Potential Risk of Thrombosis in combination with Thrombocytopenia.* Published April 19, 2021. Accessed March 14, 2023.
5. Health Canada. *Summary safety review - Janssen COVID-19 Vaccine - Assessing the Potential Risk of Thrombosis in combination with Thrombocytopenia.* Published May 4, 2021. Accessed March 14, 2023.
6. Health Canada. *Health Canada issues label change and guidance on the AstraZeneca COVID-19 vaccine* [Statement]. Published March 24, 2021. Accessed March 14, 2023.
7. Health Canada. *AstraZeneca COVID-19 Vaccine and COVISHIELD: Risk of Thrombosis with Thrombocytopenia* [Health Product Risk Communication]. Published March 24, 2021. Accessed March 14, 2023.
8. Health Canada. *Janssen COVID-19 Vaccine and the Risk of Thrombosis with Thrombocytopenia* [Health Product Risk Communication]. Published April 26, 2021. Accessed March 14, 2023.
9. Public Health Agency of Canada. *Thrombosis with thrombocytopenia syndrome: Findings from the Advisory Committee on Causality Assessment.* Updated January 11, 2023. Accessed March 14, 2023.
10. U.S. Food and Drug Administration. *Coronavirus (COVID-19) Update: FDA Limits Use of Janssen COVID-19 Vaccine to Certain Individuals* [FDA News Release]. Published May 5, 2022. Accessed March 14, 2023.

* COVISHIELD (Verity Pharmaceuticals Inc/Serum Institute of India, in partnership with AstraZeneca Canada Inc) is a viral vector-based COVID-19 vaccine that was also authorized for use in Canada; however, its authorization by interim order expired on September 16, 2021.

MONTHLY RECAP OF HEALTH PRODUCT SAFETY INFORMATION

The following is a list of health product advisories, type I recalls and summaries of completed safety reviews published in March 2023 by Health Canada.

Cayston (aztreonam) Advisory	Gilead Sciences Incorporated recalled 2 lots of the cystic fibrosis drug Cayston (aztreonam) due to the potential of cracked glass vials in those lots, which may introduce glass particles into the medication.

Cloxacillin-containing products Summary Safety Review	This safety review evaluated the risk of acute kidney injury associated with the use of cloxacillin-containing products. Health Canada's review of the available information did not establish a link. Health Canada will work with the manufacturers to update the Canadian product monographs for cloxacillin-containing products to note that cases of acute kidney injury have been reported and to increase awareness of this potential risk.
Istodax (romidepsin) Health Product Risk Communication	In 2013, Istodax (romidepsin) was authorized under a Notice of Compliance with conditions for the treatment of patients with relapsed/refractory peripheral T-cell lymphoma who are not eligible for transplant and have received at least one prior systemic therapy, pending the results of trials to verify its clinical benefit. Istodax is now available only under Celgene Inc.'s (a Bristol-Myers Squibb company) Restricted Access Program and should **not** be initiated in new patients. This is based on a Phase 3 confirmatory study that failed to demonstrate Istodax, in combination with chemotherapy, was more effective than chemotherapy alone at delaying the progression of PTCL.
Nitroglycerin Sprays Advisory	Canada is experiencing a shortage of nitroglycerin 0.4 MG/ACT sprays due to supply issues with the raw materials used to make the sprays as well as an increase in demand. Health Canada is asking people to only obtain what they need from their pharmacy; keep expired product; and check the chart in the advisory to confirm which product(s) can be used beyond their Original (Printed) Expiry Date.
Proglycem (diazoxide) Summary Safety Review	This safety review evaluated the risk of pericardial effusion associated with the use of Proglycem (diazoxide). Health Canada's review of the available information found a possible link. Health Canada is working with the manufacturer to update the Canadian product monograph for Proglycem with a warning about cases of pericardial effusion having been observed, including in infants and children.
Unauthorized health products Unauthorized children's syrups Robikids and Solmux Unauthorized health products from Kausch International Goods Unauthorized sexual enhancement 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.

NEW HEALTH PRODUCT SAFETY INFORMATION

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

Product monograph updates

The following safety labelling updates, which were recently made to the Canadian product monographs, have 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.

ella (ulipristal acetate)

The *Warnings and Precautions, Drug-Drug Interactions*, and *Patient Medication Information* sections of the Canadian product monograph for ella have been updated with **instructions on initiating or resuming a regular hormonal contraceptive** following the intake of ella.

Key messages for healthcare professionals:[1]

- Pharmacodynamic data shows that progestin-containing contraceptives may interfere with the ability of ella to delay ovulation.
- If a woman wishes to initiate or resume a regular hormonal contraceptive, she can do so, no sooner than 5 days after the intake of ella provided she uses a reliable barrier method until her next menstrual period.
- In addition, if a woman used ella due to a known or suspected failure of her hormonal contraception, refer to the prescribing information for that specific hormonal contraceptive for further instructions on what to do.

Reference

1. *ella (ulipristal acetate)* [product monograph]. St-Laurent (QC): AbbVie, 2023.

Purinethol (mercaptopurine)

The *Serious Warnings and Precautions Box, Warnings and Precautions, Adverse Reactions*, and *Patient Medication Information* sections of the Canadian product monograph for Purinethol have been updated with the risk of **macrophage activation syndrome (MAS)**.

Key messages for healthcare professionals:[1]

- MAS is a known, life-threatening disorder that may develop in patients with autoimmune conditions, in particular with inflammatory bowel disease, and there could potentially be an increased susceptibility for developing the condition with the use of Purinethol.
- If MAS occurs, or is suspected, evaluation and treatment should be started as early as possible, and treatment with Purinethol should be discontinued.
- Physicians should be attentive to symptoms of infection such as Epstein-Barr virus and cytomegalovirus, as these are known triggers for MAS.

Reference

1. *Purinethol (mercaptopurine)* [product monograph]. Toronto (ON): Teva Canada Limited; 2023.

Notice of market authorization with conditions

*A Notice of Compliance with Conditions (NOC/c) is a form of market authorization with conditions granted to a product on the basis of **promising** evidence of clinical effectiveness following review of the submission by Health Canada. Communicating a NOC/c is intended to raise awareness on the details of the drug and the type of authorization granted.*

Healthcare professionals are encouraged to report to Health Canada any adverse reactions suspected of being associated with marketed health products, including drugs authorized under the NOC/c policy.

The content of these notices reflects current information at the time of publication. Conditions associated with the NOC/c will remain until they have been fulfilled and authorized by Health Canada. For the most up-to-date information, consult Health Canada's NOC database.

Columvi (glofitamab for injection): Authorization with conditions

Health Canada has issued a Notice of Compliance, under the NOC/c policy, for Columvi (glofitamab for injection) concentrate for solution for intravenous infusion. Columvi is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from follicular lymphoma (trFL), or primary mediastinal B-cell lymphoma (PMBCL), who have received two or more lines of systemic therapy and are ineligible to receive or cannot receive CAR-T cell therapy or have previously received CAR-T cell therapy. Patients should be advised of the conditional market authorization for this indication.

For the complete prescribing information and information available for patients/caregivers, please consult the Columvi Canadian product monograph. The product monograph can be accessed through Health Canada's Drug Product Database, the Hoffmann-La Roche Limited website or by contacting Hoffmann-La Roche Limited at 1-888-762-4388. Contact the company for a copy of any references, attachments or enclosures.

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 Register
- 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)
- 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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