Health Canada Santé Canada

Canada

Health Product InfoWatch

January 2022

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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

SUBSCRIBE

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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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.

CORONAVIRUS DISEASE (COVID-19)

For the most up-to-date information on COVID-19, please visit the Government of Canada Coronavirus disease (COVID-19) Web site **Canada.ca/coronavirus**, which includes a dedicated section for healthcare professionals and for the health product industry.

The COVID-19 vaccines and treatments portal provides information for consumers, healthcare professionals and researchers on vaccines and treatments authorized for COVID-19.

For information about adverse events following immunization that individuals have reported after receiving a COVID-19 vaccine in Canada, new safety signals or other safety updates, please visit the COVID-19 vaccine safety in Canada webpage, which is updated weekly.

DRUG AND VACCINE AUTHORIZATIONS AND COMMUNICATIONS FOR COVID-19

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

Casirivimab and Imdevimab

There is a high risk of treatment failure with the casirivimab and imdevimab combination based on analysis of neutralization activity against selected mutations of the SARS-CoV-2 Omicron variant. The Canadian product monograph for casirivimab and imdevimab will be updated to include new information about this Variant of Concern.

Health Professional Risk Communication – Casirivimab and Imdevimab

Paxlovid (nirmatrelvir and ritonavir)

Paxlovid was authorized by Health Canada on January 17, 2022 for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

Paxlovid is not recommended in patients with severe renal impairment and requires a dosage reduction in patients with moderate renal impairment. Paxlovid may also interact with various medications, which could result in serious or life-threatening adverse reactions, or a loss of therapeutic effect and possible development of viral resistance. In order to provide rapid access to Paxlovid, Pfizer will distribute product cartons and blisters labelled in English-only for a period of time. As a result, important Canadian-specific information is absent from these labels.

Authorization with terms and conditions – Paxlovid (nirmatrelvir and ritonavir)
Health Professional Risk Communication – Paxlovid (nirmatrelvir and ritonavir)

Spikevax (COVID-19 Vaccine Moderna)

Health Canada has authorized a shelf-life extension, from 7 months to 9 months, for SPIKEVAX / COVID-19 Vaccine Moderna 5 mL vials. This 2-month extension may be retroactively applied to vials that are currently on the market with printed expiry dates between February 2022 and August 2022, as long as the approved storage conditions have been maintained.

Health Professional Risk Communication – Spikevax (COVID-19 Vaccine Moderna)

ANNOUNCEMENTS

Updates to MedEffect e-Notice service

The MedEffect e-Notice is a free subscription service that provides email notifications to keep subscribers up to date and informed when Health Canada publishes new health product safety information, including health professional risk communications, public advisories and the Health Product InfoWatch. The MedEffect e-Notice has been upgraded with a modernized look and feel. Subscribers will now have access to a wider range of customization features, giving more options in the type of information they receive, including product lines, and how this information is delivered. To sign up for this service, please visit the Stay Informed Medeffect Canada web page. Current subscribers received an email on January 18 to update their preferences.

Transition of tramadol to a controlled substance and narcotic

Tramadol is a synthetic opioid analgesic that has been marketed in Canada since 2005. It is regulated under the *Food and Drugs Act*, and is available by prescription only for the management of moderate to moderately severe pain. As of March 31, 2022, tramadol will be removed from the Canadian Prescription Drug List and included in the schedules of the *Controlled Drugs and Substances Act* (CDSA) and the *Narcotic Control Regulations* (NCR).

On March 31, 2021, Health Canada published in Canada Gazette, Part II, the addition of tramadol as a controlled substance and narcotic to Schedule I of the CDSA and to the NCR. This change will come into effect on March 31, 2022.

These regulatory amendments are intended to provide additional safeguards around the use of tramadol to help prevent problematic substance use and other harms, while also protecting access to these medications for patients who need them.

Tramadol products sold and distributed by manufacturers after March 31, 2022 must include the updated labelling with the “N” narcotic symbol. In order to facilitate the transition and avoid disruption in market access, any products already sold and distributed by manufacturers prior to March 31, 2022, or product remaining at wholesalers or pharmacies, may continue to be sold until market depletion.

For further information, please see the Notice of intent to amend: Prescription Drug List: Tramadol.

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 December 2021 by Health Canada.

For health product advisories related to COVID-19 vaccines and treatments, please see the Drug and vaccine authorizations and communications for COVID-19 section.

Aimovig (erenumab) Summary Safety Review	This safety review evaluated the risks of non-fatal stroke, non-fatal heart attack and cardiovascular death associated with Aimovig. Health Canada's review of the available information could not confirm a link. Health Canada will continue to monitor safety information involving Aimovig.
Amoxicillin-containing products Summary Safety Review	This safety review evaluated the risk of aseptic meningitis associated with amoxicillin-containing products. Health Canada's review of the available information concluded that there may be a link. Health Canada will work with the manufacturers to include this risk in the Canadian product monographs for amoxicillin-containing products that do not already contain this safety information.
Certain hand sanitizers that may pose health risks Advisory	Health Canada advised Canadians that certain hand sanitizers were recalled because they either contained ingredients that were not permitted by Health Canada, were not properly labelled, were unauthorized, were missing important safety information, or for other safety related issues.
Cold and flu powdered medications Advisory	CellChem Pharmaceuticals Inc. recalled all lots of cold and flu medications, sold in pouches of dissolvable powder, due to potential health risks. The products are authorized for use in adults and children 12 years of age and older. They are available over-the-counter and sold under various generic store-brand labels at many retailers across Canada.
Domperidone Summary Safety Review Health Product InfoWatch	This follow-up safety review evaluated the risks of serious ventricular arrhythmia, QT interval prolongation and sudden cardiac death associated with the authorized and off-label (lactation promotion) use of domperidone. Health Canada's review of the available information found no new safety information related to these risks for either the authorized or off-label use of domperidone. As a result, no further updates to the Canadian product monographs are warranted. Health Canada is also communicating this information to healthcare professionals.

Health products manufactured by Eco-Med Pharmaceuticals Inc. Advisory	Medical devices manufactured by Eco-Med Pharmaceuticals, Inc. and being sold by DJO LLC and DJO France were recalled voluntarily due to potential bacterial contamination with *Burkholderia stabilis*. See table of affected products in the advisory for a full list of recalled products.
Herberex Advisory	Health Canada warned consumers not to use Herberex, advertised as an herbal product for sexual enhancement, because it may pose serious health risks. Herberex was authorized as a natural health product, but Health Canada testing found the product contained nortadalafil.
Ranitidine Advisory	Pharmascience Inc. recalled 18 lots of over-the-counter ranitidine drugs (75 mg and 150 mg tablets) after tests found N-nitrosodimethylamine (NDMA), a nitrosamine impurity, close to and above the acceptable level.
Unauthorized health products Advisory – Unauthorized Dr. pen microneedling devices Advisory – Various 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.

NEW HEALTH PRODUCT SAFETY INFORMATION

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

Safety brief

Domperidone and serious ventricular arrhythmias, QT interval prolongation and sudden cardiac death

Domperidone is a prescription drug that has been marketed in Canada since 1985. It is indicated for the symptomatic management of upper gastrointestinal motility disorders associated with chronic and subacute gastritis and diabetic gastroparesis.[1] It may also be used to prevent gastrointestinal symptoms associated with the use of dopamine agonist antiparkinsonian agents. Domperidone products have not been authorized by Health Canada for use in lactation promotion. However, domperidone has been prescribed off-label to promote lactation in postpartum women.[2]

Health Canada has communicated about cardiac risks associated with domperidone use to healthcare professionals and the public.[3-5] The Canadian product monographs for domperidone were updated with a boxed warning about potential cardiac adverse events, including sudden cardiac death.[1] Updated labelling also included a maximum daily recommended dose of 30 mg, as well as new restrictions for use in patients

with certain medical conditions that may increase the risk of cardiac adverse events, or taking drugs that may interact with domperidone.

In 2021, Health Canada conducted a follow-up safety review of serious ventricular tachycardia, QT interval prolongation and sudden cardiac death to consider recent information since the completion of the safety reviews in 2014. Health Canada reviewed adverse reaction case reports from the Canada Vigilance database. The Department also analyzed new information from the scientific literature, including data from a study by the Canadian Network for Observational Drug Effect Studies (CNODES), which examined the potential risk of serious ventricular arrhythmia and sudden cardiac death in association with the off-label use of domperidone to stimulate lactation during the postpartum period.[2] Health Canada's current review of available information concluded that the evidence does not suggest new cardiac safety risks, and that the safety information for this product is appropriate at this time. However, given the potential off-label use in postpartum women, Health Canada would like to provide healthcare professionals with the following safety reminders.

Safety reminders

- Clinical information on potential cardiac risks, including QT interval prolongation, serious ventricular arrhythmias, and sudden cardiac death are described in the Canadian product monographs for domperidone.
- The recommended maximum daily dose for authorized indications is 30 mg a day.
- Healthcare professionals are encouraged to report any adverse reactions suspected of being associated with domperidone to the Canada Vigilance Program.

Health Canada will continue to monitor the safety of domperidone, 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. *Bio-Domperidone (domperidone maleate)* [product monograph]. Montreal (QC): Biomed Pharma; 2020.
2. Moriello C, Paterson JM, Reynier P, et al. Off-label postpartum use of domperidone in Canada: a multidatabase cohort study. *CMAJ Open* 2021;9(2):E500-9.
3. Djelouah I, Scott C. Domperidone: heart rate and rhythm disorders. *Can Advers Reaction Newsl* 2007;17(1): 2.
4. Domperidone Maleate - Association with Serious Abnormal Heart Rhythms and Sudden Death (Cardiac Arrest) - For Health Professionals [Dear Healthcare Professional Letter]. Ottawa (ON): Health Canada; 2012. (accessed 2021 Nov 1)
5. Domperidone Maleate - Association with Serious Abnormal Heart Rhythms and Sudden Death (Cardiac Arrest) - For Health Professionals [Dear Healthcare Professional Letter]. Ottawa (ON): Health Canada; 2015. (accessed 2021 Nov 1)

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.

Biaxin (clarithromycin)

The *Contraindications, Warnings and Precautions, Drug Interactions* and *Patient Medication Information* sections of the Canadian product monograph for Biaxin have been updated with new safety information concerning use in patients with **electrolyte disturbances (hypokalemia or hypomagnesemia)** as well as a **potential drug interaction with direct acting oral anticoagulants**. Health Canada is working with the manufacturers to update the Canadian product monographs for other clarithromycin-containing products marketed in Canada.

Key messages for healthcare professionals:[1]

- Biaxin is contraindicated in patients with electrolyte disturbances (hypokalemia or hypomagnesemia) due to the risk of QT interval prolongation and torsades de pointes.
- Caution should be exercised when clarithromycin is co-administered with direct acting oral anticoagulants, such as dabigatran, rivaroxaban, and apixaban, particularly to patients at high risk of bleeding.

Reference

1. *Biaxin (clarithromycin)* [product monograph]. Etobicoke (ON): BGP Pharma ULC, 2021.

Cyklokapron (tranexamic acid)

The *Contraindications, Warnings and Precautions, Dosage and Administration* and *Patient Medication Information* sections of the Canadian product monograph for Cyklokapron have been updated with the **risk of error(s) due to incorrect route of administration.** The *Warnings and Precautions, Dosage and Administration* and *Patient Medication Information* sections have been updated with the **increased risk for thromboembolic events when used concomitantly with hormonal contraceptives**.

Key messages for healthcare professionals:[1]

- Cyklokapron solution for injection is intended for intravenous injection or infusion only.
- Intrathecal and epidural administration of Cyklokapron is contraindicated.
- Erroneous administration of Cyklokapron solution for injection via intrathecal or epidural routes has resulted in serious harm, including death.
- Care should be exercised to confirm the correct route of administration when other injectable medications are to be administered during the same procedure with Cyklokapron.
- The risk for thromboembolic events may be increased in patients using hormonal contraceptives concomitantly. If Cyklokapron has to be used in these patients, advise them to use an effective, alternative (non-hormonal) contraceptive method.

Reference

1. *Cyklokapron (tranexamic acid)* [product monograph]. Kirkland (QC): Pfizer Canada ULC, 2021.

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.

Jemperli (dostarlimab): Authorization with conditions

Health Canada has issued a Notice of Compliance, under the NOC/c policy, for Jemperli (dostarlimab), solution for infusion, 500 mg/10 mL vial. Jemperli is indicated as monotherapy for the treatment of adult patients with mismatch repair deficient or microsatellite instability-high recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum containing regimen. 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 Jemperli Canadian product monograph. The product monograph can be accessed through Health Canada's Drug Product Database, the GlaxoSmithKline Inc. website or by contacting GlaxoSmithKline Inc. at 1-800-387-7374. 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
- Stop Illegal Marketing of Drugs and Devices
- List of drugs for exceptional importation and sale
- COVID-19: List of authorized drugs, vaccines and expanded indications
- 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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