Health Canada Santé Canada

Your health and safety… our priority. *Votre santé et votre sécurité… notre priorité.*

Health Product InfoWatch

July 2020

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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

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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.

HEALTH PRODUCTS MENTIONED IN THIS ISSUE

Pharmaceuticals and Biologics

- Imbruvica (ibrutinib)
- Imuran (azathioprine)
- Jakavi (ruxolitinib)
- Ketamine-containing products
- MabCampath (alemtuzumab)
- Metformin
- Nardil (phenelzine sulfate)
- Polivy (polatuzumab vedotin)
- Rythmol (propafenone hydrochloride)
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- Xeljanz and Xeljanz XR (tofacitinib)

Medical Devices

- Respirator masks

Natural and Non-prescription Health Products

- Certain hand sanitizers that contain technical-grade ethanol
- Certain hand sanitizers that may pose health risks
- Hand sanitizers sold in beverage containers

Other

- Various medications

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.

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.

Health Product InfoWatch 2015 - 2020 5 years

Canada

Did You Know?

Health Canada's list of authorized antiseptic skin cleansers or hand sanitizers

To check whether an antiseptic/antibacterial skin cleanser or hand sanitizer meets Health Canada's requirements and is authorized for sale in Canada:

1. Locate the Natural Product Number (NPN) or Drug Identification Number (DIN) on the product label.
2. Look for that number on the authorized hand sanitizers list.

MONTHLY RECAP OF HEALTH PRODUCT SAFETY INFORMATION

The following is a list of health product advisories, type I recalls as well as summaries of completed safety reviews published in June 2020 by Health Canada.

Certain hand sanitizers that contain technical-grade ethanol Advisory	Health Canada advised Canadians that certain hand sanitizers containing technical-grade ethanol were recalled from the market because they are not compliant with federal regulations and may pose a risk to health.
Certain hand sanitizers that may pose health risks Advisory	Health Canada advised Canadians that certain hand sanitizers were recalled from the market because they contain types of ethanol or denaturants that are not acceptable ingredients for use in hand sanitizers in Canada.
Continued supply of medications Advisory	Health Canada advised Canadians to help support the continued supply of medications by not buying more medication than required.
Hand sanitizers sold in beverage containers Advisory	Some manufacturers of hand sanitizers are having difficulty producing or sourcing containers normally used for medical or household products. Many companies have increased their production in response to the COVID-19 pandemic, but are finding that the usual packaging for these products is limited. Some manufacturers of hand sanitizers are using packaging that is commonly used for beverages. This could confuse some consumers, who may mistake hand sanitizer for water or other beverages, and lead to accidental ingestion.

Ketamine-containing products Summary Safety Review	This safety review evaluated the risk of liver and bile duct damage associated with ketamine-containing products. Health Canada's review concluded that there is a potential link. If a patient stops taking ketamine, these damages may be reversed. Health Canada will work with manufacturers to update the product safety information of all ketamine-containing products to inform about this potential risk and advise treatment discontinuation with the first signs of liver or bile duct damage.
MabCampath (alemtuzumab) Health Professional Risk Communication	Life-threatening and sometimes fatal cases of haemophagocytic lymphohistiocytosis (HLH), stroke (including ischaemic and haemorrhagic stroke), and glomerulonephritis have been reported in patients with B-cell chronic lymphocytic leukemia (B-CLL) who were receiving MabCampath (alemtuzumab). The Canadian product monograph has been updated to include this new safety information.
Metformin Information Update	Additional lots of metformin tablets were recalled because they contain or may contain a nitrosamine impurity, N-nitrosodimethylamine (NDMA), above or close to the acceptable limit. Individuals taking metformin, including a recalled product, should not stop taking it unless they have spoken to their healthcare provider as the risks from not having adequate diabetes treatment outweigh any possible effects of exposure to the levels of NDMA found in the recalled products.
Nardil (phenelzine sulfate) Health Professional Risk Communication	Due to a global shortage of Nardil (phenelzine sulfate), a potent monoamine oxidase inhibitor (MAOI) indicated for the treatment of certain types of depressed patients, intermittent shortages of the product will be experienced in Canada. Healthcare professionals are advised to ensure no new patients are started on Nardil, consider switching patients taking Nardil to an alternative treatment and avoid abrupt discontinuation of Nardil treatment to prevent withdrawal syndrome.
Respirator masks Advisory	Health Canada determined that certain respirators, which have failed to demonstrate a 95% filtration rate, may pose a health and safety risk to users, when used in a setting that requires 95% filtration (such as healthcare settings). Health Canada continues to assess all sources of information related to respirators that may not meet safety and effectiveness standards, and takes action to ensure that products that do not meet the applicable standards are relabelled as face masks for use in settings where 95% filtration is not required. Health Canada will continue to update the list of devices that must be relabelled as face masks in order to be distributed in Canada.

Xeljanz and Xeljanz XR (tofacitinib), and Jakavi (ruxolitinib) - Janus kinase (JAK) inhibitors

Summary Safety Review

This safety review evaluated the risk of venous thromboembolic events (VTE) associated with Xeljanz and Xeljanz XR (tofacitinib), and Jakavi (ruxolitinib). Health Canada's review concluded that there is a link between the risk of VTE and the use of Xeljanz (tofacitinib). The product monograph for Xeljanz/ Xeljanz XR has been updated to include this new safety information and Health Canada has also communicated this information to healthcare professionals. Health Canada's review also found a possible link between Jakavi (ruxolitinib) and VTE. Health Canada will work with the manufacturer to update the product monograph for Jakavi (ruxolitinib) to include the risk of VTE.

NEW HEALTH PRODUCT SAFETY INFORMATION

The following topics have been selected to raise awareness and, in some cases, to stimulate reporting of similar adverse reactions.

PRODUCT MONOGRAPH UPDATES

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

Imbruvica (ibrutinib)

The risk of **cerebrovascular accidents** has been included in the *Warnings and Precautions*, *Adverse Reactions* and *Patient Medication Information* sections of the Canadian product monograph for Imbruvica.

Key messages for healthcare professionals:[1]

- Cases of cerebrovascular accident (including fatalities), transient ischemic attack, and ischemic stroke (including fatalities) have been reported with the use of Imbruvica, with and without concomitant atrial fibrillation and/or hypertension, although causality with ibrutinib has not been established.
- Regular monitoring and appropriate treatment of conditions that can contribute to the occurrence of these events is recommended.

Reference

1. *Imbruvica (ibrutinib)* [product monograph]. Toronto (ON): Janssen Inc.; 2020.

Imuran (azathioprine)

The increased risk for **severe 6-mercaptopurine toxicity** in patients with inherited mutated NUDT15 gene has been updated in the *Dosage and Administration*, *Warnings and Precautions*, *Action and Clinical Pharmacology* and *Patient Medication Information* sections of the Canadian product monograph for Imuran.

Key messages for healthcare professionals:[1]

- Patients with inherited mutated NUDT15 gene are at an increased risk for severe 6-mercaptopurine toxicity, such as early leukopenia and alopecia, from conventional doses of thiopurine therapy.
- These patients generally require dose reduction, particularly those being NUDT15 variant homozygotes.
- Genotypic testing of NUDT15 variants may be considered before initiating thiopurine therapy.
- The frequency of the NUDT15 variant NUDT15 c.415C>T has an ethnic variability of approximately 10 % in East Asians, 4 % in Hispanics, 0.2 % in Europeans and 0 % in Africans.
- In any case, close monitoring of blood count is necessary.

Reference

1. *Imuran (azathioprine)* [product monograph]. Oakville (ON): Aspen Pharmacare Canada Inc.; 2020.

Rythmol (propafenone hydrochloride)

A **new contraindication** has been included in the *Contraindications* and *Consumer Information* sections of the Canadian product monograph for Rythmol.

Key messages for healthcare professionals:[1]

- Rythmol is now contraindicated in patients with severe obstructive pulmonary disease.

Reference

1. *Rythmol (propafenone hydrochloride)* [product monograph]. Etobicoke (ON): BGP Pharma ULC; 2020.

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 nature 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, in accordance with the NOC/c policy. For the most up-to-date information, consult Health Canada's NOC database.

Veklury (remdesivir): Authorization with conditions

Health Canada has issued a Notice of Compliance, under the Notice of Compliance with Conditions policy for Veklury (remdesivir), remdesivir for injection, powder for solution for infusion, 100 mg/vial (5 mg/mL when reconstituted) and remdesivir solution for injection, 100 mg/20 mL (5 mg/mL). Veklury is indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults and adolescents (aged 12 years and older with body weight at least 40 kg) with pneumonia requiring supplemental oxygen. Use of Veklury is confined to healthcare facilities in which patients can be monitored closely. Patients should be advised about the conditional market authorization for this indication.

For the complete prescribing information and information available for the patients/caregivers, please consult the Veklury Canadian product monograph. The product monograph can be accessed through Health Canada's Drug Product Database, the Gilead Sciences Canada, Inc. Web site or by contacting Gilead Sciences Canada, Inc. at 1-866-207-4267. Contact the company for a copy of any references, attachments or enclosures.

For further information on remdesivir, please visit the Government of Canada Coronavirus disease (COVID-19): for healthcare professionals Web page.

Polivy (polatuzumab vedotin): Authorization with conditions

Health Canada has issued a Notice of Compliance, under the Notice of Compliance with Conditions policy for Polivy (polatuzumab vedotin), lyophilized powder for solution for intravenous infusion, 140 mg single-use vial. Polivy, in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, who are not eligible for autologous stem cell transplant and have received at least one prior therapy. Patients should be advised about the conditional market authorization for this indication.

For the complete prescribing information and information available for the patients/caregivers, please consult the Polivy Canadian product monograph. The product monograph can be accessed through Health Canada's Drug Product Database, the Hoffmann-La Roche Limited Web site 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
- Stop Illegal Marketing of Drugs and Devices
- List of Drugs for Exceptional Importation and Sale

Suggestions?

Your comments are important to us. Let us know what you think by reaching us at HC.infowatch-infovigilance.SC@canada.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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