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Health Product InfoWatch

April 2021

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REPORTING ADVERSE REACTIONS

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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

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- Perfect Sports Core Series Pure Creatine
- Riva Senna

Other

- Counterfeit 3M N95 respirators
- Unauthorized health products

CORONAVIRUS DISEASE (COVID-19)

For the most up-to-date information on COVID-19, please visit the Government of Canada Coronavirus disease (COVID-19) website **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.

Canada

DID YOU KNOW?

The COVID-19 vaccines and treatments portal provides information for consumers, healthcare professionals and researchers on vaccines and treatments authorized for COVID-19, as well as those currently under review.

For information about adverse events following immunization that individuals have reported after receiving a COVID-19 vaccine in Canada please see visit the COVID-19 vaccine safety in Canada webpage. This page is updated weekly.

DRUG AND VACCINE AUTHORIZATIONS AND COMMUNICATIONS FOR COVID-19

The Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19 (the Interim Order) allows for the issuance of an expedited authorization for the importation, sale and advertising of drugs used in relation to COVID-19; this includes both human and veterinary drugs. Recent communications related to previously authorized COVID-19 vaccines and treatments are also highlighted in this section.

AstraZeneca COVID-19 Vaccine and COVISHIELD – Thrombosis and thrombocytopenia

Very rare events of thrombosis with thrombocytopenia, in some cases accompanied by bleeding, have been observed following vaccination with the AstraZeneca and COVISHIELD COVID-19 vaccines. Health Canada has updated the AstraZeneca and COVISHIELD COVID-19 vaccine product monographs based on its safety review regarding these very rare events following immunization. Health Canada continues to work closely with international regulators to review data as it becomes available. Should new safety information be identified, Health Canada will take further actions, including risk communications, as needed. Further information related to Health Canada's review of this risk is available at the summary safety review link.

Summary Safety Review (April 19, 2021) – AstraZeneca and COVISHIELD COVID-19 vaccines

Health Professional Risk Communication (March 24, 2021) – AstraZeneca and COVISHIELD COVID-19 vaccines

Advisory (April 14, 2021) – AstraZeneca and COVISHIELD COVID-19 vaccines

Advisory (March 11, 2021) – AstraZeneca COVID-19 Vaccine

AstraZeneca COVID-19 Vaccine – Supply

Further to the February 26, 2021 authorization of the AstraZeneca COVID-19 Vaccine in accordance with the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19, AstraZeneca is providing, at this time, vaccine supplies with COVAX and US vial and carton labels in order to expedite the distribution of the vaccine in Canada. These labels are presented in English-only and are missing some important Canadian-specific information normally found on Health Canada approved labels.

Health Professional Risk Communication (US labels, March 31, 2021) – AstraZeneca COVID-19 Vaccine

Health Professional Risk Communication (COVAX labels, March 1, 2021) – AstraZeneca COVID-19 Vaccine

Bamlanivimab – COVID-19 Treatment update

Further to the November 20, 2020 authorization of bamlanivimab for use in accordance with the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19, a potential risk of treatment failure of bamlanivimab against certain SARS-CoV-2 variants was identified through global surveillance. Bamlanivimab is expected to retain neutralizing activity against the UK origin B.1.1.7 variant. The Canadian product monograph was updated to include new information concerning SARS-CoV-2 variants of concern.

Health Professional Risk Communication – Bamlanivimab

COVISHIELD COVID-19 Vaccine – Supply

COVISHIELD COVID-19 vaccine was authorized for use in accordance with the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19. As an extraordinary measure to provide earlier access to vaccine supplies in the context of the global pandemic, Verity Pharmaceuticals Inc. is providing, at this time, vaccine vials and cartons labelled with a global product name and global label information. The labels are presented in English-only and are missing some important Canadian-specific information normally found on Health Canada approved labels.

Health Professional Risk Communication – COVISHIELD COVID-19 Vaccine

Janssen COVID-19 Vaccine – Supply

Further to the March 5, 2021 authorization of the Janssen COVID-19 Vaccine in accordance with the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19, Janssen Inc. is providing, at this time, vaccine supplies with Non-US White and Non-US Orange Labels in order to expedite the distribution of the vaccine in Canada. These labels are presented in English-only and are missing some important Canadian-specific information normally found on Health Canada approved labels.

Health Professional Risk Communication – Janssen COVID-19 Vaccine

Janssen COVID-19 Vaccine – Thrombosis with Thrombocytopenia

Very rare cases of thrombosis in combination with thrombocytopenia, in some cases accompanied by bleeding, have been observed following vaccination with Janssen COVID-19 Vaccine. A causal relationship with the vaccine is considered plausible. Health Canada has worked with Janssen Inc. to update the product monograph for Janssen COVID-19 Vaccine to include this new safety information. Health Canada continues to work closely with international regulators to review data as it becomes available on these very rare events and will make further updates to product labelling or take other actions as needed.

Health Professional Risk Communication – Janssen COVID-19 Vaccine

Pfizer-BioNTech COVID-19 Vaccine – Storage

The Pfizer-BioNTech COVID-19 Vaccine product monograph was updated to reflect alternative and more flexible storage and/or transportation conditions of the frozen vials and transportation conditions of the thawed undiluted vials. The review of data provided by Pfizer-BioNTech confirms the maintenance of the vaccine quality under these new storage and transportation conditions.

Health Professional Risk Communication – Pfizer-BioNTech COVID-19 Vaccine

ANNOUNCEMENT

TALC AND THE RISK TO HUMAN HEALTH

Health Canada and Environment and Climate Change Canada have completed a joint final screening assessment of talc.

Based on the final assessment, two exposure scenarios have been identified as potential concerns to human health:

- Inhalation of certain loose powder products containing talc, which may cause non-cancer lung effects, such as inflammation, impaired lung function and fibrosis. Examples include body powder, baby powder, or loose face powder products; and
- Exposure to the female perineal area from certain self-care products containing talc, which may cause ovarian cancer. Examples include body powder, baby powder, diaper and rash creams, genital antiperspirants and deodorants, body wipes, bath bombs, or bubble bath products.

The final screening assessment did not identify human health risks from oral exposure to talc resulting from food intake, oral and dermal exposures from the use of self-care products, or inhalation exposure from foot powder, dry hair shampoo or pressed powder products, such as face makeup. For more information, please see the talc Advisory.

Healthcare professionals are invited to comment on the talc Risk Management Approach or provide other information that would help to inform decision-making, prior to June 23, 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 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.

***Artemisia annua*-containing products** Summary Safety Review	This safety review evaluated the risk of liver injury associated with *Artemisia annua*-containing products. Health Canada's review of the available information did not establish a link. At the time of this review, Health Canada found that the available information related to this risk in Canada is too limited to warrant regulatory action. Health Canada will continue to monitor safety information involving *Artemisia annua* and will take appropriate and timely action should new health risks be identified.

Cefuroxime-containing products Summary Safety Review	This safety review evaluated the risk of Kounis syndrome associated with cefuroxime-containing products. Health Canada's review of the available information did not establish a link. Health Canada will continue to monitor safety information involving cefuroxime-containing products and will take appropriate and timely action should new health risks be identified.
Certain hand sanitizers that may pose health risks Advisory (part 1) Advisory (part 2)	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, or were missing important information.
Counterfeit 3M N95 respirators Advisory	Health Canada warned Canadians about counterfeit 3M N95 respirators in light of recent seizures of counterfeit products in Canada and at the border. Health Canada is working with 3M Canada, the manufacturer of authentic 3M N95 respirators, and the Canada Border Services Agency to address the issue of counterfeit 3M N95 respirators. 3M has established a hotline (1-800-426-8688) and published information on its website to help Canadian customers identify, prevent and report suspected fraud. Suspected counterfeit respirators can also be reported to Health Canada.
Dental amalgam Summary Safety Review	This safety review evaluated the risk of negative health effects from mercury associated with dental amalgam. Health Canada's review of the available safety information concluded that there is no clear link. The safety review did not find new evidence to suggest a change in the overall safety profile for dental amalgam. As a precaution, use of dental amalgam in children, pregnant women, and patients with kidney disease should be minimized, as recommended in the 1996 Health Canada position statement.
Diuretics Summary Safety Review Health Product InfoWatch	This safety review evaluated the risk of choroidal effusion, acute myopia and acute angle-closure glaucoma associated with diuretics, including acetazolamide. Health Canada's review of the available information showed a link, namely for products containing hydrochlorothiazide, chlorthalidone, indapamide and acetazolamide. In addition, Health Canada's review concluded that there might be a link between metolazone and the risk of these eye disorders. Health Canada will work with manufacturers to update the Canadian product monographs for products containing hydrochlorothiazide, chlorthalidone, indapamide and acetazolamide as well as metolazone to add a warning about these risks. Health Canada has also communicated this information to healthcare professionals.

Male sexual enhancement product "Harmony" Advisory	Health Canada warned consumers to not use Harmony, a male sexual enhancement capsule, because it may pose serious health risks. It was authorized as a natural health product, but Health Canada testing found it contains high levels of prescription drug tadalafil. Health Canada has suspended the product licence for Harmony (NPN 80044321).
Perfect Sports Core Series Pure Creatine Advisory	Health Canada suspended the product licence of Perfect Sports Core Series Pure Creatine, also known as Creatine Powder, (NPN 80012948) as a result of vitamin D contamination of Lot 2006CRTN807 and because of non-compliance with Good Manufacturing Practices. The product label is also missing the statement "for adult use only". Health Canada has directed the company to recall all remaining lots from the market. In addition, Health Canada has suspended the company's site licence.
Riva Senna Advisory	Laboratoire Riva Inc. recalled 2 lots (C9718 and C9719) of Riva Senna 8.6 mg tablets (NPN 80079605) due to microbial contamination. The recalled lots were sold in Quebec and Ontario.
Tumor Necrosis Factor alpha-blockers Summary Safety Review	This safety review evaluated the risk of mycosis fungoides associated with Tumor Necrosis Factor (TNF) alpha-blockers (anti-TNF alpha): Remicade (infliximab), Humira (adalimumab), Enbrel (etanercept) and Erelzi (biosimilar etanercept). Health Canada's review of the available information concluded that a link between the risk of mycosis fungoides and the use of anti-TNF alpha products could not be confirmed given limitations in the available information. The product monographs for all anti-TNF alpha products already mention the risk of lymphoma (which includes mycosis fungoides); therefore, no updates specific for mycosis fungoides are required at this time.
Unauthorized health products Unauthorized health products seized from Tokyo Beauty & Health Care in Richmond, B.C 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, 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.

Keppra (levetiracetam)

The *Warnings and Precautions, Adverse Reactions (Post-Market Adverse Drug Reactions)*, and *Consumer Information* sections of the Canadian product monograph for Keppra have been updated with **new safety information concerning QT interval prolongation**.

Key messages for healthcare professionals:[1]

- Rare cases of ECG QT interval prolongation have been observed during post-marketing surveillance in patients with and without a prior history of cardiac conditions.
- Keppra should be used with caution, particularly in patients with QTc-interval prolongation, in patients concomitantly treated with drugs affecting the QTc-interval, or in patients with relevant pre-existing cardiac disease or electrolyte disturbances.

Reference

1. *Keppra (levetiracetam)* [product monograph]. Oakville (ON): UCB Canada Inc.; 2020.

Ketalar (ketamine hydrochloride)

The *Warnings* and *Adverse Reactions* sections of the Canadian product monograph for Ketalar* have been updated with **new safety information concerning hepatobiliary toxicity** associated with the use of ketamine.

Key messages for healthcare professionals:[1]

- Hepatocellular and cholestatic pattern of elevations in liver enzymes as well as biliary ductal dilatations and hepatic fibrosis have been reported following exposure to ketamine especially with repeated doses, chronic use or misuse.
- Clinically important elevations in liver enzymes, suggestive of both hepatocellular and cholestatic changes are potential risks of acute use of ketamine. Liver enzyme elevations and biliary ductal dilatations are potential risks of repeated, chronic use or misuse of ketamine. Both the biochemical and structural hepatobiliary changes may be reversible.
- Regular monitoring of liver function is recommended with repeated use of ketamine. In cases of clinically significant liver enzyme elevations, treatment discontinuation should be considered.

References

1. *Ketalar (ketamine hydrochloride)* [product monograph]. Montréal (QC): ERFA Canada 2012 Inc.; 2020.
2. *Spravato (esketamine hydrochloride)* [product monograph]. Toronto (ON): Janssen Inc.; 2020.

* Since ketamine is a racemic mixture of arketamine and esketamine, a potential for hepatotoxicity with the use of esketamine (Spravato) cannot be excluded. Consideration should be given to periodically monitor the liver function of patients treated with Spravato and to discontinue the treatment with Spravato when clinically significant liver enzyme elevations are observed.[2] This safety information is included in the Canadian product monograph for Spravato.

Lynparza (olaparib)

The *Warnings and Precautions* and *Adverse Reactions* sections of the Canadian product monograph for Lynparza have been updated with **more detailed information about Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML)**.

Key messages for healthcare professionals:[1]

- A substantially higher incidence of MDS/AML was reported in patients with BRCAm platinum-sensitive relapsed ovarian cancer who had received at least two prior lines of platinum chemotherapy and were followed for 5 years.
- The duration of therapy with Lynparza in patients who developed MDS/AML varied from less than 6 months to greater than 4 years.
- If MDS and/or AML is confirmed, Lynparza should be discontinued and the patient be treated appropriately.

Reference

1. *Lynparza (olaparib)* [product monograph]. Mississauga (ON): AstraZeneca Canada Inc.; 2021.

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
- Drug and vaccine authorizations for 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 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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