Health Canada Santé Canada

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Health Product InfoWatch

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REPORTING ADVERSE REACTIONS

Canada Vigilance Program
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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.

Canada

MONTHLY RECAP OF HEALTH PRODUCT SAFETY INFORMATION

The following is a list of health product advisories as well as summaries of completed safety reviews published in November 2016 by Health Canada.

Bisphosphonates Summary Safety Review	This safety review evaluated the risk of osteonecrosis of the jaw associated with oral and injectable bisphosphonates (alendronate, clodronate, etidronate, pamidronate, risedronate and zoledronate). Health Canada's review concluded that there is a higher risk with the use of intravenous bisphosphonate products compared to the oral form, especially in cancer patients. Health Canada will be working with the manufacturers to update the Canadian product monographs for bisphosphonate products.
DPP-4 inhibitors Summary Safety Review	This safety review evaluated the risk of gastrointestinal obstruction associated with dipeptidyl peptidase 4 (DPP-4) inhibitors (alogliptin, linagliptin, saxagliptin, sitagliptin). Health Canada's review concluded that the evidence does not support a link between the use of DPP-4 inhibitors and gastrointestinal obstruction. Health Canada will continue to monitor this issue.
Enlite Glucose Sensor Summary Safety Review	This safety review evaluated the risk of improper glucose management associated with Enlite Glucose Sensor manufactured by Medtronic MiniMed. Health Canada's review concluded that the evidence does not suggest that there is a new safety risk associated with the Enlite Glucose Sensor at this time. Health Canada will continue to monitor this issue.
Foreign health products Foreign Product Alert	These foreign health products have been found by regulators in other countries to contain undeclared drug ingredients or heavy metals. The products are not authorized for sale in Canada and have not been found in the Canadian marketplace but it is possible they may have been brought into the country by travellers or purchased over the Internet.
Interferon beta products Summary Safety Review	This safety review evaluated the risk of pulmonary arterial hypertension associated with interferon beta products [Interferon beta-1a (Avonex and Rebif) and interferon beta-1b (Betaseron and Extavia)]. Health Canada's review concluded that pulmonary arterial hypertension is a very rare adverse reaction to interferon beta use. Health Canada has worked with the manufacturers to include this risk in the Canadian product monographs for interferon beta products.

Loratadine Summary Safety Review	This safety review evaluated the risk of QT interval prolongation associated with loratadine. Health Canada's review concluded that a link between the use of loratadine and QT interval prolongation could not be established. Health Canada will continue to monitor this issue.
MAD Nasal Intranasal Mucosal Atomization Device Advisory	Teleflex Medical recalled certain lots of "MAD Nasal Intranasal Mucosal Atomization Device" because they may not deliver a fully atomized (fine) spray of medication. This means patients may not receive the full dose, which could reduce the medication's effectiveness. The devices are used primarily by medically trained personnel but can also be used by first responders and the general public.
Ondansetron Summary Safety Review	This safety review evaluated the risk of birth defects associated with the use of ondansetron (Zofran and generics) during pregnancy. Ondansetron is not authorized for sale in Canada to treat nausea and vomiting in pregnant women. Health Canada's review concluded that there was not enough information to establish a link. Health Canada is working with the Drug Safety and Effectiveness Network to further investigate the extent of ondansetron use during pregnancy and the risk to the fetus. Health Canada has requested that manufacturers submit information they may have regarding this risk.
Phenylephrine and acetaminophen Summary Safety Review Health Product InfoWatch	This safety review evaluated the risk of interaction between phenylephrine and acetaminophen. Health Canada's review concluded that the evidence shows an interaction which may lead to an increase in the relative bioavailability of phenylephrine; however, the clinical evidence to support this interaction is insufficient. Health Canada also communicated this information to healthcare professionals.
Rivastigmine Summary Safety Review	This safety review evaluated the increased risk of death associated with rivastigmine (Exelon and generics). Health Canada's review did not find an increased risk of death in patients taking rivastigmine regardless of the formulation used. Health Canada has asked the manufacturers of Exelon to continue to provide information on the use of this product.
SGLT2 inhibitors Summary Safety Review	This safety review evaluated the potential for loss of bone minerals with a risk of brittle or fractured bones associated with sodium-glucose cotransporter-2 (SGLT2) inhibitors (canagliflozin, dapagliflozin, empagliflozin). Health Canada's review concluded that the evidence supported a link between the risks of bone fracture and loss of bone mineral density with canagliflozin. With dapagliflozin, these risks were only identified in patients who had kidney problems. No evidence was found to date with empagliflozin. Health Canada is working with the manufacturer to update the Canadian product monograph for canagliflozin to reflect these risks.

Unauthorized health product Advisory	"Phytovie Acore Vrai Calamus" herbal tea, an unauthorized natural health product, was recalled after Health Canada testing found it to contain excessive levels of beta-asarone. The product was sold by Gourmet Nutrition F.B. Inc. over the Internet and may also be available at retail stores.
Zelboraf (vemurafenib) Summary Safety Review	This safety review evaluated the risk of bone marrow toxicity or suppression associated with Zelboraf (vemurafenib). Health Canada's review concluded that the current evidence available does not support a link between Zelboraf use and bone marrow toxicity or suppression. Health Canada will continue to monitor this issue.

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 brand name pharmaceutical drugs is available on Health Canada's Web site.

Erivedge (vismodegib)

*The risk of **irreversible premature fusion of the epiphyses in pediatric patients*** has been added to the Indications and clinical use, Warnings and precautions (boxed Serious Warnings and Precautions), and Adverse Reactions sections of the Canadian product monograph for Erivedge (vismodegib).*

Key messages for healthcare professionals:[1]

- Irreversible premature fusion of the epiphyses has been reported in pediatric patients exposed to Erivedge. Premature fusion can progress after discontinuation of treatment.
- Due to safety concerns, Erivedge is contraindicated in children and adolescents aged below 18 years.

* Use of Erivedge (vismodegib) in children and adolescents aged below 18 years is contraindicated.

Reference

1. *Erivedge (vismodegib)* [product monograph]. Mississauga (ON): Hoffmann-La Roche Limited; 2016.

Invokana (canagliflozin) and Invokamet (canagliflozin and metformin hydrochloride)

*The risk of **lower limb amputation**, primarily of the toe, has been added to the Adverse Reactions section of the Canadian product monographs for Invokana (canagliflozin) and Invokamet (canagliflozin and metformin hydrochloride).*

Key messages for healthcare professionals:[2,3]

- In an ongoing cardiovascular study* of 4 327 patients with type 2 diabetes, with known or at high risk for cardiovascular disease, the incidence rates of lower limb amputation, primarily of the toe, were 7.3, 5.4 and 3.0 per 1 000 patient years of exposure to canagliflozin 100 mg, canagliflozin 300 mg, and placebo, respectively, with the imbalance occurring as early as the first 26 weeks of therapy.
- In other type 2 diabetes studies with canagliflozin, which enrolled a general diabetes population of 8 111 patients, no difference in lower limb amputation risk was observed relative to control.

* Study details available at https://clinicaltrials.gov/ct2/show/NCT01032629.

References

2. *Invokana (canagliflozin)* [product monograph]. Toronto (ON): Janssen Inc.; 2016.
3. *Invokamet (canagliflozin and metformin hydrochloride)* [product monograph]. Toronto (ON): Janssen Inc.; 2016.

Rythmodan (disopyramide)

*The risk of **agranulocytosis** has been included in the Post-Market Adverse Drug Reactions section of the Canadian product monograph for Rythmodan (disopyramide).*

Key message for healthcare professionals:[4]

- There have been post-marketing cases of agranulocytosis in patients receiving Rythmodan.

Reference

4. *Rythmodan (disopyramide)* [product monograph]. Laval (QC): sanofi-aventis Canada Inc.; 2016.

HELPFUL LINKS

- MedEffect™ Canada
- Recalls and Safety Alerts Database
- Summary Safety Reviews
- New Safety 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
- Canadian Drug Shortage Database

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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