Health Canada Santé Canada

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Health Product InfoWatch

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REPORTING ADVERSE REACTIONS

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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 August 2016 by Health Canada.

Adempas (riociguat) Health Product Risk Communication	The RISE-IIP study, which was investigating the effects of Adempas (riociguat) in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP), has been terminated early due to an increased risk of mortality and serious adverse events among subjects with PH-IIP receiving Adempas. Patients with PH-IIP should not be treated with Adempas. If any patients with PH-IIP are being treated with Adempas, their treatment should be discontinued and their clinical status carefully monitored. The Canadian product monograph will be updated to reflect the contraindication for Adempas in patients with PH-IIP.
Antidepressants Summary Safety Review	This safety review evaluated the risk of angle-closure glaucoma associated with 23 antidepressant medications available in Canada (amitriptyline, bupropion, citalopram, clomipramine, desipramine, desvenlafaxine, doxepin, duloxetine, escitalopram, fluoxetine, fluvoxamine, imipramine, maprotiline, mirtazapine, moclobemide, nortriptyline, paroxetine, phenelzine, sertraline, tranylcypromine, trazodone, trimipramine and venlafaxine). Health Canada's review concluded that there is a link between antidepressant use and the occurrence of angle-closure glaucoma. Health Canada is working with manufacturers of antidepressant products to update the Canadian product monographs to include a warning of the potential risk for angle-closure glaucoma with the use of these products.
Atypical antipsychotics Summary Safety Review	This safety review evaluated the risk of sleep apnea associated with atypical antipsychotics. Health Canada's review concluded that the data suggested a possible link between the use of aripiprazole, asenapine, clozapine, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone and sleep apnea. Health Canada recommended to update the current Canadian product monographs for these atypical antipsychotics to highlight the risk of sleep apnea.
Digoxin Summary Safety Review	This safety review evaluated the increased risk of death in patients with atrial fibrillation and patients with heart failure taking digoxin compared to patients with the same health issues but not using digoxin. Health Canada's review did not find evidence supporting a link between the use of digoxin and a higher risk of death. Health Canada will continue to monitor this issue.

Enbrel (etanercept) Summary Safety Review	This safety review evaluated the risk of potential harm to the developing babies of mothers treated with Enbrel (etanercept). Health Canada's review concluded that taking Enbrel during pregnancy was associated with a lesser risk of experiencing a miscarriage but a potential risk of carrying to full term a newborn with a birth defect. Health Canada's review could not conclude that Enbrel by itself was the cause of birth defects. Health Canada is working with the manufacturer to update the Canadian product monograph for Enbrel to include information regarding the potential harm to a developing baby when mothers are treated with Enbrel during pregnancy.
Erwinase (Erwinia L-asparaginase) Health Product Risk Communication (Batch CAMR-174) Health Product Risk Communication (Batch CAMR-177)	Small amounts of particulate matter have been observed bound to the stopper of some vials of Erwinase (Erwinia L-asparaginase). Vials of Erwinase with visible particulate matter after reconstitution should be discarded. To avoid a potential shortage, Health Canada has not objected to the temporary importation of UK-labelled product. A standard 5-micron filter needle should be used to withdraw the reconstituted product from the UK-labelled product prior to administration. Healthcare professionals should refer to the Erwinase Canadian product monograph for prescribing information.
Foreign health products Foreign Product Alert	These foreign health products have been found by regulators in other countries to contain undeclared drug ingredients. These 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.
Gilenya (fingolimod) Summary Safety Review	This safety review evaluated the risk of progressive multifocal leukoencephalopathy associated with Gilenya (fingolimod). Health Canada's review concluded that there was a possible link between progressive multifocal leukoencephalopathy and Gilenya. The Canadian product monograph for Gilenya has been updated by the manufacturer to reflect this potential risk.
Hormone replacement therapy (estrogenic and progestogenic agents) and selective estrogen receptor modulators Summary Safety Review	This safety review evaluated the risk of ovarian cancer in menopausal women associated with the use of hormone replacement therapy (HRT) and selective estrogen receptor modulators (SERMs) (raloxifene, bazedoxifene). Health Canada's review did not find enough information to confirm that the risk of ovarian cancer is increased in women undergoing HRT for less than 5 years. The current Canadian product monograph for HRT products warns about the risk of ovarian cancer during treatment, especially after 5 years of treatment or more. The safety review did not find evidence to show a link between SERMs and ovarian cancer. Health Canada will continue to monitor the situation.

Intuniv XR (guanfacine hydrochloride) Summary Safety Review	This safety review evaluated the risk of Raynaud's phenomenon associated with Intuniv XR (guanfacine hydrochloride). Health Canada's review concluded that there was not sufficient evidence to support strengthening the existing information on Raynaud's phenomenon in the Canadian product monograph for Intuniv XR. Health Canada will continue to monitor this issue.
Lidocaine viscous 2% Summary Safety Review	This safety review evaluated the risk of severe adverse reactions in infants and young children associated with lidocaine viscous 2% products. Health Canada's review concluded that there is a link between lidocaine viscous 2% and severe adverse reactions (seizures, severe brain injury, heart problems, and death) in infants and young children from 5 months to 4 years of age. Health Canada is working with the manufacturers of lidocaine viscous 2% products to update the Canadian product monographs with warnings about the risk of severe adverse reactions in infants and young children and clarify directions for approved uses.
pms-Atenolol Advisory	One lot (495259) of pms-Atenolol 100 mg was recalled by Pharmascience Inc., due to a labelling error. The lot contains foil blister packs incorrectly labelled as pms-Atenolol 50 mg and the wrong Drug Identification Number.
Propecia, Proscar and generics (finasteride 1 and 5 mg) Summary Safety Review	This safety review evaluated the risk of seizures associated with finasteride. Health Canada's review concluded that the findings do not support a link between an increased risk of seizures in patients treated with finasteride. Health Canada will continue to monitor this issue.
Revolade (eltrombopag) Health Product Risk Communication	Cases of severe drug-induced liver injury with Revolade (eltrombopag) have been reported in patients during clinical trials and post-marketing. To mitigate the risk of severe hepatotoxicity and potentially fatal liver injury, healthcare professionals should measure serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin prior to initiation of Revolade, and at specified intervals following treatment initiation. As well, Revolade should be discontinued if ALT levels exceed specified limits. The Canadian product monograph for Revolade has been updated to reflect this safety information.

Solu-Cortef (hydrocortisone sodium succinate) 100 mg/2 mL single-dose Act-O-Vial Health Product Risk Communication	Eight lots of Solu-Cortef (hydrocortisone sodium succinate) 100 mg/2 mL single-dose Act-O-Vial were recalled by Pfizer due to a labelling text error on the side panel of the carton which indicates that the reconstituted product contains 125 mg/mL hydrocortisone instead of 50 mg/mL. Solu-Cortef 250 mg/2 mL or 500 mg/4 mL Act-O-Vials (single use) can be used as alternatives; however, healthcare professionals need to be aware that the alternative products have a reconstituted concentration of 125 mg/mL. Changes to the volume for dosing will be required. Therapeutic alternatives should be considered for non-urgent medical uses.
Trifecta heart valve Summary Safety Review	This safety review evaluated the risk of structural valve deterioration associated with the use of Trifecta heart valve. Health Canada's review concluded that there was not enough long-term evidence available to make changes to the instructions for use at this time. Health Canada will continue to monitor safety information including the manufacturer's 10-year long patient studies and other patient safety reports regarding the Trifecta heart valve.
Unauthorized health product (AlgoSlim) Information Update	Health Canada informed Canadians not to use the unauthorized weight loss product AlgoSlim, distributed via mail order by E Sélection. The package does not contain unauthorized AlgoSlim and instead contains an authorized product, Slite-T, from a lot that expired in June 2012.
Velcade (bortezomib) and generics Summary Safety Review	This safety review evaluated the risk of necrotizing fasciitis associated with bortezomib. Health Canada's review concluded that there was insufficient evidence at this time to make a link between bortezomib and necrotizing fasciitis. Health Canada will continue to monitor this issue.
Yondelis (trabectedin) Summary Safety Review	This safety review evaluated the risk of capillary leak syndrome associated with Yondelis (trabectedin). Health Canada's review concluded that there is a potential risk of capillary leak syndrome with the use of Yondelis. Health Canada is recommending updates to the Canadian product monograph to include this potential risk.

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.

Diamicron (gliclazide)

*The **loss of blood glucose control or hyperglycemia with concomitant use of St. John's Wort** has been included in the Precautions and Drug Interactions sections of the Canadian product monograph for Diamicron.*

Key messages for healthcare professionals:[1]

- If gliclazide is used concomitantly with herbs such as St. John's Wort (*Hypericum perforatum*), loss of blood glucose control or hyperglycemia may occur.
- Close monitoring is required in these patients.

Reference

1. *Diamicron (gliclazide)* [product monograph]. Laval (QC): Servier Canada Inc.; 2016.

Imbruvica (ibrutinib)

*The risk of **interstitial lung disease (ILD)** has been included in the Warnings and Precautions and Adverse Reactions sections of the Canadian product monograph for Imbruvica.*

Key messages for healthcare professionals:[1]

- Cases of interstitial lung disease (ILD), including cases confirmed by biopsy, have been reported in patients receiving Imbruvica (ibrutinib).
- Monitor patients for pulmonary symptoms indicative of ILD. Advise patients to report promptly any new or worsening respiratory symptoms.
- If symptoms of ILD develop, interrupt Imbruvica, manage appropriately, consider the risks and benefits of Imbruvica before resuming treatment, and follow the dose modification guidance. If ILD is confirmed, discontinue Imbruvica.

Reference

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