Health Canada Santé Canada

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Health Product InfoWatch

January 2020

CONTENTS

REPORTING ADVERSE REACTIONS

Canada Vigilance Program
Online: Adverse Reaction and Medical Device Problem Reporting
Telephone: 1-866-234-2345
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HEALTH PRODUCTS MENTIONED IN THIS ISSUE

Pharmaceuticals and Biologics
Angiotensin II receptor blocker products (sartans)
Atoma-brand Diphenhydramine Hydrochloride 2% Anti-Itch Cream
Blincyto (blinatumomab)
Gilenya (fingolimod)
Metformin
Ranitidine
Sativex (delta-9-tetrahydrocannabinol [THC] and cannabidiol [CBD])
Xeljanz (tofacitinib)

Natural Health Products
U-Dream herbal sleep-aid products

Other
Unauthorized health products

ANNOUNCEMENT

The Health Product InfoWatch is turning 5!

The Health Product InfoWatch was launched in 2015 to replace the Canadian Adverse Reaction Newsletter (CARN) with a new format, style and publication frequency. The Editorial Team would like to take this opportunity to thank readers for their continued interest.

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, type I recalls as well as summaries of completed safety reviews published in December 2019 by Health Canada.

Angiotensin II receptor blocker products (sartans) and ranitidine Information Update	Health Canada has been working to address the issue of N-nitrosodimethylamine (NDMA) and similar nitrosamine impurities found in certain sartans since 2018 and certain ranitidine drugs more recently. Recently, Health Canada also expanded its efforts to evaluate the potential for nitrosamines in drugs other than sartans and ranitidine, along with measures to address and prevent the impurities.
Atoma-brand Diphenhydramine Hydrochloride 2% Anti-Itch Cream Advisory	Health Canada advised Canadians that Taro Pharmaceuticals Inc. recalled one lot of Atoma-brand Diphenhydramine Hydrochloride 2% Anti-Itch Cream because of a labelling error. The text printed on the tube incorrectly states that, for children under 2 years of age, "Application should be supervised by an adult" when it should instead state "Consult a doctor." There is no quality issue with the product, but the labelling error could lead to the inappropriate use of the product on children under 2 years of age.
Gilenya (fingolimod) Health Professional Risk Communication	When used during pregnancy, Gilenya (fingolimod) has been associated with an increased risk of major congenital malformations, including congenital heart disease such as atrial septal defect, and renal and musculoskeletal abnormalities. Gilenya is now contraindicated in women who are pregnant or in women of childbearing potential who are not using effective contraception. The Canadian product monograph for Gilenya has been updated to include this new contraindication and new safety information.
Metformin Information Update	Health Canada is aware that some metformin products available outside Canada have been found to contain a nitrosamine impurity, N-nitrosodimethylamine (NDMA), above the acceptable limit. As of December 2019, Health Canada is not aware of any metformin products in Canada containing NDMA above acceptable levels. The Department has asked companies to test their metformin products and is collecting samples from companies to conduct its own testing.

U-Dream herbal sleep-aid products Advisory Drug recall	Health Canada has tested several U-Dream Lite and U-Dream Full Night herbal sleep-aid products and has found that they contain a substance similar to the prescription drug zopiclone, which may pose serious health risks. Health Canada tested the products after receiving complaints of unusual adverse reactions—such as symptoms of withdrawal and dependence—suggesting that the products may contain a substance not listed on the product label. The Department has suspended all of the company's U-Dream and U-Dreams product licences.
Unauthorized health products Multiple unauthorized health products Unauthorized eye drops in Toronto, Ontario Unauthorized prescription skin products in Etobicoke, Ontario Update - Products sold by Dutta Health Centre Ayurvedic Clinic in B.C.	Health Canada advised Canadians about various unauthorized health products being sold at retail locations across Canada or online that may pose serious health risks.
Xeljanz (tofacitinib) Health Professional Risk Communication	An increased incidence rate of thrombosis, including pulmonary embolism, deep vein thrombosis, and arterial thrombosis was observed in patients treated with Xeljanz (tofacitinib) in a large, ongoing post-marketing study. The study showed that patients with rheumatoid arthritis and at least one cardiovascular risk factor should not have their dose doubled given the risk of thrombosis. The Canadian product monograph for Xeljanz/Xeljanz XR has been updated to include this new warning about thrombosis under *Serious Warnings and Precautions*.

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. Canadian product monographs can be accessed through Health Canada's Drug Product Database.

Sativex (delta-9-tetrahydrocannabinol [THC] and cannabidiol [CBD])

Removal of Notice of Compliance with Conditions indications for Sativex:

The *Indications* section of the Canadian product monograph for Sativex has been revised to **remove** the following indications, which were authorized under the Notice of Compliance with Conditions (NOC/c) policy, as the confirmatory clinical studies for these NOC/c indications did not support the therapeutic advantage of Sativex for neuropathic and cancer pain:*

- Adjunctive treatment for the symptomatic relief of neuropathic pain in adult patients with multiple sclerosis.
- Adjunctive analgesic treatment in adult patients with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain.

The *Adverse Reactions, Clinical Trials,* and *Patient Medication Information* sections have also been updated in relation to these removed NOC/c indications.

Key messages for healthcare professionals:[1]

- Sativex is now only indicated as adjunctive treatment for symptomatic relief of spasticity in adult patients with multiple sclerosis who have not responded adequately to other therapies and who demonstrate meaningful improvement during an initial trial of therapy.
- Healthcare professionals are encouraged to consider alternative options for treatment of patients with neuropathic or cancer pain.

Inclusion of information concerning use in hepatic impairment and drug interactions for Sativex:

The *Warnings and Precautions* and *Action and Clinical Pharmacology* sections of the Canadian product monograph for Sativex have been revised to include additional recommendations regarding use in patients with moderate or severe hepatic impairment.

The *Drug Interactions* and *Patient Medication Information* sections of the Canadian product monograph for Sativex have been revised to include additional information regarding potential drug interactions, such as those involving metabolizing enzymes cytochrome P450 (CYP) and uridine diphosphate-glucuronosyltransferase (UGT).

Key messages for healthcare professionals:[1]

- Administration to patients with moderate or severe hepatic impairment is not advised due to higher peak concentration and exposure to THC, CBD, and their metabolites.
- Healthcare professionals are encouraged to refer to the product monograph concerning specific drug interactions with Sativex.

Reference

1. *Sativex (delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)) [product monograph]. Cambridge (United Kingdom): GW Pharma Ltd; 2019.*

* *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. Conditions associated with the NOC/c remain until they have been fulfilled and authorized by Health Canada, in accordance with the NOC/c Policy. If the confirmatory study results do not verify the anticipated benefit within the agreed upon timeframe, the NOC/c indication may be revoked.*

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.

Blincyto (blinatumomab): Authorization with conditions

Health Canada has issued a Notice of Compliance, under the Notice of Compliance with Conditions policy for a new indication for Blincyto* (blinatumomab), lyophilized powder for solution for infusion, 38.5 mcg. The new indication for Blincyto is for the treatment of patients with Philadelphia chromosome-negative CD19 positive B-precursor acute lymphoblastic leukemia (ALL) in first or second hematologic complete remission with minimal residual disease (MRD) greater than or equal to 0.1%. 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 Blincyto Canadian product monograph. The product monograph can be accessed through Health Canada's Drug Product Database, the Amgen Canada Inc. Web site or by contacting Amgen Canada Inc. at 1-866-502-6436. Contact the company for a copy of any references, attachments or enclosures.

* Blincyto's updated product monograph with this NOC/c indication is dated December 2019.

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
- Annual trends for adverse reaction case reports and medical device problem incidents
- Stop Illegal Marketing of Drugs and Devices

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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