Health Canada Santé Canada

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Health Product InfoWatch

July 2016

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REPORTING ADVERSE REACTIONS

Canada Vigilance Program
Telephone: 1-866-234-2345
Fax: 1-866-678-6789
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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

ANNOUNCEMENT

Health Canada allowing immediate access to Naloxone Nasal Spray

As an emergency public health measure, the Minister of Health has signed an Interim Order which authorizes the immediate importation and sale of NARCAN (naloxone) Nasal spray for use in the emergency treatment of known or suspected opioid overdoses. Until now, only the injectable form of the drug has been available in Canada.

Health Canada received an application for a nasal version of naloxone in May 2016, and is currently conducting an expedited review for authorization in Canada. The Interim Order allows both individuals and commercial entities to temporarily import into Canada the product, which has been approved by the U.S. Food and Drug Administration. Health Canada is working with public health authorities to determine how it will be sold in each province or territory.

For more information, please consult the July 6, 2016 news release, notice and frequently asked questions.

In order to be sold in Canada, NARCAN Nasal spray will need to be accompanied by the U.S. labelling as well as additional information required by the Minister of Health. This additional information includes instructions for use in French and instructions on how to report adverse drug reactions.

NARCAN Nasal Spray will be available without a prescription.

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 June 2016 by Health Canada.

Alpha-lipoic acid-containing products Summary Safety Review Health Product InfoWatch	This safety review evaluated the potential risk of hypoglycemic episodes associated with alpha-lipoic acid (ALA)-containing natural health products. Health Canada's review concluded that ALA may cause insulin autoimmune syndrome, which can result in hypoglycemia. Health Canada is considering updates to the labelling standard for ALA to inform consumers to stop using the product and to consult a healthcare professional if they experience symptoms of hypoglycemia. Health Canada has also communicated this information to healthcare professionals.
Atarax and generics (hydroxyzine) Summary Safety Review Health Product Risk Communication	This safety review evaluated the potential risk of QT prolongation (QTP) and torsade de pointes (TdP) associated with hydroxyzine (Atarax and generics). Health Canada's review concluded that hydroxyzine has the potential to block hERG channels and other types of cardiac channels, resulting in a potential risk of QTP and cardiac arrhythmia events including TdP. Health Canada is working with the manufacturers to update the Canadian Product Monographs, including indications, contraindications, and dosage information. Health Canada has also communicated this information to healthcare professionals.
Avonex (interferon beta-1a) Summary Safety Review	This safety review evaluated the potential risk of nephrotic syndrome associated with Avonex (interferon beta-1a). Health Canada's review concluded that there is a potential risk of nephrotic syndrome with the use of Avonex. Health Canada has asked the manufacturer to update the Canadian Product Monograph to include this risk.

Denosumab (Prolia and Xgeva) Summary Safety Review	This safety review evaluated the potential risk of hearing loss and deafness associated with denosumab (Prolia and Xgeva). Health Canada's review concluded that the findings were not sufficient to confirm any additional link between denosumab and hearing loss or deafness 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, toxic substances or high levels of 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.
Tysabri (natalizumab) Summary Safety Review	This safety review evaluated the potential risk of hemolytic anemia associated with Tysabri (natalizumab). Health Canada's review concluded that there is currently insufficient evidence to support a direct link between the use of Tysabri and hemolytic anemia. However, post-market cases of anemia were reported. The manufacturer has updated the Canadian Product Monograph for Tysabri with new information about the risk of anemia.
Uloric (febuxostat) Summary Safety Review	This safety review evaluated the potential risk of Drug Reaction/Rash with Eosinophilia and Systemic Symptoms (DRESS) associated with Uloric (febuxostat). Health Canada's review concluded that the data, though limited, suggested a possible link between DRESS and febuxostat. The Canadian Product Monograph for Uloric has been updated to include this potential risk.
Unauthorized health product (Animal Test) Advisory	Health Canada reminded Canadians regarding the serious risks posed by the unauthorized health product "Animal Test" after identifying additional retailers and a distributor selling the product. The product is marketed as a dietary supplement and is labelled to contain yohimbine.
W-18 Information Update	Health Canada has clarified its position on W-18, a potentially harmful substance. W-18 has been referred to as a synthetic opioid although no pharmacological data is available about the mode of action. Health Canada is moving to add W-18 and related compounds to Schedule I of the *Controlled Drugs and Substances Act*. Health Canada also emphasized that it is not currently known whether naloxone would be effective if it were administered to someone who had taken W-18.

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.

SAFETY BRIEF

Truvada for pre-exposure prophylaxis to reduce the risk of HIV-1 infection in adults at high risk – recommendations to support the appropriate use

Truvada (emtricitabine/tenofovir disoproxil fumarate) was approved in Canada in 2006 for the treatment of HIV-1 infection for adults in combination with other antiretroviral agents. It is now approved in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults at high risk for HIV-1 infection (see textbox for additional information).[1] Truvada should only be prescribed as part of a comprehensive prevention strategy with strict adherence to the recommended dosing regimen to maximize the reduction in the risk of HIV-1 infection.

The Canadian product monograph (CPM) for Truvada has been updated to include the PrEP indication and the important warnings, precautions and safety information associated with this indication. In addition, materials supporting the appropriate use of Truvada for PrEP have been developed by the manufacturer.

Risk of drug resistance with improper use of Truvada for PrEP:

Truvada used for a PrEP indication must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initial use and periodically (at least every 3 months) during use. Drug-resistant HIV-1 variants may emerge in individuals with undetected HIV-1 infection who are taking only Truvada, because Truvada alone does not constitute a complete treatment regimen for the management of HIV-1 infection. Patients should be counselled to strictly adhere to the recommended Truvada dosing schedule. The effectiveness of Truvada in reducing the risk of acquiring HIV-1 is strongly correlated with adherence as demonstrated by measurable drug levels in clinical trials.

Healthcare providers should confirm a negative HIV-1 test immediately prior to initiating Truvada for PrEP. Truvada for PrEP should not be prescribed to patients with HIV-1 infection or to individuals with signs or symptoms consistent with acute viral infections (e.g., fever, fatigue, myalgia, skin rash, etc.). If clinical symptoms consistent with acute viral infection are present, and recent (less than 1 month) exposures to HIV-1 are suspected, PrEP initiation should be delayed for at least one month along with reconfirmation of negative HIV-1 status.

Healthcare professionals prescribing Truvada for PrEP should:

- Complete a risk evaluation of uninfected individuals in order to identify individuals at high risk of HIV-1 infection.
- Counsel uninfected individuals to strictly adhere to the recommended Truvada dosing schedule.
- Counsel patients about safer sex practices, including consistent and correct use of condoms, knowledge of their HIV-1 status and that of their partner(s), and regular testing for other sexually transmitted infections that can facilitate HIV-1 transmission (such as syphilis and gonorrhea). **Truvada for PrEP should only be used as part of a comprehensive HIV prevention strategy**.
- Test patients to confirm that they are HIV-1 negative immediately before starting Truvada for a PrEP indication. Truvada should not be prescribed to individuals with any signs or symptoms consistent with recent acute viral infections.
- Screen patients at least every 3 months for HIV-1 status to reconfirm that they are HIV-1 negative while taking Truvada for PrEP. If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, Truvada PrEP should be discontinued until negative infection status is confirmed using a test approved by Health Canada as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection.

Web site training and educational materials:

Web site training and educational materials developed by the manufacturer for Truvada for PrEP are available at the following Web address : www.truvada.ca. The training and educational materials include a Prescriber Individual Agreement Form, a Checklist for Prescribers, a Training Guide for Healthcare Providers, a Prescriber Education Slide Deck and a Prescriber Safety Brochure.

Reporting of adverse reactions in patients receiving Truvada for PrEP:

All cases of serious or unexpected adverse reactions in patients receiving Truvada for PrEP should be reported to Health Canada or Gilead Sciences Canada, Inc.

Factors that may help to identify individuals at high risk:[1]

- has partner(s) known to be HIV-1 infected, or
- engages in sexual activity within a high prevalence area or social network and one or more of the following:
  - inconsistent or no condom use
  - diagnosis of sexually transmitted infections
  - exchange of sex for commodities (such as money, food, shelter, or drugs)
  - use of illicit drugs or alcohol dependence
  - incarceration
  - partner(s) of unknown HIV-1 status with any of the factors listed above

Reference

1. *Truvada (emtricitabine/tenofovir disoproxil fumarate)* [product monograph]. Mississauga (ON): Gilead Sciences Canada, Inc.; 2016.

PRODUCT MONOGRAPH UPDATE

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.

Lamisil (terbinafine)

Lamisil (terbinafine) tablets are now ***contraindicated*** *for patients with chronic or active hepatic disease. This information has been included in the Contraindications, Warnings and Precautions and Adverse Reactions sections of the Canadian product monograph.*

Key messages for healthcare professionals:[1]

- Serious and life-threatening hepatic adverse reactions (including hepatic failure leading to death and liver transplant) have been reported in patients with or without pre-existing chronic or active hepatic disease receiving Lamisil tablets for the treatment of onychomycosis and dermatomycosis.
- Before prescribing Lamisil tablets, a baseline liver function test should be performed to assess any pre-existing liver disease since hepatotoxicity may occur in patients with or without pre-existing liver disease.
- Periodic monitoring (after 4 to 6 weeks of treatment) of liver function tests is recommended. Lamisil should be immediately discontinued in case of elevation of liver function tests.
- Patients prescribed Lamisil tablets should be warned to report immediately to their physician any symptoms of persistent nausea, decreased appetite, fatigue, vomiting, right upper abdominal pain or jaundice, dark urine or pale feces.

Reference

1. *Lamisil (terbinafine)* [product monograph]. Dorval (QC): Norvatis Pharmacetuicals 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

Health Canada
Marketed Health Products Directorate
Address Locator 0701D
Ottawa ON K1A 0K9
Telephone: 613-954-6522
Fax: 613-952-7738

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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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