Health Canada Santé Canada

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Health Product InfoWatch

April 2015

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REPORTING ADVERSE REACTIONS

Canada Vigilance Program
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HEALTH PRODUCTS MENTIONED IN THIS ISSUE

Pharmaceuticals and Biologics

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Other

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Foreign Health Products
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Unauthorized Health Product

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 March 2015 by Health Canada.

0.9% Sodium Chloride Injection USP and 5% Dextrose Injection USP Health Product Risk Communication	Baxter recalled one lot of 0.9% Sodium Chloride Injection USP, 50 mL and one lot of 5% Dextrose Injection USP, 50 mL due to the potential for leakage of the parenteral solution bag. Leakage of a parenteral solution bag may result in delay or interruption of therapy, microbial contamination and air in the system. If used in IV admixture, there is potential for delivery of a more concentrated drug solution than intended.
Altimate Fat Burner Maximum Burn Information Update	Following Health Canada's advisory regarding "Altimate Fat Burner Maximum Burn" being sold by Nature's Source in Vaughan, Ontario, the Department received a complaint about the product also being sold at Nature's Source, in Oakville, Ontario. Altimate Fat Burner Maximum Burn is an unauthorized health product labelled to contain DHEA, yohimbe, caffeine and ephedrine.
Attention Deficit Hyperactivity Disorder (ADHD) Drugs Information Update Summary Safety Review (amphetamines and suicidality) Summary Safety Review (methylphenidate and suicidality)	These safety reviews evaluated the potential risk of suicidality associated with amphetamine and methylphenidate products. Cases of suicidality have been reported with the use of both types of products for the treatment of ADHD. However, there is limited evidence showing that either were the cause of suicidality. Stronger, clearer warnings on the risk of suicidal thoughts and behaviours are being incorporated into the prescribing information for these drugs. Health Canada has also communicated this risk to Canadians.
Cisplatin Injection, Gemcitabine for Injection, USP and Topotecan HCl for Injection Health Product Risk Communication	Mylan Pharmaceuticals ULC, in consultation with Health Canada, initiated a voluntary recall for one lot of Cisplatin Injection 1 mg/mL, 2 lots of Gemcitabine for Injection, USP (1 g and 2 g per vial, respectively) and 2 lots of Topotecan for Injection 4 mg per vial due to the potential presence of foreign particulate matter. Inadvertent injection of foreign particulate matter could result in risks to patient health.

Foreign Health Products Foreign Product Alert	These foreign health products have been found by regulators in other countries to contain undeclared drug ingredients, or unacceptable levels of microbial contamination. 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.
Jamp-Methotrexate (USP 50mg/2mL) Advisory Health Product Risk Communication	Jamp Pharma Corporation, in consultation with Health Canada, voluntarily recalled one lot of Jamp-Methotrexate USP 50 mg/2 mL (lot 7801372) due to the potential presence of foreign particulate matter. The risks associated with subcutaneous injection of foreign particulate matter include local reaction at the injection site and/or swelling or possible allergic reaction and infection.
Methotrexate Injection (USP 50mg/2mL) Advisory Health Product Risk Communication	Mylan Pharmaceuticals ULC, in consultation with Health Canada, voluntarily recalled one lot of Methotrexate Injection USP 50 mg/2 mL (lot 7801370) due to the potential presence of foreign particulate matter. The risks associated with subcutaneous injection of foreign particulate matter include local reaction at the injection site and/or swelling or possible allergic reaction and infection.
Miracle Mineral Solution Information Update	Health Canada reminded Canadians that consuming a product sold as “Miracle Mineral Solution” (MMS) may pose serious health risks, following a Health Canada seizure of an MMS product from a vendor in Burin, Newfoundland on March 25, 2015.
Tumour Necrosis Factor (TNF) Blockers Summary Safety Review	This safety review evaluated the potential risk of glioblastoma in patients using TNF blockers. Given the evidence available at the time of this review, no increased risk of glioblastoma after exposure to TNF blockers was found. Health Canada will continue its ongoing monitoring of adverse reaction information involving TNF blockers, as it does for all health products on the Canadian market, and assess potential harms.
Unauthorized Health Product Advisory	Health Canada seized a health product being injected at Art Nails Ltd., located in Vancouver, B.C., which appeared to be unauthorized as it contained no labelling. All products administered by injection in Canada must be authorized by Health Canada and must have approved labelling.

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.

REVIEW ARTICLE

Goldenseal and cytochrome P450 inhibition

Key points

- Goldenseal (*Hydrastis canadensis*) is a herbal ingredient used to aid or alleviate a variety of digestive disorders.
- Both *in vitro* and *in vivo* studies suggest that goldenseal has an inhibitory effect on certain cytochrome P450 (CYP) isoforms, including CYP3A4 and CYP2D6.
- Healthcare professionals are reminded to ask patients about the use of natural health products when prescribing and dispensing medications, particularly those known to be metabolized by CYP.

Goldenseal (*Hydrastis canadensis*) is a herbal ingredient that is used to aid or alleviate a variety of digestive disorders.[1] Although cytochrome P450 (CYP)-mediated interactions are well-documented for certain substances, including herbal ingredients and food (e.g., St. John's Wort and grapefruit juice), the potential for goldenseal to inhibit CYP enzymes and interact with drugs may not be as well known.

Both *in vitro* and *in vivo* studies examining the effects of goldenseal on the CYP metabolic system have been conducted. *In vitro* studies have shown that goldenseal has inhibitory effects on CYP enzymes, including CYP3A4 and CYP2D6.[2,3] A series of small-scale clinical studies have corroborated these findings.[4-6] Gurley et al. first observed that goldenseal strongly inhibited CYP3A4/5 and CYP2D6 in healthy human volunteers.[4] In a subsequent investigation, goldenseal use produced significant changes to the pharmacokinetic parameters of midazolam, a clinically recognized CYP3A4 substrate.[5]

In contrast, one clinical study observed that goldenseal did not significantly affect the pharmacokinetics of indinavir, another CYP3A4 substrate.[7] It was postulated that goldenseal may alter the oral bioavailability of drugs that are subject to a high degree of first-pass metabolism by CYP3A4 in the gut wall, but is not likely to affect drugs metabolized primarily in the liver. As such, indinavir, which has a high oral bioavailability and is metabolized primarily in the liver, would not likely be affected by goldenseal.

The clinical significance of goldenseal's inhibitory potential is further influenced by a variety of factors, including age-related and gender differences in CYP expression, CYP gene polymorphisms, the presence of disease, and the use of concomitant health products which can inhibit or induce CYP activity.[8] Additional studies that address the variability in CYP expression between individuals and that include larger sample sizes and consistent dosages of goldenseal are needed to further characterize this potential safety risk.

Natural health product identification in adverse reaction reports

It is important to include as many health product identifiers as possible in the adverse reaction reporting form, especially when reporting adverse reactions suspected of being associated with natural health products. This assists Health Canada in conducting accurate, thorough assessments of adverse reactions.

Examples of natural health product identifiers include:

- Exact product brand name (including modifying prefix or suffix)
- Natural Product Number (NPN) or Homeopathic Medicine Number (DIN-HM)
- List of ingredients (or a copy or picture of the label or container) and their amount per serving
- Lot number
- Expiration date
- Company name
- Where the product was purchased (e.g., Internet, pharmacy, Canada vs. other countries, etc.)

Other regulatory agencies have identified goldenseal as a potential inhibitor of CYP.[8,9] As of Nov. 30, 2014, there were no Canadian or international reports of adverse reactions assessed by Health Canada as having been associated with interactions between goldenseal-containing health products and other health products.

It is important for healthcare professionals and consumers to be aware that herbal products may affect drug metabolism through various mechanisms, particularly through enzyme induction or inhibition. Goldenseal is just one example of a herbal ingredient with the potential of being involved in a drug-herb interaction. Another example of a potential herb-drug interaction which was recently communicated by Health Canada involved a suspected interaction between *Ginkgo biloba* and efavirenz, a drug used to treat HIV.[10]

Healthcare professionals are reminded to ask patients about the use of natural health products (NHPs) when prescribing and dispensing medications, especially those known to be metabolized by CYP. Health Canada encourages the reporting of all suspected cases of interactions, including those that occur with the use of NHPs, as well as drugs and food products, to the Canada Vigilance Program.

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HELPFUL LINKS

- MedEffect™ Canada
- Recalls and Safety Alerts Database
- Summary Safety Reviews
- Canada Vigilance Adverse Reaction Online Database
- Drug Product Database
- Canadian Drug Shortage Database
- The Drug and Health Product Register

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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