Health Canada Santé Canada

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Health Product InfoWatch

September 2020

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REPORTING ADVERSE REACTIONS

Canada Vigilance Program
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HEALTH PRODUCTS MENTIONED IN THIS ISSUE

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CORONAVIRUS DISEASE (COVID-19)

For the most up-to-date information on COVID-19, please visit the Government of Canada Coronavirus disease (COVID-19) Web site **Canada.ca/coronavirus**, which includes a dedicated section for healthcare professionals and for the health product industry.

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.

Health Product InfoWatch 2015 - 2020 5 years

Canada

Did you know?

Canadian Paediatric Surveillance Program 2019 results

The Canadian Paediatric Surveillance Program (CPSP) is a joint project of the Public Health Agency of Canada and the Canadian Paediatric Society. It contributes to the improvement of the health of children and youth in Canada through national surveillance and research into childhood disorders that are high in disability, morbidity and economic costs to society. Featured in the CPSP 2019 report are studies and surveys of: serious and life-threatening adverse drug reactions; vaping-related illness and injury; serious and life-threatening events associated with recreational cannabis use; among others. To learn more, read the report: Canadian Paediatric Surveillance Program 2019 results.

MONTHLY RECAP OF HEALTH PRODUCT SAFETY INFORMATION

The following is a list of health product advisories, type I recalls and summaries of completed safety reviews published in August 2020 by Health Canada.

Certain hand sanitizers that may pose health risks Advisory	Health Canada advised Canadians that certain hand sanitizers were recalled because they either contain ingredients that are not permitted by Health Canada or are not properly labelled and are missing important information.
Prescription cough and cold products containing opioids Health Professional Risk Communication	Prescription cough and cold products containing codeine, hydrocodone or normethadone are NOT indicated for use in children and adolescents (younger than 18 years of age). There is a risk of opioid toxicity due to the variable and unpredictable metabolism of codeine or hydrocodone. The benefits of symptomatic treatment of cough associated with allergies or the common cold do not outweigh the risks of use of opioids in these patients. Health Canada continues to work with the manufacturers of affected prescription opioid-containing products to include this new safety information in their respective Canadian product monographs.
Ranitidine Information Update Drug recall	Pharmascience Inc. recalled one lot of prescription PMS-Ranitidine (150 mg strength tablet) as a precaution after tests found N-nitrosodimethylamine (NDMA), a nitrosamine impurity, at close to the acceptable level. Health Canada also provided an update on the status of ranitidine drugs in Canada, including enhanced safety measures the Department is putting in place to detect NDMA. A table with detailed information on the recalled lot (lot 619003) is provided in the information update.

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

Hypersensitivity reactions, including anaphylaxis, reported with oral use of *Andrographis paniculata*-containing natural health products

Key messages

- Cases of hypersensitivity reactions, including anaphylaxis, suspected of being associated with oral ingestion of *Andrographis paniculata (A. paniculata)*-containing health products have been reported in Canada and internationally.
- The information in the Canadian reports was insufficient to adequately assess the causal association between the hypersensitivity reactions and products containing *A. paniculata*.
- Healthcare professionals are encouraged to report any case of hypersensitivity suspected of being associated with products containing *A. paniculata* to Health Canada for the continued monitoring and assessment of this potential health risk.

A. paniculata (Common andrographis, Indian chiretta)* is a plant which has been used in Ayurvedic medicine and traditional Chinese medicine for prophylaxis and symptomatic treatment of upper respiratory infections, lower urinary tract infections and acute diarrhea.[1-3] Natural health products (NHPs) with *A. paniculata*, either as a single or multi-ingredient, are available for sale in Canada in several dosage forms including tablets, capsules, tinctures and other liquid forms.

Canadian context

As of April 30, 2020, Health Canada received 3 Canadian reports of hypersensitivity reactions suspected of being associated with a product containing *A. paniculata*. Two cases were deemed serious. The first serious case involved a 56 year-old woman who experienced anaphylactic shock within 10 minutes of taking 2 capsules of a NHP containing *A. paniculata* (Cold-Tek). The second serious case involved a 40 year-old woman who experienced abdominal and chest pain, diarrhea, dyspnea, erythema, seizure, urticaria and vomiting 3 hours after taking Andrographis Complex. All 3 reports were deemed unassessable for the relatedness to *A. paniculata* due to limited information or the presence of other suspect ingredients.

International context

The Australian Therapeutic Goods Administration (TGA) investigated this issue[4] and released a Safety advisory in 2015 about the risk of anaphylactic / allergic reactions with *A. paniculata*-containing health products.[5] According to the TGA's safety review, it appears likely that *A. paniculata* plays a causative and/or contributing role in anaphylactic / allergic reactions, including when present in multi-ingredient formulations.[2,5] The TGA required that a warning statement be included on the labels of all listed medicines containing *A. paniculata* on the Australian market: "*Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) stop use and seek immediate medical attention*".[6]

New Zealand's Medsafe also issued an Alert Communication in 2017 about the potential risk of allergic reactions with *A. paniculata*-containing products.[7]

*For information on *A. paniculata* and other natural health product ingredients, consult the Natural Health Products Ingredients Database.

Cases of hypersensitivity reactions with the use of *A. paniculata*-containing products have been reported in the literature.[8,9] However, further investigation of the causal association between the ingredient *A. paniculata* and hypersensitivity is needed.[8] Some authors have also indicated that hypersensitivity reactions could potentially be related to product contamination and the lack of product standardization across brands.[8,10]

The exact pathophysiological mechanism that mediates the potential association between *A. paniculata*-containing products and hypersensitivity reactions remains unclear.[2]

Healthcare professionals are encouraged to report any case of hypersensitivity suspected of being associated with *A. paniculata*-containing NHPs to Health Canada for the continued monitoring and assessment of this potential risk (see "Natural health product identification in adverse reaction reports").

Natural health product identification in adverse reaction reports

Healthcare professionals who suspect an adverse reaction to a NHP are strongly encouraged to report it. It is important to include as much information as possible and as many NHP identifiers as possible in the adverse reaction reporting form. This assists Health Canada in conducting accurate, thorough assessments of adverse reactions.

Consumers are also recommended to hold on to the product, as Health Canada may request a sample for further investigation, if needed.

Examples of NHP 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 the amount per serving
- Lot number
- Expiration date
- Company name
- Where the product was purchased (e.g., Internet, pharmacy, Canada vs. other countries, etc.)

References

1. *Herba Andrographidis.* In: WHO monographs on selected medicinal plants. Vol. 2. Geneva (Switzerland): World Health Organization; 2004. p. 12-24. (accessed 2020 July 28).
2. *Safety review of Andrographis paniculata and anaphylactic / allergic reactions.* Canberra (Australia): Therapeutic Goods Administration; 2015 Oct 8. (accessed 2020 July 28).
3. Committee on Herbal Medicinal Products (HMPC). *Assessment report on Andrographis paniculata Nees, folium.* London (UK): European Medicines Agency; 2014 Aug 27. (accessed 2020 July 28).
4. Advisory Committee on the Safety of Medicines. *ACSOM meeting statement, Meeting 23, 11 July 2014.* Canberra (Australia): Therapeutic Goods Administration; 2015 March 5. (accessed 2020 July 28).
5. *Products containing Andrographis paniculata. Safety advisory - risk of allergic reactions.* Canberra (Australia): Therapeutic Goods Administration; 2015 Oct 8. (accessed 2020 July 28).
6. *High-moderate risk changes to permissible ingredients - Andrographis paniculata.* Canberra (Australia): Therapeutic Goods Administration; 2019 Dec 2. (accessed 2020 July 28).
7. *Safety Information. Early Warning System - Alert Communication. Andrographis paniculata - potential risk for allergic reactions.* Wellington (New Zealand): Medsafe; 2017 March 24. (accessed 2020 July 28).
8. Suwankesawong W, Saokaew S, Permsuwan U, et al. Characterization of hypersensitivity reactions reported among *Andrographis paniculata* users in Thailand using Health Product Vigilance Center (HPVC) database. *BMC Complement Altern Med* 2014;14:515.
9. Coon JT, and Ernst E. *Andrographis paniculata* in the treatment of upper respiratory tract infections: a systematic review of safety and efficacy. *Planta Med* 2004;70(4):293-8.
10. Richard EJ, Murugan S, Bethapudi B, et al. Is *Andrographis paniculata* extract and andrographolide anaphylactic? *Toxicol Rep* 2017;4:431-437.

Did you know? Licensed Natural Health Products Database

To get information on the ingredients in Andrographis Complex, Cold-Tek, or other natural health products on the Canadian market, search the Licensed Natural Health Products Database:

https://health-products.canada.ca/lnhpd-bdpsnh/index-eng.jsp.

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
- Stop Illegal Marketing of Drugs and Devices
- List of Drugs for Exceptional Importation and Sale

Suggestions?

Your comments are important to us. Let us know what you think by reaching us at HC.infowatch-infovigilance.SC@canada.ca

Health Canada
Marketed Health Products Directorate
Address Locator 1906C
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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