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Health Product InfoWatch

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REPORTING ADVERSE REACTIONS

Canada Vigilance Program

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HEALTH PRODUCTS MENTIONED IN THIS ISSUE

Pharmaceuticals and Biologics

Bexsero (multicomponent meningococcal B vaccine [recombinant, adsorbed])
CellCept (mycophenolate mofetil)
Clear Care Cleaning and Disinfecting Solution
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Pneumococcal vaccines
Tarceva (erlotinib)
Zostavax (zoster vaccine live, attenuated [Oka/Merck])

Natural Health Products

Pseudoephedrine-containing products

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 January 2016 by Health Canada.

CellCept (mycophenolate mofetil) and Myfortic (mycophenolate sodium) Health Product Risk Communication	New contraindications are being added to the CellCept (mycophenolate mofetil) and Myfortic (mycophenolate sodium) Canadian Product Monographs concerning the risk of spontaneous abortions and congenital malformations following exposure during pregnancy.
Galexos (simeprevir) Summary Safety Review	This safety review evaluated the potential risk of severe liver problems and related death associated with the use of Galexos (simeprevir). Health Canada's review concluded that the level of evidence related to the risk of severe liver problems should be reflected in the prescribing information, which has now been updated.
Oral fluoroquinolones Summary Safety Review	This safety review evaluated the potential risk of retinal detachment associated with the use of oral fluoroquinolones. Health Canada's review concluded that a link could not be ruled out at this time. Health Canada recommended that the labelling be revised to highlight the urgency to see a healthcare professional if patients experience vision problems during or following oral fluoroquinolone administration.
Tarceva (erlotinib) Health Product Risk Communication	Tarceva (erlotinib) is not effective for maintenance treatment in patients with locally advanced or metastatic non-small cell lung cancer whose tumours do not have an epidermal growth factor receptor activating mutation. The Canadian prescribing and consumer information for Tarceva will be updated to reflect the new data.

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

Key points

- Ischemic colitis has been reported with a variety of medications, including pseudoephedrine. A small

Pseudoephedrine and ischemic colitis

Pseudoephedrine is a direct and indirect acting sympathomimetic which is used for the symptomatic relief of nasal congestion.[1] In Canada, it is available as a self-care product, either as a single ingredient or as a combination product with other ingredients such as antihistamines, analgesics, or antitussive agents.

Key points (continued)

number of published case reports suggest a possible association between pseudoephedrine use and ischemic colitis.

- The contribution of medications, including over-the-counter medicines and natural health products such as pseudoephedrine, is important to consider in the management of ischemic colitis.
- Healthcare professionals are encouraged to report to Health Canada any cases of ischemic colitis suspected of being associated with pseudoephedrine or any other health products, and to provide detailed information when describing cases.

Did you know?

In Canada, single ingredient pseudoephedrine products are licenced as natural health products (NHPs) and have a Natural Product Number (NPN). Pseudoephedrine combination products are licenced as pharmaceuticals and have a Drug Identification Number (DIN).

Did you know?

Dechallenge and Rechallenge information is useful for assessing adverse reaction information in the reports you submit to Health Canada.

Pseudoephedrine acts directly on α-adrenergic receptors in the mucosa of the respiratory tract, producing vasoconstriction and shrinkage of swollen nasal mucous membranes.[2] This results in a decreased blood flow through the nasal mucosa and a reduced nasal airway resistance. Systemic vascular effects in the heart and peripheral circulation have been previously reported with pseudoephedrine in the literature.[3]

Ischemic colitis is an inflammation of the colon secondary to reduced blood perfusion that leads to bowel wall ischemia.[4] It is caused by a decrease in systemic perfusion or an anatomic occlusion. It has a vast clinical spectrum of injury ranging from mild and transient ischemia to acute fulminant colitis.[5] Ischemic colitis predominantly affects the elderly and is usually associated with underlying occlusive vascular disease.[4,6] This condition may also be associated with hypercoagulable states, as well as various medications (e.g., antibiotics, chemotherapeutic agents, diuretics, hormonal therapies, illicit drugs, nonsteroidal anti-inflammatory drugs, psychotropic medications, statins, triptans, vasoactive substances).[4,7] The clinical presentation is variable but patients typically present with a sudden onset of crampy abdominal pain, diarrhea and an urge to defecate. Bright red or maroon blood in the stools is frequently present as well. Other symptoms include anorexia, nausea and vomiting. This condition can easily be confused with other digestive problems, given that symptoms are similar.[8] The diagnosis is based on a combination of clinical suspicion, radiographic, endoscopic and histological findings.[7] Segmental gastrointestinal involvement is characteristic. The proposed mechanism for ischemic colitis in association with pseudoephedrine is vasoconstriction in the mesenteric circulation in susceptible patients.[9,11]

Health Canada's literature review of ischemic colitis and pseudoephedrine identified 9 published cases.[5,9-13] There were 7 women and 2 men; ages ranged from 33 to 58 years. All patients reported using pseudoephedrine (as a single ingredient or in a combination product), within a week of hospital admission. In 8 cases, pseudoephedrine doses ranged from 60 to 240 mg per day. In one case, the patient took up to 300 to 900 mg daily over a two year period, exceeding recommended daily intakes. All the patients presented with a sudden onset of severe abdominal pain followed by bloody stools. In most cases, endoscopic examination was reported to have revealed a segmental colitis supporting the diagnosis of ischemic colitis. Some patients were using concomitant medications, including amoxicillin, antihistamines, female hormones, narcotics, benzodiazepines, acetaminophen, and nonsteroidal anti-inflammatory drugs. Dechallenge was positive in all cases; however, in some cases, concomitant products were discontinued at the same time. All patients recovered without sequelae.

Of the 9 case reports identified in the literature, only 1 involved the use of a single-ingredient pseudoephedrine product without other concomitant medications or significant past medical history for ischemic colitis.[9] This case involved a 49-year-old woman who took Sudafed 120 mg twice daily for 5 days prior to her hospital admission; the last dose was taken about 12 hours before onset of her gastrointestinal symptoms.

Did you know? (continued)

Dechallenge is the response to withdrawal of the drug. Abatement of reaction after the drug is stopped or the dose is reduced is considered a positive dechallenge.

Rechallenge is the response to reintroduction of the drug. Reappearance of the adverse reaction after reintroduction of the drug is considered a positive rechallenge.

What to include in your adverse reaction reports to Health Canada

In addition to the **name of the health product** and **description of the adverse reaction**, it is important to include as many as possible of the following elements:

- Patient characteristics (age, sex, height and weight);
- Dosing information and indication for use of the suspected health product;
- Therapy dates: when the suspected health product was started and stopped;
- Changes to therapy with the suspected health product and impact on the patient (e.g., dechallenge/rechallenge information);
- Treatment of the adverse reaction (including date the adverse reaction occurred and was resolved, if applicable);
- Investigations to exclude alternate causes for the adverse reaction;
- Relevant history and pre-existing conditions;
- Relevant tests/lab data; and
- Other health products taken (including over-the-counter and natural health products) with therapy dates and dosing information.

As of May 19, 2015, Health Canada had not received any Canadian reports of ischemic colitis suspected of being associated with the use of pseudoephedrine. A review of international data from the World Health Organization's Global Individual Case Safety Reports Database System (VigiBase) identified 24 international cases of ischemic colitis suspected of being associated with pseudoephedrine as of May 2, 2015, including 7 that reported the use of single-ingredient pseudoephedrine.*

Cases of ischemic colitis suspected of being associated with the use of pseudoephedrine are limited. Nonetheless, Health Canada continues to monitor the risk of ischemic colitis with pseudoephedrine use. Healthcare professionals are encouraged to ask their patients about the use of all health products (including over-the-counter and natural health products) and to report any case of ischemic colitis suspected of being associated with pseudoephedrine to Health Canada.

References

1. Brayfield A (ed). *Martindale: The complete drug reference*. [online] London (UK): Pharmaceutical Press: 2015. (accessed Jan 21, 2016)
2. Pseudoephedrine hydrochloride, pseudoephedrine sulfate. In: McEvoy GK, editor. *AHFS Drug Information STAT!*Ref *Online Electronic Medical Library*. Bethesda (MD): American Society of Health-System Pharmacists; updated Nov 4, 2015. (accessed Jan 21, 2016)
3. Salerno SM, Jackson JL, Berbano EP. Effect of oral pseudoephedrine on blood pressure and heart rate. *Arch intern med* 2005;165(15):1686-94.
4. Tyagi S, Cappell MS. Chapter 162. Large bowel disorders. In: McKean SC, Ross JJ, Dressler DD, et al., editors. *Principles and Practice of Hospital Medicine*. New York (NY): McGraw-Hill; 2012.
5. Moszkowicz D, Mariani A, Trésallet C, et al. Ischemic colitis: the ABCs of diagnosis and surgical management. *J Visc Surg* 2013;150(1):19-28.
6. Klestov A, Kubler P, Meulet J. Recurrent ischaemic colitis associated with pseudoephedrine use. *Intern Med J* 2001; 31(3):195-6.
7. Grubel P, Lamont JT, Nandakumar G. Colonic ischemia. In: Collins KA, editor. *UpToDate*. Waltham (MA); updated Feb 13, 2015. (accessed Jan 5, 2016)
8. Theodoropoulou A, Koutroubakis IE. Ischemic colitis: clinical practice in diagnosis and treatment. *World J Gastroenterol* 2008;14(48):7302-8.
9. Sherid M, Samo S, Husein H, et al. Pseudoephedrine-induced ischemic colitis: case report and literature review. *J Dig Dis* 2014;15(5):276-80.
10. Dowd J, Bailey D, Moussa K, et al. Ischemic colitis associated with pseudoephedrine: four cases. *Am J Gastroenterol* 1999;94(9):2430-4.
11. Traino AA, Buckley NA, Bassett ML. Probable ischemic colitis caused by pseudoephedrine with tramadol as a possible contributing factor. *Ann Pharmacother* 2004;38(12): 2068-70.
12. Schneider RP. Ischemic colitis caused by decongestant? *J Clin Gastroenterol* 1995;21(4): 335-6.
13. Lichtenstein GR, Yee NS. Ischemic colitis associated with decongestant use. *Ann Intern Med* 2000;132(8):682.

* World Health Organization (WHO) adverse reaction information provided by: The WHO Collaborating Centre for International Drug Monitoring. This information is not homogeneous with respect to the sources of the information or the likelihood that the health product caused the suspected adverse reaction. Also, this information does not represent the opinion of the WHO.

PRODUCT CONFUSION ALERT

Risk of eye injury with improper use of hydrogen peroxide-based contact lens solutions

Key points

- Eye injuries have been reported due to improper use of hydrogen peroxide-based contact lens solutions.
- Eye care professionals and other healthcare professionals are encouraged to advise consumers that hydrogen peroxide-based contact lens solutions are different than multi-purpose or saline solutions and to advise on safe and proper use.
- Health Canada is working with Alcon Canada Inc., the manufacturer of Clear Care Cleaning and Disinfecting Solution (Clear Care) to revise the labelling and packaging of their product to promote safe and proper use.

Hydrogen peroxide-based contact lens solutions are intended for cleaning, daily protein removal, disinfecting and storing of lenses. Currently available products in Canada include Clear Care (marketed in 2002), Lens Care System (marketed in 2014 and available as several different store brands), and Peroxiclear (marketed in 2014). Others such as Aosept and Oxysept are no longer sold in Canada.

When used properly, hydrogen peroxide found in contact lens solutions is a very effective chemical disinfectant.[1] However, hydrogen peroxide-based solutions are neither multi-purpose solutions nor saline contact lens solutions. All hydrogen peroxide-based contact lens solutions must only be used with a specially designed lens case containing a neutralizing disc, which is provided with the product. The disc in the lens case neutralizes the hydrogen peroxide to create a gentle saline solution similar to tears. Lenses must be soaked in the specialized lens case for a minimum number of hours (as indicated in the directions for use) before the lenses can be safely inserted in the eyes. Hydrogen peroxide-based solutions should never be used to rinse contact lenses prior to inserting them into the eyes.

Unneutralized hydrogen peroxide is irritating to the eyes. The most common adverse events related to hydrogen peroxide-based contact lens solutions reported to Health Canada were: eye burns, eye irritation, eye pain, ocular hyperaemia (redness), blurred vision and reduced visual acuity. Other less commonly reported adverse reactions were: corneal abrasion, corneal epithelium defect, corneal injury, corneal irritation, corneal perforation, eye swelling, increased lacrimation and visual impairment. These adverse reactions are consistent with published information on the effects of unneutralized hydrogen peroxide in the eyes.[2]

In 2013, Health Canada issued an Information Update about the risk of eye injuries from improper use of hydrogen peroxide-based contact lens solutions. Reports received since that time by Health Canada indicate that eye injuries continue to occur. In 2015, Health Canada analysed adverse reaction reports involving Clear Care, both to assess the effectiveness of labelling and packaging changes undertaken by the company in 2013 and to determine additional strategies to reduce the risk of eye injuries.

Health Canada's analysis of these reports identified several factors that may contribute to consumer confusion resulting in improper use of the product. Some or all of the factors may be common to all hydrogen peroxide-based contact lens solution products. The primary factors were:

- Limited user knowledge that hydrogen peroxide-based contact lens solutions are not the same as multi-purpose or saline solutions, and instructions for safe and proper product use are different;
- Product placement at the point of purchase (e.g., hydrogen peroxide-based

solutions are found in close proximity to multi-purpose and/or saline solution eye products); and
- Safety messages on the label and package were not prominent, and not always reviewed by or adhered to by users.

Eye care professionals and other healthcare professionals are encouraged to advise consumers regarding the safe and proper use of all hydrogen peroxide-based contact lens solutions. The following warnings in particular should be emphasized:

- Hydrogen peroxide-based solutions are different from multi-purpose and saline contact lens solutions.
- DO NOT squirt solution directly into eyes; burning or stinging will result.
- DO NOT use a flat lens case. Hydrogen peroxide-based solutions only work with the special lens case with neutralizing disc provided.
- DO NOT remove lenses from case until the specified time indicated in the directions for use has passed. The solution needs time to neutralize.
- NEVER rinse contact lenses with the solution before putting them in eyes. To rinse your lenses, use sterile saline.
- If unneutralized solution gets into eyes, it will cause burning and stinging. If this happens, remove contact lenses immediately and flush (wash) eyes with a large amount of water or sterile saline.
- Stop use and ask a doctor if burning or irritation continues.

Health Canada is currently working with Alcon Canada Inc., the manufacturer of Clear Care, to revise safety messages on the label and introduce packaging improvements, including a Product Facts table.*

If you require further information, please contact the Patient Safety Section of Health Canada.

References

1. Wing D, Gellatly K. Contact Lens Care. In: Repchinsky C, ed. *Therapeutic Choices for Minor Ailments*. Ottawa, ON: Canadian Pharmacists Association; 2013: 145.
2. Hydrogen peroxide, In NLM: TOXNET Toxicology Data Network. Hazardous Substances Data Bank (HSDB). Bethesa, MD: National Institutes of Health, Health & Human Services; 1993. http://toxnet.nlm.nih.gov. Reviewed December 5, 2013. Accessed January 20, 2016.

* The Product Facts table is modeled after the Canadian “Nutrition Facts” table for foods and the U.S. “Drugs Facts” box. It provides a standardized format and location for important product information, so that consumers can find and compare information quickly and easily.

VACCINE SAFETY REVIEW

Report for April 1, 2015 to June 30, 2015

Post-market surveillance is essential to monitor the safety and effectiveness of vaccines and other health products. The monitoring of the safety of vaccines is a shared responsibility between Health Canada and the Public Health Agency of Canada (PHAC). Market authorization holders are required to report serious adverse events following immunization (AEFIs) to the Canada Vigilance Program in the Marketed Health Products Directorate at Health Canada. The Canada Vigilance Program also receives voluntary AEFI reports from healthcare professionals and consumers. Provincial and Territorial public health authorities report AEFIs from publicly funded vaccine programs to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) in PHAC to monitor the safety of immunization programs.

This Vaccine Safety Review summarizes AEFI reports received by the Canada Vigilance Program between April 1, 2015 and June 30, 2015. To access reports published by CAEFISS, please visit the CAEFISS website.

- From April 1, 2015 to June 30, 2015, the Canada Vigilance Program received 171 reports of adverse events for which vaccines were the suspected cause.
- There were more reports received during this period than was previously received during the same period of 2013 (106 reports) and 2014 (149 reports). This increase was because of the reports involving Bexsero (multicomponent meningococcal B vaccine [recombinant, adsorbed], 44 reports) and Zostavax (zoster vaccine live, attenuated [Oka/Merck], 38 reports).
- There were 68 (40%) serious reports. Most of these involved patients with underlying medical conditions and were unlikely related to the vaccination.
- The most frequently reported AEFIs were pyrexia, vaccination site pain, vaccination site erythema, pain in the extremities, headache, vaccination site swelling, myalgia, fatigue, nausea, and dizziness. The majority of these adverse events involved Bexsero, Zostavax, and pneumococcal vaccines. These are known events following immunization and are captured in the respective Canadian product monographs.
- No new safety signals (potential safety issues) were identified during this period.
- The benefits of vaccines authorized in Canada continue to outweigh the risks.
- Health Canada, in collaboration with PHAC, will continue to closely monitor the safety of vaccines authorized in Canada.

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.

Piperacillin/Tazobactam for Injection and Piperacillin for Injection

*The risk of **Drug Reactions with Eosinophilia and Systemic Symptoms (DRESS)** has been included in the Warnings and Precautions and Adverse Reactions sections of the Piperacillin Sodium/Tazobactam Sodium Powder for Injection Canadian product monograph. DRESS has also been included in the Adverse Reactions section of the Piperacillin for Injection Canadian product monograph.*

Key message for healthcare professionals:[1,2]

- Serious skin reactions, such as Drug Reactions with Eosinophilia and Systemic Symptoms (DRESS), have been reported in patients receiving piperacillin/tazobactam and reported rarely with piperacillin.
- If patients develop a skin rash they should be monitored closely and piperacillin/tazobactam discontinued if lesions progress.

References

1. *Piperacillin Sodium/Tazobactam Sodium Powder For Injection* [product monograph]. Boucherville (QC): Sandoz Canada Inc.; 2015.
2. *Piperacillin for Injection* [product monograph]. Saint-Laurent (QC): Hospira Healthcare Corporation; 2015.

Manufacturers of authorized generic products are in the process of updating their respective labelling.

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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