



# Health Product InfoWatch

July 2017

## HEALTH PRODUCTS MENTIONED IN THIS ISSUE

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### REPORTING ADVERSE REACTIONS

Canada Vigilance Program  
 Online: [Adverse Reaction and Medical Device Problem Reporting](#)  
 Telephone: 1-866-234-2345  
 Fax or mail: Form available online

### SUBSCRIBE

To receive the Health Product InfoWatch and notifications of health product advisories electronically, subscribe to [MedEffect™ e-Notice](#) or to [MedEffect™ Canada RSS feeds](#).

### Pharmaceuticals and Biologics

- Bisphosphonates, oral and injectable
- Brilinta (ticagrelor)
- Cefazolin for Injection
- Dipeptidylpeptidase-4 inhibitors
- Evotaz (atazanavir and cobicistat)
- Finasteride
- Mefloquine
- Narcan (naloxone)
- Reyataz (atazanavir)
- Sodium bicarbonate injection
- Tecfidera (dimethyl fumarate)
- Tysabri (natalizumab)
- Volulyte (hydroxyethyl starch)
- Voluven (hydroxyethyl starch)

### Other

- Foreign health products
- Unauthorized health 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.

## ANNOUNCEMENTS

### Consultation – New measures to inform Canadians of the risks of prescription opioids

As part of the Government of Canada's work to reduce problematic opioid use and its related harms, Health Canada is proposing [regulations](#) that would make a warning sticker and patient information handout mandatory with all prescription opioids at the time of sale. The sticker would be applied by the pharmacist to the prescription opioid container to warn patients about the potential risks associated with opioid use, including dependence, addiction and overdose. The handout would contain broader information on the safe use of opioids, and on the risks associated with these drugs. Through the proposed regulations, the Minister of Health would also be able to require that pharmaceutical companies develop and implement risk management plans for all opioids to identify, mitigate and monitor risks associated with opioid use.

To finalize these regulations, Health Canada is [asking Canadians](#) to provide their comments via the [Canada Gazette Web site](#). These consultations will be open until August 31, 2017.

[News Release](#)

### Government of Canada enables new access to drugs in urgent public health situations

The Government of Canada has taken action to make more treatment options available for the opioid crisis and other emergency situations by implementing new regulations that allow the import of drugs that are urgently needed in Canada.

Health Canada has published an initial [List of drugs for an urgent public health need](#) that are authorized for sale in the United States, the European Union or Switzerland, but are not yet authorized in Canada. Health Canada will now permit these drugs to be imported into Canadian jurisdictions that have notified Health Canada of an urgent public health need.

Under these regulations, every healthcare institution authorized by the laws of a province to provide acute care services is required to report serious adverse drug reactions that involve a drug from the List to Health Canada.

[News Release](#)  
[Questions and Answers](#)

## 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 June 2017 by Health Canada.

<b>Brilinta (ticagrelor)</b> <a href="#">Summary Safety Review</a>	This safety review evaluated the risk of severe cutaneous adverse reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms and acute generalized exanthematous pustulosis, associated with Brilinta (ticagrelor). Health Canada's review concluded that there was not enough information available to confirm a link. Health Canada will continue to monitor this issue.
<b>Cefazolin for Injection</b> <a href="#">Drug Recall</a>	Cefazolin Sodium 10 g/vial (lot number 303723) has been recalled by Fresenius Kabi Canada Ltd. as the affected lot may contain presence of foreign matter.
<b>Dipeptidylpeptidase-4 inhibitors</b> <a href="#">Summary Safety Review</a>	This safety review evaluated the risk of heart failure associated with dipeptidylpeptidase-4 (DPP-4) inhibitors. While Health Canada was carrying out the review, the manufacturers of DPP-4 inhibitors updated the Canadian product monographs to include information regarding the risk of heart failure. Health Canada's review of the available information concluded that the recently updated Canadian product monographs accurately describe the risk.
<b>Finasteride</b> <a href="#">Summary Safety Review</a>	This safety review evaluated the risk of serious muscle-related adverse reactions associated with finasteride (Propecia, Proscar and generic products). Health Canada's review concluded that the risk of serious muscle-related adverse reactions with the use of finasteride could not be ruled out. Health Canada has recommended that the manufacturers update the Canadian product monographs of finasteride-containing products to inform about this risk.
<b>Foreign health products</b> <a href="#">Foreign Product Alert</a>	These foreign health products have been found by regulators in other countries to contain undeclared drug ingredients. These 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.

<p><b>Mefloquine</b></p> <p>Summary Safety Review Statement from Health Canada</p>	<p>This safety review evaluated the risk of rare long-lasting and permanent neurological and psychiatric adverse events associated with mefloquine. Health Canada’s review concluded that there was limited evidence supporting this association. The review also found that some individuals were prescribed mefloquine even though they had contraindications against its use. Health Canada will be working with the manufacturer to update the Patient Medication Information section of the Canadian product monograph to better explain the type of neurological adverse events that may, very rarely, become permanent. A checklist will also be developed to assist healthcare professionals in deciding whether to prescribe mefloquine to individual patients.</p>
<p><b>Narcan (naloxone) nasal spray</b></p> <p>Information Update</p>	<p>Health Canada advised healthcare professionals and Canadians that the Canadian authorized version of Narcan (naloxone) nasal spray has transitioned onto the market. Last July, an Interim Order was issued by the Minister of Health, permitting the importation, sale and distribution of Narcan approved in the United States for a period of one year. Health Canada has now authorized the Canadian version of Narcan. Narcan is the same product in Canada and the United States with minor labelling differences being the only distinctions.</p>
<p><b>Sodium bicarbonate injection</b></p> <p>Information Update Drug Recall</p>	<p>Health Canada informed Canadians of the current shortage of injectable sodium bicarbonate product in Canada. The global supply of the vials has been tight since late May due to manufacturing delays. In addition, Pfizer Canada recalled 2 lots (lot numbers 72119EV and 72120EV) of 8.4% sodium bicarbonate injection, USP, 50 mL vials, due to possible microbial contamination in the manufacturing process. The recall did not affect the pre-filled syringe format.</p>
<p><b>Tecfidera (dimethyl fumarate)</b></p> <p>Summary Safety Review</p>	<p>This safety review evaluated the risk of kidney injury associated with Tecfidera (dimethyl fumarate). Health Canada’s review concluded that there is limited evidence at this time suggesting kidney injury with Tecfidera. The findings of this review are already reflected in the Canadian product monograph. Health Canada has asked the manufacturer to provide additional safety information on this risk as it becomes available.</p>

<p><b>Tysabri (natalizumab)</b></p> <p>Summary Safety Review</p>	<p>This safety review evaluated the risk of hematological abnormalities in newborns whose mothers were treated with Tysabri (natalizumab) during pregnancy. Health Canada’s review concluded that there is a potential for hematological abnormalities to happen in these newborns. The Canadian product monograph has been updated to reflect this risk.</p>
<p><b>Unauthorized health products</b></p> <p>Advisories:</p> <ul style="list-style-type: none"> <li>Jupiter and Kratom Zone</li> <li>Matrix Red and White Vein</li> <li>Thai and Medicine Man</li> <li>Lone Wolf</li> <li>Poppers and sexual enhancement products</li> <li>Rhino 69 Extreme 10K</li> <li>Super Panther 7K</li> <li>Update - Sexual enhancement products</li> </ul>	<p>Health Canada advised Canadians about various unauthorized health products being sold at retail locations across Canada or online.</p>
<p><b>Volulyte and Voluven (hydroxyethyl starch)</b></p> <p>Summary Safety Review</p>	<p>This safety review evaluated the risk of acute kidney injury in non-critically ill patients associated with hydroxyethyl starch (Voluven and Volulyte). Health Canada’s review concluded that there was not enough information to establish a link. Health Canada has requested additional safety information from the manufacturer as it becomes available.</p>

## 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 brand name pharmaceutical drugs is available on [Health Canada's Web site](#).

### Bisphosphonates, oral and injectable

Additional information concerning the risk of **osteonecrosis of the jaw (ONJ)** has been added to the *Warnings and Precautions* section of the Canadian product monographs (CPMs) for all oral and injectable bisphosphonates (alendronate, clodronate, etidronate, pamidronate, risedronate and zoledronic acid).

#### Key messages for healthcare professionals:<sup>1-8</sup>

**For oral and injectable formulations**, the following should be considered when evaluating a patient's risk of developing ONJ:

- Potency of the medicinal product that inhibits bone resorption (higher risk for highly potent compounds).
- Route of administration (higher risk for parenteral administration).
- Cumulative dose of bone resorption therapy.
- Co-morbid conditions (e.g., anemia, coagulopathies) and smoking.
- Periodontal disease, poorly fitting dentures, history of dental disease.

**In addition**, the following has been added to the CPMs of the **injectable formulations**:

- The start of treatment or of a new course of treatment should be delayed in patients with unhealed open soft tissue lesions in the mouth.
- If ONJ occurs while on treatment, temporary interruption should be considered until the condition resolves and contributing risk factors are mitigated where possible.

#### References

1. *Aclasta (zoledronic acid injection)* [product monograph]. Dorval (QC): Novartis Pharmaceuticals Canada Inc.; 2017.

2. *ACT Etidronate (etidronate disodium tablets) and ACT Etidrocal (etidronate disodium tablets and calcium carbonate tablets)* [product monograph]. Mississauga (ON): Actavis Pharma Company; 2017.

3. *Actonel (risedronate sodium tablets) and Actonel DR (risedronate sodium delayed-release tablets)* [product monograph]. Mississauga (ON): Warner Chilcott Canada Co.; 2017.
4. *Bonfos (clodronate disodium capsules and clodronate disodium for injection)* [product monograph]. Mississauga (ON): Bayer Inc.; 2017.
5. *Clasteon (clodronate disodium capsules and clodronate disodium injection)* [product monograph]. Mississauga (ON): Sunovion Pharmaceuticals Canada Inc.; 2017.
6. *Fosamax (alendronate sodium tablets) and Fosavance (alendronate sodium/cholecalciferol tablets)* [product monograph]. Kirkland (QC): Merck Canada Inc.; 2017.
7. *Pamidronate Disodium for Injection (pamidronate disodium)* [product monograph]. Kirkland (QC): Hospira Healthcare Corporation; 2017.
8. *Zometa (zoledronic acid for injection)* [product monograph]. Dorval (QC): Novartis Pharmaceuticals Canada Inc.; 2017.

## Evotaz (atazanavir and cobicistat) and Reyataz (atazanavir)

The risk of **chronic kidney disease** has been included in the *Warnings and Precautions* and *Adverse Reactions* sections of the Canadian product monographs for Reyataz and Evotaz.

### Key messages for healthcare professionals:<sup>1-2</sup>

- Chronic kidney disease (CKD) has been reported in patients treated with atazanavir, with or without ritonavir. Some cases resulted in fatal outcomes or requiring hemodialysis.
- Reyataz and Evotaz should be used with caution, particularly in those patients with other risk factors for CKD.

### References

1. *Evotaz (atazanavir and cobicistat)* [product monograph]. Montreal (QC): Bristol-Myers Squibb Canada; 2017.
2. *Reyataz (atazanavir)* [product monograph]. Montreal (QC): Bristol-Myers Squibb Canada; 2017.

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## 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](#)
- [Drug Shortages Canada](#)

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## Suggestions?

Your comments are important to us. Let us know what you think by reaching us at [InfoWatch\\_InfoVigilance@hc-sc.gc.ca](mailto: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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