Health Canada Santé Canada

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Health Product InfoWatch

September 2015

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REPORTING ADVERSE REACTIONS

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HEALTH PRODUCTS MENTIONED IN THIS ISSUE

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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

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 August 2015 by Health Canada.

Enbrel (etanercept) Summary Safety Review	This safety review evaluated the potential link between schizophrenia-like symptoms and the use of Enbrel (etanercept). The review did not find enough information to support an association. Health Canada will continue to monitor this issue.
"L'il Critters Vitamin D3" and "Vitafusion Calcium Adult Gummy Vitamins" Information Update	All lots of "L'il Critters Vitamin D3" (NPN 80025335) and "Vitafusion Calcium Adult Gummy Vitamins" (NPN 80029584) were recalled after the company's testing identified levels of vitamin D that exceeded what is indicated on the product label.
Foreign Health Products Foreign Product Alert (15 foreign products) Foreign Product Alert (5 foreign products)	These foreign health products have been found by regulators in other countries to contain undeclared drug ingredients or high levels of heavy metals. 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.
Xarelto (rivaroxaban) Summary Safety Review	This safety review evaluated the potential risk of liver injury associated with Xarelto (rivaroxaban). A clear link between the use of Xarelto and liver injury could not be established. Health Canada published an article in the August 2015 issue of the Health Product InfoWatch to encourage the reporting of related adverse reactions, and to provide detailed information when describing cases.

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.

CASE REPORT

Recent Canadian cases are selected based on their seriousness, frequency of occurrence or the fact that the reactions are unexpected. Case Reports are considered suspicions and are presented to stimulate reporting of similar suspected adverse events.

Negative pressure wound therapy devices and the risk of bleeding

Health Canada received a report from the Office of the Chief Coroner involving a negative pressure wound therapy (NPWT) device. NPWT devices use topical negative pressure to treat acute wounds and to promote the closure of difficult-to-heal chronic wounds.[1] In principle, they apply a localized vacuum to a wound site which can help remove fluids and infectious materials, and draw the edges of the wound together.[2] NPWT devices include a vacuum pump, drainage tubing and a dressing set. In Canada, NPWT devices are regulated as class II medical devices (IV being the highest risk class).

The report described the death of an elderly patient treated with NPWT. The NPWT device was used as part of wound management for a femorotibial bypass with an in-situ saphenous vein graft, where the wound had developed an infection. The patient had multiple medical problems including coronary artery disease, peripheral arterial disease with previous aortobifemoral bypass, atrial fibrillation (treated with warfarin), hypertension, hypercholesterolemia, congestive heart failure and chronic obstructive pulmonary disease. The patient also had a previous history of a gastrointestinal bleed and stable renal dysfunction.

NPWT was administered in a hospital setting for several weeks. While a patient assessment (conducted several days prior to the patient's death) indicated some improvement following antibiotic therapy, the wound base was reported to be necrotic and the graft easily visible and palpable upon follow-up examination. NPWT was ordered to continue with the addition of an interface dressing of Aquacel Silver. Some days later, the patient was reported as being well with no complaints, but was found unresponsive with a large amount of blood surrounding the wound site approximately one hour later. It was noted that the NPWT dressing was in place at the time of discovery and that blood leakage was observed around the device.

The cause of death was described as the rupture of an infected saphenous vein graft. Therapeutic anticoagulation was noted as a contributing factor. It was also noted in the report that the patient presented with other risk factors (infection and lack of tissue coverage over vascular structures) that can increase the risk of potential fatal bleeding.

As of June 1, 2015, Health Canada has not received any additional reports of bleeding suspected of being associated with NPWT devices. The United States Food and Drug Administration (FDA) has previously issued safety communications on the serious complications, particularly bleeding and infection, associated with the use of NPWT devices.[3-5] These communications, which include recommendations for healthcare professionals and patients, were issued after a number of cases of death and injuries associated with NPWT devices were reported to the FDA.

To mitigate the potential risk of bleeding associated with NPWT, healthcare professionals involved in wound management therapy are reminded to select patients for NPWT carefully, after reviewing the most recent device labelling (including contraindications, warnings and precautions), and in consideration of patient risk factors. The patient's full healthcare team should be prepared to take emergency measures if life-threatening complications such as bleeding occur. Patients should likewise be educated by healthcare professionals to watch for signs of bleeding and to urgently alert clinical staff should bleeding occur.

Health Canada encourages the reporting of bleeding and other adverse incidents suspected of being associated with the use of NPWT devices to the Health Products and Food Branch Inspectorate through the toll free hotline (1-800-267-9675).

References

1. Fisher A, Brady B. Vacuum assisted wound closure therapy. *Issues Emerg Health Technol* 2003;Mar(44):1-6.
2. Sullivan N, Snyder DL, Tipton K, et al. *Negative pressure wound therapy devices: technology assessment report*. Rockville, MD: Agency for Healthcare Research and Quality; 2009.
3. *FDA preliminary public health notification: serious complications associated with negative pressure wound therapy systems*. Silver Spring (MD): US Food and Drug Administration; 2009 Nov 13. (accessed 2015 Aug 5).
4. *Advice for patients: serious complications with negative pressure wound therapy devices*. Silver Spring (MD): US Food and Drug Administration; 2009 Nov 13. (accessed 2015 Aug 5).
5. *Update on serious complications associated with negative pressure wound therapy systems: FDA safety communication*. Silver Spring (MD): US Food and Drug Administration; 2011 Feb 24. (accessed 2015 Aug 5).

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.

Malarone (atovaquone and proguanil)

*The risk of a **drug interaction** between Malarone (atovaquone and proguanil) and efavirenz has been included in the Drug Interactions subsection of the Malarone Canadian product monograph.*

Key message for healthcare professionals:[1]

- Coadministration of efavirenz with Malarone (atovaquone and proguanil) resulted in decreased exposures to atovaquone and proguanil.
- When given with efavirenz or boosted protease-inhibitors, atovaquone concentrations have been observed to decrease as much as 75%.
- Since decreased concentrations of atovaquone and proguanil may result in a decrease of antimalarial efficacy, concomitant administration should be avoided whenever possible.

Reference

1. *Malarone (atovaquone and proguanil)* [product monograph]. Mississauga (ON): GlaxoSmithKline Inc.; 2015.

Phosphodiesterase Type 5 (PDE5) inhibitors: Adcirca (tadalafil), Cialis (tadalafil), Levitra (vardenafil), Revatio (sildenafil), Staxyn (vardenafil) and Viagra (sildenafil)

*The coadministration of PDE5 inhibitors with guanylate cyclase stimulators, such as riociguat, is now **contraindicated**. This information has been included in the Contraindications section of respective PDE5 inhibitor Canadian product monographs.**

Key message for healthcare professionals:[1-6]

- The coadministration of PDE5 inhibitors with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may lead to potentially life-threatening episodes of symptomatic hypotension or syncope.

References

1. *Adcirca (tadalafil)* [product monograph]. Toronto (ON): Eli Lilly Canada Inc.; 2015.
2. *Cialis (tadalafil)* [product monograph]. Toronto (ON): Eli Lilly Canada Inc.; 2015.
3. *Levitra (vardenafil)* [product monograph]. Mississauga (ON): Bayer Inc.; 2015.
4. *Revatio (sildenafil)* [product monograph]. Kirkland (QC): Pfizer Canada Inc.; 2015.
5. *Staxyn (vardenafil)* [product monograph]. Mississauga (ON): Bayer Inc.; 2015.
6. *Viagra (sildenafil)* [product monograph]. Kirkland (QC): Pfizer Canada Inc.; 2015.

* The Revatio Canadian product monograph is currently being updated.

HELPFUL LINKS

- MedEffect™ Canada
- Recalls and Safety Alerts Database
- Summary Safety Reviews
- New 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

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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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