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Health Product InfoWatch

August 2016

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REPORTING ADVERSE REACTIONS

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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 July 2016 by Health Canada.

Alere INRatio and INRatio 2 PT/INR Monitoring Systems Advisory Information Update	Health Canada advised Canadians that Alere Inc., is withdrawing Alere INRatio and INRatio 2 Prothrombin Time Monitoring Systems from the Canadian market. There is a risk that the Alere devices provide an inaccurate low reading of blood clotting time.
Blincyto (blinatumomab) Health Product Risk Communication	There have been reported cases of life-threatening, sometimes fatal pancreatitis associated with the use of Blincyto. If pancreatitis is suspected, Blincyto should be either temporarily interrupted or discontinued. The Canadian Product Monograph has been updated to reflect this new safety information.
Codeine-containing products Summary Safety Review Information Update	This safety review evaluated the risk of respiratory depression in children and adolescents associated with the use of codeine-containing products. There are well-described reports of life-threatening breathing problems in patients under 18 years of age, when prescription codeine is used as part of treating pain after surgery to remove tonsils or adenoids. Therefore, Health Canada is working with manufacturers to update the Canadian Product Monograph so that prescription codeine is no longer used in children and adolescents for this purpose. Health Canada has also communicated this information to Canadians.
Diclectin (doxylamine and pyridoxine combination) Summary Safety Review	The safety of Diclectin was recently reviewed by Health Canada as part of its routine health product monitoring. Health Canada's review found that Diclectin's benefits continue to outweigh its risks, when used as authorized. The review also showed no change in the safety profile of Diclectin in pregnant women. Health Canada will continue to monitor this issue.
Foreign health products Foreign Product Alert (6 products) Foreign Product Alert (7 products) Foreign Product Alert (15 products)	These foreign health products have been found by regulators in other countries to contain undeclared allergens, 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.

Hydrocodone-containing products Summary Safety Review Information Update	This safety review evaluated the risk of respiratory depression in children and adolescents associated with the use of hydrocodone-containing products. The majority of cases of serious breathing problems identified in the safety review involved children under 6 years of age and usually involved higher-than-recommended doses. Therefore, Health Canada will work with the manufacturers to update the Canadian Product Monograph to indicate that its use in children under 6 years of age is no longer recommended. Health Canada has also communicated this information to Canadians.
Inferior vena cava filters Health Product Risk Communication	Serious complications have been reported in patients implanted with an inferior vena cava (IVC) filter, including caval perforation, caval thrombosis, filter fracture and fragment embolization, intracardiac migration, cardiac perforation, cardiac tamponade, and death. Healthcare professionals should carefully consider the indications for IVC filters. Retrievable IVC filters are intended for short-term placement and, when possible, should be removed when anticoagulation therapy can be started or if a patient's risk of pulmonary embolism subsides.
Kogenate FS and Helixate FS (Antihemophilic Factor [Recombinant]) Summary Safety Review	This safety review evaluated the risk of developing inhibitory antibodies (IA) to Kogenate FS and Helixate FS in previously untreated patients with severe hemophilia A. Health Canada's review concluded that the evidence does not suggest any additional concerns regarding the risk of developing IAs toward Kogenate FS and Helixate FS. Health Canada will continue to monitor the situation.
Personnelle sunscreen lotion Information Update	Health Canada advised Canadians not to use two Personnelle sunscreen lotions (DIN 02395983 and 02395975) because of microbial contamination. The affected sunscreen was sold at Jean Coutu retail locations.
Unauthorized health products (B-Hard on Demand and Wonderblue) Advisory	Health Canada advised Canadians that "B-Hard on Demand" and "Wonderblue" have been seized from Désirs et Plaisirs in St-Jérôme, Québec. These products were found to contain undeclared prescription drug substances and other drugs substances.
Unauthorized health products (TRT and Freak'n Test) Advisory	Health Canada advised Canadians that TRT and Freak' n Test have been seized from Next Level Fitness in Richmond and Surrey, British Columbia. These products were labelled to contain a prescription drug substance (L-dopa).

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

Adverse incidents with injectable dermal fillers – facial vascular compromise: Update

Key points

- Scientific publications have described serious adverse incidents, including facial vascular compromise, associated with dermal fillers due to inadvertent vascular injection.
- As of June 2016, Health Canada has received a total of 16 adverse incident reports describing facial vascular compromise with dermal filler injections.
- Healthcare professionals are reminded of the importance of having adequate training, experience and knowledge to prevent adverse incidents from inadvertent vascular injection such as arteriole embolus, blindness and necrosis.

Injectable soft tissue dermal fillers have become an integral part of aesthetic medicine for patients who want non-invasive rejuvenation. They are used to restore volume and to smooth and efface superficial wrinkles and deep folds of the face, among other indications.[1] Dermal fillers can be classified as temporary (absorbable), regulated in Canada as a Class III medical device, or permanent (nonabsorbable), regulated as Class IV. Key components of different absorbable products include hyaluronic acid (HA), calcium hydroxylapatite, poly-L-lactic acid (PLLA), and collagen. Poly-methylmethacrylate (PMMA) is the key component of permanent non-absorbable products. At the time of this review, a total of 88 dermal filler devices (83 HA, 1 PMMA, 3 calcium hydroxylapatite, 1 PLLA) were licensed for sale in Canada.

In July 2010, Health Canada previously informed healthcare professionals about the risks related to the use of dermal fillers.[2] At that time, Health Canada had received 32 adverse incident reports of pain, edema, nodules, abscesses, lip necrosis and partial loss of vision suspected of being associated with the use of HA dermal fillers.

Since that time, additional scientific publications as well as a United States Food and Drug Administration communication have described serious adverse incidents, including facial vascular compromise, associated with dermal fillers due to inadvertent vascular injection.[3-16] Inadvertent vascular injection may lead to embolization and in rare cases may result in permanent vision impairment, blindness, stroke, and necrosis of the underlying facial tissue.[3-15] Although vascular complications are statistically rare following the injection of dermal fillers, these complications are still considered relevant because of the increased popularity of these devices for cosmetic purposes.[7,12,15] Retinal blindness has been reported with the use of all types of dermal fillers.[4-6,9,12-15] Nevertheless, the true incidence of this complication remains unknown because of underreporting.[7]

As of June 2016, Health Canada has received 16 incident reports describing facial vascular compromise with dermal fillers. Six of these reports described ocular complication including 4 reports of vision disorders/partial vision loss and 2 of blindness, one report described partial deafness (outcome unknown), 6 reports described necrosis, one arteriole embolus, and 4 reports described vascular compromise/violaceous reticulated pain. In general, symptoms presented immediately or within a few hours of injection; some were reported after 2, 5, or 7 days. Injection sites varied and included: malar area, marionette lines, nasolabial folds, lips and lip corners, pre-jowl sulcus, nasojugal folds, glabellar area, lateral nasal and periorbital areas, chin and temple. The devices implicated included HA, calcium hydroxylapatite, PMMA and PLLA soft tissue fillers.

To mitigate the potential risks associated with the unintentional injection of dermal fillers into the facial blood vessels, healthcare professionals are reminded that they should have the appropriate training, experience and knowledge of the:

- facial anatomy and corresponding vasculature
- anatomical variation among patients
- injection sites that have an increased risk of adverse events associated with unintentional injection of filler into blood vessels
- contraindications, warnings and precautions, and differences with respect to device indications
- importance to promptly recognize and manage relevant filler associated intravascular injection complications

Healthcare professionals are also reminded that patients should be informed about the risks associated with the injection procedure including the possibility of these rare but serious adverse events and the importance of seeking immediate medical attention should signs related to intravascular injections develop such as:[16]

- unusual pain
- vision changes
- blanching of the skin
- any neurological changes associated with a stroke (during or after a procedure) including:
    - sudden difficulty speaking
    - numbness or weakness in face, arms, or legs
    - difficulty walking
    - face drooping
    - severe headache, dizziness, or confusion

Health Canada encourages the reporting of vascular compromise and other serious and unexpected adverse incidents with dermal fillers by using the Health Product Complaint Form or by calling the toll free hotline: 1-800-267-9675.

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16. *Unintentional injection of soft tissue filler into blood vessels in the face: FDA Safety Communication*. Silver Spring (MD): US Food and Drug Administration; May 2015. (accessed 2016 July 5).

Did you know?

Health Canada provides information for consumers on injectable dermal fillers on its website, to help inform decision-making by Canadians considering cosmetic injections.

VACCINE SAFETY QUARTERLY SUMMARY

Report for October 1, 2015 to December 31, 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 October 1, 2015 and December 31, 2015. To access reports published by CAEFISS, please visit the CAEFISS website.

- From October 1, 2015 to December 31, 2015, the Canada Vigilance Program received 201 reports of adverse events for which vaccines were the suspected cause.
- The largest proportion of the reports received (50 %) were for influenza vaccines, which is expected during the "Influenza Immunization Awareness Campaign in Canada".
- There were 78 (39%) serious reports. Most of these involved patients with underlying medical conditions and were unlikely related to the vaccination.
- The most frequently reported AEFIs were injection site erythema, pyrexia, urticaria, and headache. The majority of these adverse events involved influenza vaccines. These are known events following immunization and are included 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.

Note that because of updated information received by the Canada Vigilance Program, there may be differences in the number of AEFI reports and adverse events retrieved at different dates.

PRODUCT MONOGRAPH UPDATE

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.

Adalat XL (nifedipine extended-release tablets)

*The use of Adalat XL tablets in patients with moderate or severe hepatic impairment is now **contraindicated**. This information has been included in the Contraindications and Warnings and Precautions sections of the Adalat XL Canadian product monograph.*

Key messages for healthcare professionals:[1]

- The use of Adalat XL in patients with moderate or severe hepatic impairment is contraindicated as there is no tablet strength (< 20 mg/dose) nor formulation (the gastrointestinal therapeutic system or GITS formulation cannot be divided) that can be safely used in these patients.

Reference

1. *Adalat XL (nifedipine extended-release tablets)* [product monograph]. Missisauga (ON): Bayer Inc.; 2016.

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 License 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.

Pub.: 150182
ISSN: 2368-8025