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Canadian Adverse Reaction Newsletter

Volume 20 • Issue 4 • October 2010

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In this Issue

Scope

This quarterly publication alerts health professionals to potential signals detected through the review of case reports submitted to Health Canada. It is a useful mechanism to stimulate adverse reaction reporting as well as to disseminate information on suspected adverse reactions to health products occurring in humans before comprehensive risk–benefit evaluations and regulatory decisions are undertaken. The continuous evaluation of health product safety profiles depends on the quality of your reports.

Reporting Adverse Reactions

Canada Vigilance Program
Phone: 866 234-2345
Fax: 866 678-6789
Online: www.healthcanada.gc.ca/medeffect

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Statins and interstitial lung disease

Key points

- During the last 15 years, 29 cases of interstitial lung disease (ILD) suspected of being associated with statins have been published.
- Health Canada has received 8 adverse reaction (AR) reports of ILD, or pathologies associated with ILD, suspected of being associated with statins.
- Drug-induced ILD is a rare but serious AR and may be life-threatening. Health care professionals are encouraged to report to Health Canada any cases of ILD suspected of being associated with statins.

HMG–CoA reductase inhibitors, or statins, are widely used cholesterol-lowering drugs. In Canada, marketed statins include atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin. Their date of marketing ranges from 1988 for lovastatin to 2003 for rosuvastatin.

Interstitial lung disease (ILD) is a heterogeneous group of disorders that could be acute or chronic and, if left untreated, could lead to pulmonary fibrosis and pulmonary insufficiency.[1,2] Signs and symptoms include difficulty breathing, nonproductive cough and diffuse crackles heard on auscultation. ILD has been reported in association with several drugs, such as amiodarone, azathioprine, carbamazepine, cyclophosphamide, methotrexate and nitrofurantoin.[1,2]

During the last 15 years, 29 cases of ILD suspected of being associated with statins have been published.[3–14] Of these cases, 16 described a positive dechallenge (abatement of adverse reaction after the drug is stopped or the dose is reduced) with or without immunosuppressive treatment,[3,4,6,8–11,14] and 3 cases described a positive rechallenge (reappearance of adverse reaction after reintroduction of the drug).[4,9] In some of these reports, ILD was part of systemic clinical features consistent with potential drug-induced diseases such as lupus,[7] polymyositis,[4,12] dermatomyositis[5] and Churg–Strauss syndrome.[14]

A systematic review of the suspected association between ILD and statins has recently been published.[15] Although the mechanism of potential statin-induced ILD is unknown, some authors suggested it could be mediated by the inhibition of phospholipases; an effect of the statins on mitochondrial metabolism; or immune mediated.[15]

As of Mar. 31, 2010, Health Canada received 8 adverse reaction (AR) reports of ILD, or pathologies associated with ILD, suspected of being associated with the following statins: atorvastatin ($n = 3$), pravastatin ($n = 2$), rosuvastatin ($n = 2$) and simvastatin ($n = 1$). Pulmonary fibrosis ($n = 3$), ILD or interstitial pneumonia ($n = 2$), sarcoidosis ($n = 1$), Churg–Strauss syndrome ($n = 1$) and

polyarteritis nodosa with severe coughing ($n = 1$) were described in the reports. Six of the 8 cases were reported as serious.* Six cases were reported by health care professionals. In 2 cases, the pulmonary condition improved after the statin was stopped and the ILD treated. Two of the cases received by Health Canada were published.[14]

Drug-induced ILD is a rare but serious AR and may be life-threatening.[1] It can mimic other ILDs and is considered a condition of exclusion rather than a specific entity.[15] Information was limited in the reports received by Health Canada. Additional clinical information such as criteria for diagnosis, information on statin therapy, dechallenge and rechallenge, and concomitant conditions and medications would be necessary to characterize this suspected AR. Health care professionals are encouraged to report to Health Canada any cases of ILD suspected of being associated with statins.

*In the *Food and Drugs Act* and Regulations, a serious AR is defined as "a noxious and unintended response to a drug that occurs at any dose and that requires in-patient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death."

Patrice Tremblay, MD, Health Canada

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Potential interference of computed tomography scanning with electronic medical devices

The US Food and Drug Administration (FDA) has received a small number of reports of potential interference of computed tomography (CT) scanning with implanted or externally worn electronic medical devices, including pacemakers, defibrillators, neurostimulators, and implanted or externally worn drug-infusion pumps.[1] In the FDA notification, there was no mention of permanent effects in patients. Adverse incidents suspected of being associated with CT scanning include unintended stimuli from neurostimulators, malfunctions of insulin-infusion pumps and transient changes in the output pulse rate of pacemakers. The potential for interference of CT scanning with electronic devices has also been described in the literature.[2–5] Most cases of interference are transitory and cause interruption only during the period of direct irradiation of the device itself.[2] In some cases, however, the output of the device can be affected and the device may require reprogramming.[2]

In Canada, there is no evidence to date that CT scanning has resulted in the malfunction of electronic medical devices. Health Canada will continue to monitor this potential for interaction and will share information if evidence becomes available to suggest that there is a safety risk to Canadian patients. Any cases of serious or unexpected adverse incidents suspected of being associated with the interference of CT scanning with implanted or externally worn electronic devices should be reported to the Health Products and Food Branch Inspectorate (www.hc-sc.gc.ca/dhp-mps/compli-conform/info-prod/md-im/index-eng.php).

References

1. *FDA preliminary public health notification: possible malfunction of electronic medical*

Case Presentation

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

Red Bull Energy Drink: suspected association with seizure

Health Canada received a report of an 18-year-old man who drank 2 cans (355 mL each) of Red Bull Energy Drink over a half hour, on an empty stomach, for fatigue and hunger after a night of studying. About 1 hour later, while at school, he experienced 2 grand mal seizures. He was previously well and was not taking any medication. He had no history of seizure or head injury. Although he had occasionally consumed Red Bull Energy Drink in the past, during the night before the seizure he had not consumed any caffeinated drinks. At the emergency department, the patient was afebrile and had normal vital signs. His blood work showed insignificant electrolyte abnormality, and a drug screen was negative. Electrocardiography and a computed tomography scan of the head were normal. The patient was released from hospital the same day, with only acetaminophen as treatment. At 1-year follow-up, the patient has remained seizure free.

In Canada, Red Bull Energy Drink is regulated as a natural health product (NHP). A 355-mL can contains, among its ingredients, caffeine 113.6 mg, taurine 1420 mg, glucuronolactone 852 mg, inositol 71 mg, niacinamide 25.6 mg, pantothenic acid 8.5 mg, riboflavin 2.3 mg, vitamin B_{12} 1.4 µg and vitamin B_6 2.8 mg. According to the product label, not more than 1 can (355 mL) per day should be consumed. It is not recommended for children, pregnant or breast-feeding women, caffeine sensitive persons, or to be mixed with alcohol.[1]

Four cases of seizure associated with energy drinks have been published.[2] These cases described discrete new-onset seizures occurring in adults following heavy consumption. In 2 of these cases, the energy drinks were taken on an empty stomach.

Health Canada encourages the reporting of suspected adverse reactions to energy drinks and other NHPs to the Canada Vigilance Program (www.healthcanada.gc.ca/medeffect).

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New consumer form for reporting adverse reactions

In June 2010, Health Canada issued a new Consumer Side Effect Reporting Form to make it easier for consumers to report adverse reactions (ARs) to health products to the Canada Vigilance Program. The new form is one of 3 Canada Vigilance AR reporting forms available to Canadians. The other 2 forms are for health care professionals and industry.

Reporting ARs is important to health product safety. Each report may contribute to improving the safe use of health products, including prescription and nonprescription medications and natural health products. Information received from AR reports may help identify previously unrecognized, rare or serious ARs and may lead to changes in product safety information or other regulatory actions. Consumers are encouraged to seek assistance from their health care professional to report an AR to Health Canada.

The Consumer Side Effect Reporting Form, as well as information about the Canada Vigilance Program and how to report an AR, are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

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.

Quarterly summary of health professional and consumer advisories

(posted on Health Canada's Web site: May 22, 2010 – August 22, 2010)

Date*	Product	Subject
Aug 19	ExtenZe	Unauthorized sexual enhancement supplements may pose health risks
Aug 18	SeXXX Drive	Unauthorized health product containing undeclared hydroxyhomosildenafil
Aug 17	Energy drinks	It's Your Health: Safe use of energy drinks
Aug 16	Fulda Unitang Herbs Sleep Plus	Unauthorized herbal sleep aid may pose health risks
Aug 12	Adrenalin	Risk of inadvertent injection
July 29	Counterfeit Viagra	Unauthorized product on the Montréal market
July 29	Foreign products	Alerts – Huo Luo Jing Dan, Kam Chik San, Magic Power Coffee, Que She, Sheng Yuan Fang
July 28 & Aug 3	Relistor	Association with gastrointestinal perforation
July 27	Prescription drugs online	Health Canada warns about buying products from www.globalpharmacycanada.com
July 23	Marigold Natural Pharmacy products	Unauthorized products may pose health risks
July 22	SX Male Enhancement	Unauthorized product containing undeclared acetildenafil
July 14	Foreign products	Alerts – 1 Body Beautiful; USA Yaku Cell Slimming Capsules, Dong Gua Pai You Su, Qing Gua Pai You Su, and Mu Gua Pai You Su; US recall of over 30 sexual enhancement supplements from Atlas Operations Inc.; Stallion, SZM Formula for Men, Tomcat Ali and Volcanic; Vitalex for men and Vitalex for women
July 13	UP Ultimate Performance For Men	Unauthorized product containing undeclared sildenafil
July 13	RotaTeq	Presence of porcine circovirus (PCV) DNA
July 12	Rotarix	Presence of porcine circovirus type 1 (PCV-1)
July 8	Avandia, Avandamet and Avandaryl	Status of rosiglitazone drugs in Canada
July 5	Foreign products	Alerts – LiPO-4 Cap, LiPO-8 Cap and Glucomi 600 Cap; Po Chai Pills (capsule form); Stud Capsule For Men
June 17	Vitamin D	Proper dosing of liquid vitamin D supplements in infants
June 16	Foreign products	Alerts – Vita Breath; Qingzhi Santian Shou; Comecoo, Zhongcaoyao-Jiankangjianfei
June 15	Unauthorized products	Unauthorized products labelled in Russian, Ukrainian or Kazakh removed from the Montréal market
June 15	Mirena	Potential risk of uterine perforation
June 11	Cancidas	Recall – potential for cracked vials
June 10	Colleague Volumetric Infusion Pumps	Information concerning the recall in the United States
June 8	Insulin products	It's Your Health: Insulin products
June 8	Vigofit and Once More	Unauthorized products seized in British Columbia
June 4	Ciprofloxacin Injection	Recall – possible contamination
June 3	OM Fusion products	Unauthorized products removed from the market
May 31 & June 3	Champix	Changes to the Canadian product monograph
May 26	Unauthorized products	Unauthorized products seized at Your Vitamin Store in British Columbia
Apr 7	Risperdal Consta	Needle detachments associated with the needle assembly

Advisories are available at www.healthcanada.gc.ca/medeffect.
*Date of issuance. This date may differ from the posting date on Health Canada's Web site.

Canadian Adverse Reaction Newsletter

Health Canada
Marketed Health Products Directorate
AL 0701D
Ottawa ON K1A 0K9
Tel: 613 954-6522
Fax: 613 952-7738

Editorial Team

Ann Sztuke-Fournier, BPharm
(Editor-in-Chief)
Jared Cousins, BSP
Mary Joy, RPh, BScPhm
Hoa Ly, BSc
Patricia Carruthers-Czyzewski, BScPhm, MSc
Gilbert Roy, BPharm
Christianne Scott, BPharm, MBA

Acknowledgement

We thank the following members of the Expert Advisory Committee on the Vigilance of Health Products for their review of material for this issue: Colleen J. Metge, BSc(Pharm), PhD; Dugald Seely, ND, MSc; and Sylvia Hyland, RPh, BScPhm, MHSc. We also thank Darija Muharemagic, master's student in chemistry, for her participation in the production of the newsletter.

Suggestions?

Your comments are important to us. Let us know what you think by reaching us at mhpd_dpsc@hc-sc.gc.ca

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Canada Vigilance Program
Phone: 866 234-2345
Fax: 866 678-6789
Online: www.healthcanada.gc.ca/medeffect

ISSN 1499-9447, Cat no H42-4/1-20-4E

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