Health Canada Santé Canada

Canada

Canadian Adverse Reaction Newsletter

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www.healthcanada.gc.ca/carn

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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 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

Contact Health Canada or a Regional AR Monitoring Office free of charge

Phone: 866 234-2345
Fax: 866 678-6789

Online form available at:

www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/form/index_e.html

Benadryl Total: medication incident and stroke

In October 2006, Health Canada received a report of a suspected adverse reaction involving a medication incident related to product labelling and packaging.

A 64-year-old woman consulted her family physician after experiencing an allergic reaction. She was given epinephrine (0.3 mg subcutaneously) and was advised to take Benadryl (diphenhydramine) 3 times daily for 3 days. Inadvertently, the patient bought Benadryl Total (diphenhydramine, pseudoephedrine and acetaminophen). She was unaware that this product contained pseudoephedrine and acetaminophen. After the second day of use, the patient experienced a stroke that affected her vision and speech. No other risk factors for stroke were reported other than age and use of pseudoephedrine.

Health products with sound-alike names and look-alike packaging and labelling can cause confusion for both consumers and health professionals and contribute to inappropriate product selection (Fig. 1). Such errors may result in serious patient harm.[1,2] Health professionals are reminded that product line extensions can sometimes lead to confusion for their patients in choosing the intended product. Patients are encouraged to always read the product's label carefully and to consult their pharmacist whenever they select self-care products.

Michel Trottier, BScPhm, RPEBC, RPh, Health Canada

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Fig. 1: Packages of Benadryl (left) and Benadryl Total (right).

Newsletter and Advisories by email

To receive the Newsletter and health product Advisories ***free*** by email, join Health Canada's ***MedEffect*** mailing list. ***Go to www.healthcanada.gc.ca/medeffect***

Rosiglitazone and parotid gland enlargement: update

The thiazolidinedione rosiglitazone (Avandia) is an insulin sensitizer that is indicated for use either as monotherapy or in combination with metformin or a sulfonylurea in patients whose type 2 diabetes is inadequately controlled by diet and exercise alone.[1] In the January 2006 issue of the *Canadian Adverse Reaction Newsletter*, it was reported that Health Canada had received 5 domestic reports of parotid gland enlargement suspected of being associated with the use of rosiglitazone.[2] As of Dec. 31, 2006, 1 additional domestic report was received. All 6 cases involved patients who experienced visibly evident enlargement of one or both parotid glands while taking the drug. In 4 cases the adverse reaction was alleviated or resolved when the rosiglitazone therapy was stopped; in the remaining 2 cases this information was not provided.

The parotid glands are the largest of the salivary glands and are located in the facial subcutaneous tissue, over the posterior aspect of each mandibular ramus. There is considerable variation in the size of parotid glands of healthy individuals,[3] but on clinical examination they are not visible and are not readily palpable. Nontender parotid gland enlargement has been associated with a number of medical disorders (e.g., diabetes mellitus, obesity and hyperlipidemia) and medications (e.g., iodides, phenylbutazone and propylthiouracil).[4–7]

Rosiglitazone is a highly selective and potent agonist for the peroxisome proliferator–activated receptor gamma (PPARγ).[1] Although rosiglitazone appears to be associated with some effects that are not mediated by PPARγ, binding of rosiglitazone to PPARγ seems to be an important component of its mechanism of action.[8] In addition, PPARγ-responsive genes participate in the regulation of fatty acid metabolism and in the maturation of preadipocytes, predominantly of subcutaneous origin.[1] Although PPARγ is also implicated in various functions in the parotid glands,[9–11] the activity of rosiglitazone in the parotid glands is not fully understood. Further studies are required to confirm whether the drug causes noticeable parotid gland enlargement by acting directly on the parotid tissue through its agonist activity on PPARγ, or indirectly through induction of weight gain or elevation of serum lipid levels, or by another mechanism.

Parotid gland enlargement may be due to diabetes alone and may become clinically evident during treatment with rosiglitazone. When a diabetic patient taking rosiglitazone experiences nontender parotid gland enlargement, the drug may be considered as a possible cause.

Health professionals are encouraged to report any cases of parotid gland enlargement in patients receiving rosiglitazone.

Bruce Eveleigh, MD, Health Canada

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Adverse reaction reporting: education modules

Health Canada has developed 2 new education modules on adverse reaction (AR) reporting of marketed health products (pharmaceuticals, biologics [e.g., fractionated blood products, and therapeutic and diagnostic vaccines], natural health products and radiopharmaceuticals). In addition to the existing module for naturopathic doctors, modules for other health professionals and for consumers are now available on the MedEffect Canada Web site (www.healthcanada.gc.ca/medeffect).

The online module *Health Professional Reporting of Adverse (Drug) Reactions* provides an interactive tool to help health professionals report suspected adverse reactions to Health Canada. The online module for consumers, *Reporting Side Effects from Your Medicine: What You Need to Know*, comes with a guidebook and provides comprehensive learning tools to help consumers and patients report side effects, either to their health professional or to Health Canada.

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.

MedEffect Canada

MedEffect Canada is Health Canada's resource centre for Canadians to obtain health product safety information and to report adverse reactions.

MedEffect Canada's Web site (www.healthcanada.gc.ca/medeffect) provides health professionals and the general public centralized access to:

- Recent health product safety information, such as health professional and public communications, warnings, advisories and recalls
- MedEffect e-Notice subscription
- *Canadian Adverse Reaction Newsletter*
- The Adverse Reaction Database, which contains information on suspected adverse reactions to Canadian marketed health products reported to Health Canada
- Adverse reaction reporting forms and guidance documents
- A learning centre with education modules on how to report adverse reactions
- Other relevant information about postmarket monitoring of adverse reactions

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.

Norethindrone (Micronor): suspected association with decreased breast milk production

In Canada norethindrone (Micronor), a progestin-only oral contraceptive, has been marketed since 1972. From the date of marketing to Apr. 20, 2007, Health Canada received 13 domestic reports of decreased puerperal lactation (breast milk production) suspected of being associated with the use of norethindrone. Some reports noted that the infants had lost weight or were not gaining weight. The cases involved postpartum women aged 22–35 years (median 30 years). The age was not specified in 2 cases. Norethindrone therapy was started more than 6 weeks after delivery in 9 cases and less than 6 weeks after delivery in 3 cases; this information was not provided in 1 case. The reaction onset was reported in 9 of the cases and ranged from 3 to 16 days after the start of the norethindrone therapy. Upon withdrawal of the norethindrone therapy, 10 women experienced improved milk production, 3 of whom had used health products to improve lactation (domperidone, fenugreek and blessed thistle).

How to report an adverse reaction?

There are multiple ways to report an adverse reaction (AR) to Health Canada. To report an AR, go to: www.healthcanada.gc.ca/medeffect

- complete and submit your report **online** or
- download and print a paper copy of the reporting form* and submit it:
  - by **toll-free fax**: 866 678-6789 (faxes are automatically directed to the appropriate Regional AR Monitoring Office)
  - by **mail**: to one of the Regional AR Monitoring Offices (addresses can be found on the back of the AR reporting form or at www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/centres/index_e.html)

You can also report an AR by **toll-free phone**: 866 234-2345 (calls are automatically directed to the appropriate Regional AR Monitoring Office).

Manufacturers, please report ARs to the National AR Monitoring Office at:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
Health Canada
Address Locator 0701C
Ottawa ON K1A 0K9
Tel: 613 957-0337
Fax: 613 957-0335

By submitting a suspected AR report, you are contributing to the ongoing collection of safety and effectiveness information that occurs once health products are marketed.

*The Adverse Reaction Reporting Form is also available in the *CPS* (*Canadian Compendium of Pharmaceuticals and Specialties*).

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.

Summary of health professional and consumer advisories posted by Health Canada from Feb. 15 to May 14, 2007
(advisories are available at www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/index_e.html)

Date	Product	Subject
May 11	Depakene & ratio-Valproic	Recall of 2 Valproic acid drugs, Depakene 500 mg and ratio-Valproic 500 mg
May 3	Urat Madu	Foreign product alert
Apr 24	FiberChoice plus Multivitamins	Foreign product alert
Apr 19 & 16	Aranesp and Eprex	Safety information and new prescribing information for the erythropoiesis-stimulating agents — Amgen Canada and Janssen-Ortho, Inc.
Apr 18	Actos	Association between long-term treatment and fractures in women — Eli Lilly Canada Inc.
Apr 18	Herbal sleep supplement	Advisory not to use an herbal supplement that can be habit-forming
Apr 16	Defibrillators	Urgent medical device information — subset of implantable cardiac defibrillators and cardiac resynchronization therapy defibrillators — Boston Scientific
Apr 13	Lexscl Fat Rapid Loss	Foreign product alert
Apr 13	V.MAX, Rhino Max (Rhino V Max)	Foreign product alert
Apr 13	Lanmei Keili Ji	Foreign product alert
Apr 13	Weight loss products	*It's Your Health*: The safe use of health products for weight loss
Apr 10	Iressa	Safety information on use in patients with squamous cell carcinoma of the head and neck — AstraZeneca Canada Inc.
Apr 4	Salivart oral moisturizer	Certain lots contaminated with mould or yeast
Mar 31	Permax	Parkinson's drug Permax and heart valve conditions
Mar 30	Zelnorm	Voluntary suspension of sales owing to cardiovascular ischemic events — Novartis Pharmaceuticals Canada Inc.
Mar 29	Vigorect Oral Gel Shooter	Warning not to use an unauthorized product
Mar 27	Trasylol	Hypersensitivity reactions and renal dysfunction — Bayer Inc.
Mar 27	Tamiflu	Changes to Canadian labelling
Mar 24	XOX For Men	Warning not to use an unauthorized natural health product
Mar 16	Patient restraints	Safety information on the use of waist and torso patient restraints
Mar 14	MIAOZI slimming capsules	Advisory not to use an unauthorized product
Mar 13 & 9	Gadolinium-containing agents	Nephrogenic systemic fibrosis / nephrogenic fibrosing dermopathy
Mar 12 & 7	Omniscan	Nephrogenic systemic fibrosis / nephrogenic fibrosing dermopathy — GE Healthcare Canada
Mar 12	ReNu MultiPlus	Warning not to use certain lots of contact lens solution
Mar 9	Exjade	Acute renal failure and reports of cytopenias — Novartis Pharmaceuticals Canada Inc.
Mar 8 & 7	Medical equipment	Information concerning unpredictable events due to daylight savings time change
Mar 5	Waist Restraint	Safety information on Pinel rotating waist restraint — Pinel Medical Inc.
Feb 28	EMPowerPlus	Reports of adverse reactions in patients with serious mental health conditions
Feb 28 & 23	Rosiglitazone	Safety information on rosiglitazone-containing products: Avandia, Avandamet and Avandaryl — GlaxoSmithKline Inc.
Feb 27	Confirm Clearly Smart Pregnancy Test	Association of test and refills with false-positive results — Durex Canada, Division of SSL Canada Inc.
Feb 23	Sleepees	Advisory not to use an herbal supplement that can be habit-forming
Feb 21	Baraclude	Information for treatment in patients co-infected with HIV and HBV — Bristol-Myers Squibb Canada
Feb 16	External defibrillators	Safety information and corrective action — DDU-100 Series automatic external defibrillators — Defibtech, LLC

To receive the Newsletter and health product Advisories free by email, join Health Canada's ***MedEffect*** mailing list. ***Go to*** **www.hc-sc.gc.ca/dhp-mps/medeff/subscribe-abonnement/index_e.html**

Report adverse reactions

Reporting information about adverse reactions may contribute to:

- The identification of previously unrecognized rare or serious adverse reactions
- Changes in product safety information, or other regulatory actions
- International data regarding benefits, risks and effectiveness of health products
- Improved health product safety knowledge that benefits all Canadians

Canadian Adverse Reaction Newsletter

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

Health professionals/consumers report toll free:
Tel 866 234-2345
Fax 866 678-6789

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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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