

Product Update

Drug advisories

GlaxoSmithKline Inc. (GSK) is advising health care professionals of the ADOPT study results that highlight safety concerns with products containing rosiglitazone (i.e., **Avandia**, **Avandamet**, **Avandaryl**). This multicentre, double-blind trial primarily assessed the time-to-treatment-failure in 4360 newly diagnosed type 2 diabetes patients receiving rosiglitazone, metformin, or glyburide monotherapy for a median of 4 years. Rosiglitazone resulted in a slower progression to treatment failure. A review of the safety data demonstrated that female patients taking rosiglitazone had a higher rate of fractures as compared to metformin- or glyburide-treated women (9.3% vs 5.1% and 3.5%, respectively). Unlike those associated with postmenopausal osteoporosis, most fractures occurred in the upper arm, hand, or foot. GSK advises that the cause for these fractures is unclear at this time. Assessment of fracture risk and maintenance of bone health in rosiglitazone-treated patients, and in particular female patients, is recommended. Health care professionals are encouraged to report adverse reactions, including any case of serious fracture in rosiglitazone-treated patients.

Bristol-Myers Squibb is advising caution when pre-

scribing **Baraclude** (entecavir) in HIV/HBV co-infected patients not receiving highly active antiretroviral therapy (HAART). In a recent case report, a 31-year-old patient developed HIV drug resistance after 6 months of Baraclude treatment in 2006. The gentleman had received HAART for less than a year in 2000 and since then the disease had remained clinically stable.

Durex Canada is recalling and discontinuing the sale of **Confirm Clearly Pregnancy Test Starter Kits** and **Confirm Clearly Refills**. Consumers have reported false-positive and inconsistent results at a rate higher than expected.

A recent Canadian Adverse Reaction Newsletter highlights a possible link between **domperidone** and prolonged QT interval or Torsade de Pointes. Unlike arrhythmia, these 2 adverse effects do not appear in the Motilium product monograph. An association of corrected QT prolongation and Torsade de Pointes with domperidone has been reported in the medical literature. From 1985 to 2006, Health Canada received 9 reports of heart rate and rhythm disorders occurring with domperidone use. Six of these reports included 2 cases of prolonged QT interval and 4 reports of Torsade de Pointes. Domperidone is mainly metabolized via the cytochrome P450 3A4 pathway. Inhibitors of this path-

way (e.g., ketoconazole, macrolides, SSRIs, grapefruit juice) can increase the plasma concentration of domperidone, leading to a prolonged QT interval.

Health Canada warns consumers of a potential health risk with the use of **EMPowerPlus**, a vitamin/mineral supplement. The product has been associated with reports of worsening psychiatric symptoms in patients with underlying mental health conditions. In some cases the product was given in combination with prescription medications or substituted for prescription medication. A Health Canada public advisory and an information bulletin were previously issued in 2003 concerning the use of EMPowerplus for the treatment of serious medical conditions. With the receipt of the adverse reactions, Health Canada remains concerned about the health risks associated with the use of this product.

Health Canada advises consumers not to use **MIAOZI Slimming Capsules**, a product available through the Internet that is advertised for its weight loss properties. Manufactured by Bainian Pharmacy Group of Hong Kong, these capsules are not licensed for sale in Canada. The green capsules, packaged in silver and green blister packs, were recently intercepted by Canada Customs and found to contain the appetite suppressant sibutramine. This ingredient is

contraindicated in many health conditions or diseases and has the potential to interact with many medications.

Health Canada is informing Canadians that **Permax** (pergolide), a drug used for the treatment of Parkinson's disease, has been withdrawn from the US market amid concerns about an association with cardiac valvulopathy, a condition involving inflammation or stiffening of the heart valves. Two new studies regarding the risk of heart valve problems associated with Permax were published in January 2007. Health Canada is in the process of reviewing these studies and other information to determine what further action will be required regarding Permax.

A consumer warning has been issued by Health Canada regarding 2 lots of **ReNu MultiPlus** soft contact lens solution. Bausch and Lomb has recalled lots GC6038 and GC6052 because their iron content is higher than it should be and may result in reduced efficacy and infection leading to eye injury. The lots affected are 480 mL bottles found in Club Packs and Vision Packs bearing the DIN 02230538. For more information, contact the company's consumer affairs at 1-888-459-5000.

Health Canada is warning consumers not to use **Sleepees**, an herbal sleep aid not authorized for sale in

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Canada. The product contains estazolam, a benzodiazepine. The distributor, Old World Network Inc. in Vancouver, BC, has recalled the product. Consumers should return the product to the place of purchase.

Health Canada wishes to inform Canadians that the Canadian labelling for **Tamiflu** has recently been updated to include new safety information resulting from adverse reaction reports of abnormal or suicidal behaviour in Japanese children or teenagers taking this drug. As of February 28, 2007, there have been no Canadian reports of deaths or psychiatric adverse events such as abnormal or suicidal behaviour in children or teenagers.

At Health Canada's request, Novartis Pharmaceuticals Canada Inc. is suspending marketing and sales of **Zelnorm** (tegaserod hydrogemaleate) tablets in Canada to permit further evaluation of important safety information. Zelnorm is a serotonin 5-HT₄ receptor partial agonist indicated for the symptomatic treatment of irritable bowel syndrome with constipation in female patients whose main symptoms are constipation and abdominal pain and/or discomfort and for the treatment of chronic idiopathic constipation in patients under 65 years of age. A recent retrospective analysis

of pooled clinical trial data showed that the incidence of cardiovascular ischemic events in patients taking Zelnorm was higher than in those taking placebo. Novartis is asking Canadian pharmacists and distributors to return the product to the company. Patients taking Zelnorm should discontinue treatment and contact their physician for advice about alternative therapies.

New products

Champix (varenicline tartrate by Pfizer Canada), a new oral smoking cessation treatment for adults, is expected on the market in late April 2007. By binding to the $\alpha_4\beta_2$ nicotinic acetylcholine receptors in the brain, varenicline acts as an agonist and reduces the craving for nicotine. It also blocks the effect of nicotine at these receptors. Studies demonstrate better results with 12 weeks of Champix 1 mg twice daily as compared to both placebo and twice daily bupropion SR 150 mg. The most common adverse events are nausea, abnormal dreams, constipation, flatulence, and vomiting. Patients begin treatment one week before their "quit date" with a dose of 0.5 mg per day for 3 days, titrate up to twice a day for 4 days, then to 1 mg twice daily for 12 weeks. Success rates are improved when treatment is combined with patient counselling for smoking cessation. Tablets will be available in 2 strengths: 0.5 mg and 1 mg.

Citrodan (anhydrous magnesium citrate oral solution by Odan Laboratories Ltd. www.odanlab.com) is a laxative for the treatment of occasional constipation. The clear, lemon-flavoured, noncarbonated, sugar-free product is available in plastic bottles of 300 mL that contain 15 gm of magnesium citrate.

Duotrav (by Alcon Canada Inc.) combines the prostaglandin travaprost 0.004% and the beta-blocker timolol maleate 0.5% in one ophthalmic solution. The product is approved to reduce elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who do not respond to one of these agents alone, or other agents that lower IOP. The recommended dose is one drop in the affected eye(s) once daily each morning. Duotrav is available in 2.5 mL bottles and can be stored at room temperature or in the fridge (2°–25°C).

Fosrenol (lanthanum carbonate hydrate by Shire Biochem Inc.) is a soon-to-be marketed oral phosphate binding agent for dialysis patients with end-stage renal disease (ESRD). The active ingredient binds to dietary phosphorus in the gut and forms an insoluble complex that is not absorbed, but is excreted in the feces. The recommended starting dose is 750 to 1500 mg daily, divided and taken with or after meals. The dose should be

increased gradually every 2 to 3 weeks to achieve an appropriate serum phosphorus level. Tablets must be chewed before swallowing. Four tablet strengths will be available: 250, 500, 750, and 1000 mg.

Infergen (interferon alfacon-1 by Valeant Canada Ltd.) is approved for the retreatment of chronic hepatitis C virus (HCV) infection in adults with compensated liver disease who have anti-HCV serum antibodies and/or the presence of HCV RNA who have failed to respond or relapsed after prior administration of an interferon alfa. The recommended dose is 15 mcg SC once daily and requires no dose adjustment for genotype or patient weight. Infergen is available in single-dose, preservative-free, prefilled vials.

NasoGEL and **NasaMist** are 2 new OTC products available from NeilMed Pharmaceuticals, Inc. NasoGEL is a water-soluble saline gel that moisturizes dry nasal passages for a prolonged period. Each tube contains 28.4 grams. NasaMist is a buffered saline solution available in a 75 mL spray bottle that is suitable for use in adults, children and infants.

Resolve (cestemenol-350; www.resolve retailer.com) is a natural product that claims to aid with smoking cessation. The active ingredient is derived from *Passiflora incarnate* (passion flower) and

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Abies balsamea L. (balsam fir). At present, evidence is lacking for the use of passion flower and balsam fir in this indication and study results for cestemenol-350 efficacy have not been published.

New dosage form/strength

Apo-digoxin (Aptex Inc.) is the first generic digoxin product to be marketed in Canada. It is available in tablet strengths of 0.0625 mg, 0.125 mg, and 0.25 mg.

Aranesp (darbepoetin alfa by Amgen Canada Inc.) prefilled syringes will be replaced with **SingleJect Prefilled Syringes with UltraSafe Needle Guard**. The new needle device is designed to reduce the risk of accidental needle-stick injury by keeping the needle covered after use.

Purdue Pharma has added an 80 mg capsule to its line of once-daily **Biphentin** (controlled-release methylphenidate hydrochloride) capsules for the treatment of attention deficit hyperactivity disorder (ADHD) in children, adolescents, and adults. There are 7 other available strengths, ranging from 10 mg to 60 mg.

Diovan (valsartan by Novartis Pharmaceuticals Canada Inc.) tablets are now available in a 320 mg strength for once-daily administration. Other available strengths include 40 mg,

80 mg, and 160 mg tablets. All **heparin** products from Pharmaceutical Partners of Canada are now latex-free.

A recent change in the nonmedicinal ingredients of **Marinol** (dronabinol by Solvay Pharma Inc.) capsules has resulted in a change in storage requirements. The 5 and 10 mg capsules are now formulated with iron oxide (red, black, or yellow) and should be kept in the original container and stored in a cool place between 2°–8°C.

RAN-Fentanyl Transdermal System (fentanyl patch by Ranbaxy Pharmaceuticals Canada Inc.) is a new generic fentanyl patch that is available in strengths of 25 mcg/hour, 50 mcg/hour, 75 mcg/hour, and 100 mcg/hour.

New indication

In addition to 2.5 mg, 5 mg, 7.5 mg, 10 mg and 15 mg, **Zyprexa** (olanzapine by Eli Lilly Canada Inc.) is now available as a 20 mg tablet. Monotherapy with the antineoplastic agent **Alimta** (pemetrexed by Eli Lilly Canada Inc.) is a treatment option for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) previously treated with chemotherapy. **Alimta**, in combination with cisplatin, is also indicated for first-line treatment of patients with malignant pleural mesothelioma who have unresectable disease or who are not candidates for curative surgery.

Barriere-HC (1% hydrocortisone/silicone cream by Shire Biochem Inc.) will be discontinued when current supplies have run out. No alternatives are available.

Product withdrawals

Boehringer Ingelheim Canada Ltd. advises that, in accordance with the Montreal Protocol, the CFC-containing **Combivent Metered Dose Inhaler** (ipratropium bromide/salbutamol sulfate 200-dose) will be discontinued by June 30, 2007, at the latest. No alternative product containing HFA is available.

Dilaudid Suppositories 3 mg (hydromorphone by Abbott Laboratories Ltd.) have been discontinued. Generics are available.

Two products from Stiefel Canada Inc. will no longer be available. **Duofilm Gel** for

Kids (salicylic acid 11%) and **Stieva-A Gel** (tretinoin 0.01%) have been discontinued effective April and June 2007, respectively. **Stieva-A Cream** is still available.

HumaPen Ergo insulin delivery device will be discontinued in April 2007 by Eli Lilly Canada Inc. The pen can continue to be used for 3 years from the date of first use. Patients currently using this pen, or those newly prescribed Humalog insulin products, can receive 1 complimentary **HumaPen Luxura**. For more information contact the Customer Response Centre at 1-888-545-5972.

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Highlights from the April 2007 issue of Health Canada's Canadian Adverse Reaction Newsletter, Volume 17, Issue 2

- Quetiapine: pancreatitis and thrombocytopenia
- Case presentation: Telithromycin and toxic epidermal necrolysis
- Bitter orange (synephrine): update on cardiovascular reactions
- Adverse reaction reporting — 2006
- Summary of advisories posted by Health Canada from Nov.15, 2006 to Feb.14, 2007. Advisories are available at:

For further information, go to
www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/index_e.html.