Product Update

ADVISORIES

Rasilez / Rasilez HCT: Novartis Pharmaceuticals Canada Inc. and Health Canada inform health care professionals of the potential risks of cardiovascular and renal adverse events in patients with type 2 diabetes and renal impairment treated with **Rasilez** (aliskiren) or **Rasilez HCT** (aliskiren/hydrochlorothiazide), based on data from an interim review of the ALTITUDE trial. In this trial, patients receiving Rasilez in addition to standard of care, which included an ACE inhibitor or an ARB, had an increased incidence of adverse events, specifically, nonfatal stroke, renal complications, hyperkalemia and hypotension after 18 to 24 months. The company advises that Rasilez should not be initiated in patients with diabetes who are on an ACE inhibitor or ARB and that Rasilez should be stopped in patients who are also on an ACE inhibitor or ARB. Advise patients with diabetes who are currently taking a combination of Rasilez and an ACE inhibitor or an ARB to discuss their treatment options with their health care provider.

Avastin: Hoffmann-La Roche Ltd. and Health Canada remind health care professionals that **Avastin** (bevacizumab, single-use sterile preservative-free vials for IV use) is not authorized for intravitreal use; the product is only authorized for intravenous administration for specific indications as presented in the product monograph. Infectious endophthalmitis leading to blindness following the use of Avastin has been reported in the US, and the company believes this may have occurred as a result of contamination following repackaging for unauthorized intravitreal injection without aseptic technique. Analysis of the situation is ongoing.

Champix: Health Canada has completed its review of the cardiovascular safety of **Champix** (varenicline). Although the number of patients who experienced serious heart-related events in the group treated with Champix was slightly increased in the clinical trial involving 700 smokers with cardiovascular disease (CVD), the trial was not adequately designed to test for cardiovascular safety of Champix. As a result, the possibility of an increased risk of heart attack or stroke in patients with CVD can neither be confirmed nor discounted at this time. Advise patients to seek immediate medical attention if they are or think they are experiencing signs and symptoms of heart attack or stroke while taking Champix. Smoking continues to be a major risk factor for CVD; discussing the risks and benefits of smoking cessation with patients may help determine an appropriate treatment regimen to help patients lower their risk of CVD.

Celexa: Lundbeck Canada and Health Canada inform health care professionals that the product monograph for **Celexa** (citalopram hydrobromide) has been revised to include the new maximum daily dose of 40 mg (previously 60 mg/day) and information about the potential for QT interval prolongation. For patients with hepatic impairment, who are ≥ 65 years, or those who take cimetidine concomitantly, the recommended maximum daily dose is 20 mg. Celexa is contraindicated in patients with congenital long QT syndrome or known QT interval prolongation. ECG monitoring is recommended in patients with risk factors for torsade de pointes (heart failure or recent myocardial infarction) or in patients taking concomitant medications that prolong the QT interval, as well as in patients with liver impairment. Advise patients to discuss

further with their health care provider before stopping or reducing the dose.

Compliments Muscle and Back Pain Relief Regular Strength: A labelling error in the French dosing directions for **Compliments Muscle and Back Pain Relief Regular Strength** caplets (acetaminophen/methocarbamol 325 mg/400 mg) has resulted in a recall of 5 lots from the Canadian market by Vita Health. Lots recalled are 0K078B27ZI, 0K078B29VL, IA100B2AQH, 1H106B2GVP and 1H106B2HJJ. Under "Posologie" in the French dosing section, it reads "Adultes et enfants de 2 ans et plus" where it should read "Adultes et enfants de 12 ans et plus." The instructions as they are may present serious risks for children <12 years. For further information regarding the recall, including how to return the affected product, advise patients to contact Vita Health at 1-800-665-8820.

Epipen / EpiPen Jr / Auto-Injectors: Pfizer Canada Inc. and Health Canada remind health care professionals of the correct method of removing the blue safety cap for the **Epipen** (epinephrine 0.3 mg) and **EpiPen Jr** (epinephrine 0.15 mg) **Auto-Injectors**. For the emergency treatment of severe allergic reactions including

anaphylaxis, it is important that the blue safety cap be removed by pulling the cap straight up while the device is held with the orange tip pointing downward. Pulling the blue safety cap sideways or bending and twisting it off may prevent the device

ADVISORIES (cont'd)

from working properly and potentially result in failure to deliver the drug. A periodic review of instructions on the correct use of the device may help ensure that it has not been unintentionally activated. Patients can order training materials such as DVDs free of charge at www.EpiPen.ca or at 1-877-EPIPEN1.

Excedrin Extra Strength/ Excedrin Tension Headache: A voluntary recall by Novartis Consumer Health Inc. in the US has been extended to Canada for all lots of OTC **Excedrin Extra Strength** and **Excedrin Tension Headache** caplets (acetaminophen/caffeine 500 mg/ 65 mg) with expiration dates of December 20, 2014, and earlier. The US FDA has received reports of chipped and broken pills, and inconsistent bottle packaging clearance practices, which may result in an assortment of products in the same bottle. Consumers may be at risk of receiving an unintended ingredient and/or an undesired dose of the packaged ingredient. For further information regarding the recall, including how to return the affected product, advise patients to contact Novartis at 1-888-788-8181.

Multaq: Sanofi-aventis Canada Inc. and Health Canada inform health care professionals of updates to the product monograph of **Multaq** (dronedarone) regarding cardiovascular and pulmonary safety information and a revised indication. Contraindications to Multaq include patients with permanent atrial fibrillation of any duration in which sinus rhythm cannot be restored and attempts to restore it are no longer considered, patients with history of or current heart failure, regardless of New York Heart Association functional class, patients with left ventricular systolic dysfunction, patients with certain conduction abnormalities and patients with liver or lung toxicity related to the previous use of amiodarone. Added sections to the product monograph include cardiovascular and renal monitoring recommendations and the need for pulmonary clinical evaluation.

Please refer to the product monograph for further information.

Sublinox: Meda Valeant Pharma Canada Inc. and Health Canada inform health care professionals of the association of **Sublinox** (zolpidem tartrate) with complex sleep behaviours, especially in combination with CNS-active medications. Immediate discontinuation of Sublinox is recommended in patients who report complex sleep behaviours, i.e., engaging unknowingly in activities that they do not remember. Personal or family history of sleepwalking is a contraindication to its use. Advise patients to discuss further with their health care providers if insomnia has not remitted after 7 to 10 days of treatment with Sublinox.

Ursodiol: The manufacturers of **ursodiol** (Aptalis Pharma Canada Inc., Dominion Pharmacal, Pharmascience Inc., Pharmel Inc. and Teva Canada Ltd.) and Health Canada inform health care professionals of an increase in serious liver adverse events, including liver transplantation and death, in patients taking ursodiol at twice the recommended dose. According to a 5-year randomized controlled trial in 150 patients with primary sclerosing cholangitis (PSC), ursodiol 28 to 30 mg/kg/day did not improve survival relative to placebo. In addition, at this dose, patients on ursodiol experienced a higher rate of serious adverse events, including death and liver transplantation, regardless of the improvement in serum AST and ALP levels. Advise patients with PSC taking ursodiol to discuss this further with their health care providers.

NEW PRODUCTS

Aczone (dapsone 5% by Valeant Canada LP) is a topical gel for the treatment of acne vulgaris in patients ≥ 12 years. **Aczone** should be applied in a thin layer and gently rubbed into clean, dry, affected skin twice a day. Reassess use of Aczone if there is no improvement after 12 weeks. Common adverse events in clinical trials include oiliness/peeling, dryness and erythema. A temporary local yellow or orange discoloration

of skin and facial hair was observed in a clinical trial when benzoyl peroxide was applied after Aczone. Resolution occurred in 4 to 57 days. The combination of Aczone with trimethoprim/sulfamethoxazole in patients with G6PD deficiency may result in increased risk of hemolysis. Aczone is available in 30 g and 60 g tubes.

Gelnique (10% oxybutynin chloride by Watson Laboratories Inc.) is a topical gel for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and frequency. The recommended dose is one metered dose from the dispenser (pump) or contents of one sachet applied once daily to dry, intact skin on the abdomen, upper arms/shoulders or thighs. Advise patients to rotate application sites

daily and to avoid applying Gelnique to recently shaved skin surface or skin areas with eczema, seborrhea or psoriasis. Common adverse events in clinical trials were dry mouth and application-site reactions, e.g., dermatitis, pruritus, erythema. Gelnique is available in a 30 g metered-dose pump and in cartons of 30 individual use 1 g sachets (100 mg / g each).

Ozurdex (dexamethasone 0.7 mg by Allergan Inc.) is an intravitreal implant for the treatment of macular edema following central retinal vein occlusion and the treatment of noninfectious uveitis affecting the posterior segment of the eye. Contraindications include advanced glaucoma and active or suspected ocular or periocular infections. The recommended dose is the administration of the entire contents of one single use Ozurdex 0.7 mg device (preservative-free) into the affected eye by a qualified oph-

thalmologist carried out under controlled aseptic conditions. No more than 2 consecutive injections should be used and an interval of approximately 6 months should be allowed between the 2 injections.

Sublinox (zolpidem tartrate 10 mg orally disintegrating tablets by MEDA AB) is a nonbenzodiazepine hypnotic, scheduled as a controlled substance, for the short-term treatment and symptomatic relief of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakenings. If used for more than 2 to 3 consecutive weeks, the patient requires a complete re-evaluation. The recommended dose is 10 mg once daily placed under the tongue immediately before bedtime and only when patients are able to stay in bed for a full night before being active again. Sublinox is not recommended for patients ≥ 65 years; the 10 mg dose, which cannot be split, causes drowsiness and dizziness, thereby increasing the risk for falls. Contraindications include myasthenia gravis or a personal or family history of sleepwalking. Advise patients not to take Sublinox with alcohol or other CNS depressants, as this may increase the risk of complex sleep-related behaviours with amnesia (i.e., driving while not fully awake).

Visanne (dienogest 2 mg by Bayer Inc.) is a progestin for the management of pelvic pain associated with endometriosis. The recommended dose is 2 mg once daily (1 tablet) started on any day of the menstrual cycle and taken continuously at the same time daily regardless of any vaginal bleeding. Common adverse effects reported included headache and breast discomfort, including engorgement and breast pain. If contraception is required while on Visanne, advise patients to use nonhormonal methods, e.g., barrier methods. Long-term bone mineral density and fracture risk data are not available, as efficacy has not been tested beyond 15 months.

Zytiga (abiraterone acetate 250 mg tablets by Janssen Inc.) is an androgen biosynthesis inhibitor used in combination with prednisone for the treatment of metastatic prostate cancer (castration-resistant prostate cancer) in patients who have received prior chemotherapy containing docetaxel. Zytiga may harm a developing fetus due to its mechanism of action; therefore, women who are or may be pregnant should not handle Zytiga without protection, e.g., gloves. The recommended dose is 1 g as a single daily dose taken orally on an empty stomach, swallowed whole with water, with no food consumption 2 hours prior and 1 hour after administration. Zytiga is not recommended for patients with pre-existing moderate or severe hepatic impairment. Complete discontinuation is advised if patients develop severe hepatotoxicity (ALT or AST 20 times the upper limit of normal).

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NEW INDICATIONS

Actemra (tocilizumab by Hoffmann-La Roche Ltd.) is now approved for the treatment of active systemic juvenile idiopathic arthritis in patients 2 years of age and older, who have responded inadequately to previous therapy with one or more nonsteroidal anti-inflammatory drug and systemic corticosteroids.

Multaq (dronedarone by Sanofi-aventis Canada Inc.) has undergone revisions to its indication for atrial fibrillation. Multaq is now indicated for the treatment of patients with paroxysmal or persistent atrial fibrillation who are in sinus rhythm or who are intended to be cardioverted, to reduce the risk of cardiovascular hospitalization due to atrial fibrillation. Multaq should only be prescribed after alternative treatment options have been considered.

Remicade (infliximab by Janssen Inc.) now has an expanded indication in the treatment of Crohn's disease. Remicade is indicated for the reduction of signs and symptoms, induction and maintenance of clinical remission and mucosal healing in adults and pediatric patients, as well

as the reduction of corticosteroid use in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to a corticosteroid and/or aminosalicylate. Remicade can be used alone or in combination with conventional therapy.

Rituxan (rituximab by Hoffmann-La Roche Ltd.) in combination with glucocorticoids is now approved for the induction of remission in adult patients with severely active granulomatosis with polyangiitis (GPA, also known as Wegener's granulomatosis) and microscopic polyangiitis (MPA). Consideration should be given to current treatment guidelines for vasculitis.

Xarelto (rivaroxaban by Bayer Inc.) is now approved for the prevention of stroke and systemic embolism in patients with atrial fibrillation. The recommended dose is 20 mg once daily with food. In patients with CrCl 30 to 49 mL/min, the recommended dose is 15 mg once daily with food.

Zinecard (dexrazoxane by Pfizer Canada Inc.) is indicated for reducing (preventing) the incidence and severity of cardiotoxicity associated with doxorubicin administration for the treatment of *metastatic* breast cancer in patients who have already experienced a partial response or at least maintained stable disease. The change in wording of the indication from breast cancer to metastatic breast cancer is recent.

NEW GENERICS

Brimonidine P 0.15% eye drops are now available from Apotex Inc. This is a new alternative to Alphagan P.

Candesartan 4 mg, 8 mg, 16 mg and 32 mg tablets are now available from Cobalt Pharmaceuticals. This is a new alternative to Atacand.

Clopidogrel 75 mg tablets are now available from Apotex Inc., Cobalt Pharmaceuticals, Sandoz Canada and Teva Canada. These are new alternatives to Plavix.

Diltiazem CD 120 mg, 180 mg, 240 mg and 300 mg capsules are now available from Cobalt Pharmaceuticals. These are new alternatives to Cardizem CD.

Diltiazem T 120 mg, 180 mg, 240 mg, 300 mg and 360 mg capsules are now available from Cobalt Pharmaceuticals. This is a new alternative to Tiazac.

Dorzolamide-timolol 2%/0.5% eye drops are now available from Apotex Inc. This is a new alternative to Cosopt.

Latanoprost 0.005% eye drops are now available from Cobalt Pharmaceuticals. This is a new alternative to Xalatan.

Losartan 50 mg and 100 mg tablets are now available from Apotex Inc., Cobalt Pharmaceuticals and Sandoz Canada. Losartan 25 mg tablets are also now available from Cobalt Pharmaceuticals and Sandoz Canada. These are new alternatives to Cozaar.

Losartan/hydrochlorothiazide 50/12.5, 100/12.5 and 100/25 mg tablets are now available from Sandoz Canada. These are new alternatives to Hyzaar (50/12.5, 100/12.5) and Hyzaar DS (100/25).

Memantine 10 mg tablets are now available from Apotex Inc. This is a new alternative to Ebixa.

Montelukast 10 mg tablets are now available from Apotex Inc. This is a new alternative to Singulair.

Mycophenolate 250 mg capsules and 500 mg tablets are now available from Apotex Inc., Sandoz Canada and Teva Canada. This is a new alternative to CellCept.

Olanzapine 5 mg, 10 mg, 15 mg and 20 mg oral disintegrating tablets are now available from Apotex Inc. This is a new alternative to Zyprexa Zydis.

DISCONTINUED PRODUCTS

Hydromorphone injectable products, specifically Dilaudid-HP-Plus 20 mg/mL injection and Dilaudid-XP 50 mg/mL injection, from Purdue have now been discontinued.

NEW STRENGTHS

Xarelto (rivaroxaban Bayer Inc.) is now available in 10 mg, 15 mg and 20 mg tablets.

NEW APPEARANCE/ NAME CHANGE

PMS-Phenobarbital 15 mg, 30 mg, 60 mg and 100 mg tablets will now be marketed as PHENOBARB. The product has changed ownership from Pharmascience Inc. to Pendopharm, Division of Pharmascience Inc. The DIN remains the same for all the strengths; however, the appearance of the tablets will be changed.

NEW COMBINATION PRODUCT

Jalyn modified-release capsules are a combination of a dutasteride 0.5 mg soft gelatin capsule and tamsulosin 0.4 mg sustained-release pellets by GlaxoSmith-Kline Inc. ■

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