



CARDIOVASCULAR EFFECTS OF AZITHROMYCIN, ESCITALOPRAM & DOMPERIDONE

Health authorities are warning of potentially serious abnormal heart rhythms with azithromycin, escitalopram and domperidone.

Azithromycin was recently highlighted in a study published in the *New England Journal of Medicine* comparing the risks of cardiovascular death in patients treated with azithromycin (Zithromax®), amoxicillin, ciprofloxacin (Cipro®), levofloxacin (Levaquin®) and no antibacterial drug. A small increase in deaths from cardiovascular causes and from any cause was reported with a 5 day course of azithromycin. The risk is similar with levofloxacin.

Azithromycin is a macrolide antibiotic. Other drugs in this class (erythromycin, clarithromycin) have been associated with prolongation of the QT interval, an abnormal heart rhythm that can lead to torsades de pointes. Although the risk of cardiovascular effects with azithromycin appears to be low, the FDA in the United States has issued a warning and precaution to avoid use of azithromycin in patients:

- with known prolongation of the QT interval or with conditions that predispose them to arrhythmias (e.g. uncorrected hypokalemia or hypomagnesemia)
- with clinically significant bradycardia
- taking Class IA antiarrhythmics (quinidine, procainamide) or Class III antiarrhythmics (amiodarone, sotalol)

The elderly tend to be more susceptible to drug-induced effects on the QT interval.

Escitalopram (Cipraxel®), a selective serotonin reuptake inhibitor for depression, has been linked by Health Canada to a dose-related risk of QT prolongation. As a result, a maximum daily dose of 10 mg is now recommended for patients who are 65 years of age or older, or have liver problems, or are taking omeprazole or cimetidine (due to increased levels of escitalopram).

Escitalopram is contraindicated in patients with congenital long QT syndrome or patients with QT interval prolongation. Concomitant use of escitalopram with other drugs that may affect the QT interval or drugs that may affect electrolyte levels (e.g. diuretics, laxatives, etc.) is discouraged.

Domperidone, a gastrointestinal motility agent, is associated with an “increased risk of serious ventricular arrhythmias or sudden cardiac death, particularly in patients taking daily doses greater than 30 mg and in patients older than 60 years of age”. Domperidone should be initiated at the lowest possible dose and titrated upward cautiously if the expected benefit outweighs the risk. As with escitalopram, concomitant use of domperidone with drugs that prolong the QT interval or in patients with existing QT prolongation, underlying cardiac disease (e.g. congestive heart failure) or electrolyte disturbances should proceed with caution. [MPT](#)

H2-BLOCKERS MAY CAUSE CONFUSION IN THE ELDERLY

Patients with dementia or delirium tend to experience increased central nervous system effects when using H2-blockers. Cimetidine has been listed in the Beer’s list for a number of years as being inappropriate for use in the elderly. The list has been revised to include all H2-blockers.

What are the clinical implications? Not all H2-blockers have to be avoided in the elderly, however individuals “with delirium or at high risk of delirium (e.g. age > 65 years, severe illness, hip fracture), dementia or cognitive impairment” are at increased risk of developing or suffering a progression of cognitive impairment. H2-blockers are renally eliminated. Thus it is recommended that their doses be reduced for a CrCL < 50 ml/min and a CrCL < 30 ml/min for cimetidine.

Cimetidine and ranitidine have medium to high anticholinergic activity while famotidine and nizatidine tend to have low anticholinergic activity. A higher anticholinergic load is known to increase the risk of delirium and cognitive dysfunction. The anticholinergic burden increases when other drugs with anticholinergic activity are added. [MPT](#)

DRUG NEWS

Onbrez Breezhaler® (indacaterol maleate) 75 µg capsules for inhalation Novartis (not currently a benefit of ODB)

Onbrez is a long-acting, beta-agonist bronchodilator capsule to be used with the supplied device for inhalation of the powder. It is indicated for the maintenance treatment of COPD (chronic obstructive pulmonary disease), including chronic bronchitis and emphysema. It is not a rescue medication and is not indicated for asthma or to treat acute exacerbations of COPD.

Onbrez shares the same cardiovascular concerns as other long-acting beta-agonists. This drug class is associated with a higher risk of asthma-related deaths. Exercise caution in people with convulsive disorders, thyrotoxicosis and a hyperresponsive response to sympathomimetics.

Adverse Effects: The following adverse effects tended to be more commonly reported and were of mild to moderate severity: cough, nasopharyngitis, headache, nausea, oro-pharyngeal pain, muscle spasms and viral upper respiratory tract infections. More serious effects include increased pulse, increased blood pressure and significant hypokalemia.

Dose, Administration & Storage: The contents of one 75 µg capsule is to be inhaled once daily using the Breezhaler inhalation device. The capsule must be handled with dry hands and placed into the capsule chamber of the inhalation device (never in the mouthpiece) immediately before use. After piercing the capsule (by depressing the button once only) the patient should breath out forcefully and place the round piece of the inhalation device in the mouth. With the lips closed around the mouthpiece, the contents of the capsule should be inhaled rapidly and steadily while holding the device upright. A whirring sound is heard and a “sweetness” is tasted as the drug is delivered into the lungs. If no whirring sound is heard the capsule is likely stuck in the

chamber and should be freed by opening the device and tapping the base. Following the inhalation of the dose, the breath should be held for at least 5 to 10 seconds. When the total dose is delivered the capsule should appear clear and contain no powder. If any powder remains, the steps for inhalation should be repeated. Once empty, the capsule should be discarded.

Onbrez capsules are supplied in blister packs of 30 capsules. The product should be stored in a dry place in the original package until immediately before use. **DN**

Sublinox® (zolpidem tartrate) sublingual orally disintegrating 10 mg tablets Meda Valeant (not currently a benefit of ODB)

Sublinox, a non-benzodiazepine hypnotic, is indicated for the short-term treatment of insomnia in people with difficulty in falling asleep or who have frequent nocturnal or early morning awakenings and impaired daytime functioning. Sublinox is similar in onset to zopiclone (about 15 to 30 minutes) but has a slightly shorter duration of action (7 hours vs ≥ 8 hours with zopiclone). Peak concentrations occur 30 to 80 minutes after dosing. The drug is primarily renally excreted. Like benzodiazepines, Sublinox is a controlled drug.

Use in people 65 years and older is not recommended due to the fall risk (due to drowsiness and dizziness) with the 10 mg tablet. Other adverse effects include diarrhea, complex sleep-related behaviours (e.g. driving while not fully awake), severe anaphylactic and anaphylactoid reactions, anterograde amnesia, abnormal thinking, behavioural changes, drug abuse and dependence, rebound insomnia and CNS effects. Combining with other CNS depressant drugs or alcohol increases CNS depressant effects. Sublinox should be dosed immediately prior to bedtime by allowing the tablet to dissolve under the tongue. The tablet should not be chewed, split, swallowed or taken with water. **DN**

(Refer to the product monograph for complete information)

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