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Topic “Under Construction” for a future edition of the Geri-RxFiles

## INTRODUCTION

### Drug Therapy in the Older Adult

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**Frailty Assessment Links:** <http://geriatricresearch.medicine.dal.ca/pdf/Clinical%20Faily%20Scale.pdf>

*AGS Geriatric Evaluation and Management Tools:*

<http://familymed.uthscsa.edu/gerifellowship/redirect/articles/CLC/Geriatrics%20Eval%20Management%20Tool%20for%20Frailty.pdf>

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FDA Feb/10 notified healthcare professionals and patients that it is reviewing clinical trial data about a potentially serious effect on the heart from the use of Invirase (saquinavir) in combination with Norvir (ritonavir), antiviral medications given together to treat HIV infection. The data suggest that together the two drugs may affect the electrical activity of the heart, known as prolonged QT or PR intervals.

FDA Nov/10 is requesting that manufacturers of the painkiller propoxyphene pull the drug from the market because of concerns over cardiotoxicity. (Propoxyphene is marketed alone as Darvon & combined with acetaminophen as Darvocet.) The agency's request is based on data showing that, even when taken at therapeutic doses, the drug can lead to potentially dangerous changes in the heart's electrical activity, including prolonged PR & QT intervals & widened QRS complex. FDA advises clinicians to stop prescribing propoxyphene and to ask current users to discontinue the drug. FDA's MedWatch alert

FDA Dec/10 The injectable form of dolasetron mesylate (Anzemet) should not be used to prevent nausea or vomiting related to chemotherapy because the drug increases the risk for torsade de pointes, the FDA announced on Friday. The FDA recommends against using Anzemet injections in patients with

congenital long-QT syndrome. The warning does not apply to Anzemet tablets because the risks for developing an abnormal heart rhythm are not as high as with the injections. FDA MedWatch alert (Free)

FDA July/11 FDA has added a warning to the label of the atypical antipsychotic quetiapine (Seroquel) cautioning about potential increases in the QT interval. Postmarketing cases of QT prolongation have been reported in some 17 patients, according to the New York Times. These patients had overdosed on quetiapine, had other illnesses, or were taking other medications that can cause electrolyte imbalance or QT prolongation.

FDA Aug/11 The antidepressant citalopram (marketed as Celexa) should not be prescribed at doses above 40 mg/day because higher dosages can cause arrhythmias, the FDA has warned.

FDA Sep/11 The U.S. Food and Drug Administration (FDA) is informing the public of an ongoing safety review of the anti-nausea drug Zofran (ondansetron, ondansetron hydrochloride and their generics). Ondansetron may increase the risk of developing abnormal changes (QT prolongation & torsades) in the electrical activity of the heart.

FDA July/12 Alerting clinicians that a single 32-mg intravenous dose of ondansetron (Zofran and generics) may lead to QT interval prolongation, which in turn may put patients at risk for torsades de pointes.

FDA Dec/12 is working with the manufacturers of all 32 mg dose Ondansetron Injectable Products (brand and generic) to voluntarily recall them from the market due to QT serious cardiac toxicity.

FDA Mar/13 is warning the public that azithromycin (Zithromax or Zmax) can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm. Patients at particular risk for developing this condition include those with known risk factors such as existing QT interval prolongation, low blood levels of potassium or magnesium, a slower than normal heart rate, or use of certain drugs used to treat abnormal heart rhythms, or arrhythmias.

Funk KA, Bostwick JR. A Comparison of the Risk of QT Prolongation Among SSRIs. *Ann Pharmacother.* 2013 Oct;47(10):1330-41.

Health Canada Aug/10 Droperidol Injection USP is associated with severe arrhythmia (eg. QT) and the Canadian Monograph of this product has been updated to reflect this risk.

Health Canada Nov/10 Darvon-N (dextropropoxyphene) - Recall and Withdrawal in Canada - Paladin Labs Inc. Paladin Labs Inc. in collaboration with Health Canada would like to inform healthcare professionals of the voluntary recall and withdrawal of the opioid analgesic Darvon-N (dextropropoxyphene) in Canada. (widen the QRS complex, prolong the QT interval and therefore increase the risk of serious abnormal heart rhythms.)

Health Canada Feb/12 has recently approved vandetanib (CAPRELSA) to treat medullary thyroid cancer in adult patients where either the tumour cannot be removed by surgery or it has spread from the thyroid gland to other parts of the body. CAPRELSA can cause serious QT heart rhythm changes which may result in sudden death, if left untreated.

Health Canada Mar/12: Domperidone should be used at the lowest possible dose. The risk of serious ventricular arrhythmias and sudden cardiac death may be higher in patients taking daily doses greater than 30 mg, and in patients over 60 years old.

Health Canada Oct/12: Ondansetron can cause a dose-dependent prolongation of the electrocardiographic-corrected QT interval (QTc), which can lead to Torsade de Pointes, a potentially life-threatening heart rhythm abnormality. The new maximum recommended single intravenous (IV) dose of ZOFRAN<sup>®</sup> is 16 mg infused over 15 minutes.

Health Canada Oct/13 has completed a safety review of the drug Sensipar (cinacalcet) that identified a possible link between the drug and abnormal heart rhythm (QT) associated with low blood calcium.

Health Canada Feb/14: TELZIR (fosamprenavir) should not be used with the antiarrhythmic drugs amiodarone, lidocaine (systemic), or quinidine, as this may cause serious and/or life-threatening reactions such as abnormal heart rhythm (arrhythmias). In addition, Telzir should not be used with delavirdine, another antiviral drug to treat HIV, because it may reduce the effectiveness of delavirdine.



Health Canada Mar/14: REMERON / REMERON RD (mirtazapine) – Abnormal Heart Rhythm - Merck Canada Inc. Cases of abnormal heart rhythm (eg. QT prolongation) have been reported with the antidepressant REMERON / REMERON RD (mirtazapine) mainly with drug overdose or when taking other drugs known to cause heart rhythm problems. The product information has been updated.

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Krantz MJ, Martin J, et al. QTc Interval Screening in Methadone Treatment. *Ann Intern Med.* 2009 Jan 19. [Epub ahead print] Recommendation 1 (Disclosure): Clinicians should inform patients of arrhythmia risk when they prescribe methadone. Recommendation 2 (Clinical History): Clinicians should ask patients about any history of structural heart disease, arrhythmia, and syncope. Recommendation 3 (Screening): Obtain a pretreatment electrocardiogram for all patients to measure the QTc interval and a follow-up electrocardiogram within 30 days and annually. Additional electrocardiography is recommended if the methadone dosage exceeds 100 mg/d or if patients have unexplained syncope or seizures. Recommendation 4 (Risk Stratification): If the QTc interval is greater than 450 ms but less than 500 ms, discuss the potential risks and benefits with patients and monitor them more frequently. If the QTc interval exceeds 500 ms, consider discontinuing or reducing the methadone dose; eliminating contributing factors, such as drugs that promote hypokalemia; or using an alternative therapy. Recommendation 5 (Drug Interactions): Clinicians should be aware of interactions between methadone and other drugs that possess QT interval-prolonging properties or slow the elimination of methadone.

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MHRA Dec/11 Citalopram and escitalopram are associated with dose-dependent QT interval prolongation and should not be used in those with: congenital long QT syndrome; known pre-existing QT interval prolongation; or in combination with other medicines that prolong the QT interval. ECG measurements should be considered for patients with cardiac disease, and electrolyte disturbances should be corrected before starting treatment. For citalopram, new restrictions on the maximum daily doses now apply: 40 mg for adults; 20 mg for patients older than 65 years; and 20 mg for those with hepatic impairment. For escitalopram, the maximum daily dose for patients older than 65 years is now reduced to 10 mg/day; other doses remain unchanged.

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