

Pharmacy & Therapeutics Update (TMC, FMC, MPH) Drug Information for Health Care Professionals



Volume 4, Issue 10

December 24th, 2009

Dronedaron (Multaq®)

Ryan Kammer, PharmD, BCPS

rtkammer@novanthealth.org

Dronedaron (Multaq®) is an antiarrhythmic agent indicated to reduce hospitalization related to atrial fibrillation or flutter, in patients with a recent episode who are in sinus rhythm or will be cardioverted. Dronedaron is pharmacologically similar to amiodaron, however the iodine has been removed, and the addition of a side group has reduced its half-life and tissue accumulation. This has resulted in less thyroid and pulmonary toxicity to date.

Dronedaron is dosed at 400mg PO twice daily with meals to increase bioavailability. It is metabolized via CYP3A4 and moderately inhibits CYP3A4, CYP2D6, and P-glycoprotein. Contraindications include: class IV heart failure, class II-III heart failure with recent (within 30 days) decompensation or referral to heart failure clinic, 2nd or 3rd degree heart block, heart rate <50 bpm, concomitant strong CYP3A4 inhibitors, concomitant QTc prolonging drugs, QTc ≥500 msec. Dronedaron can increase the QTc interval and the serum creatinine (about 0.1 mg/dl though GFR not affected), and cause bradycardia and gastrointestinal side effects.

Compared to amiodaron, dronedaron is less effective and more expensive, but has demonstrated less toxicity to date. Dronedaron has been added to the Formulary with initiation restricted to Cardiology. Continuation of established therapy will not be restricted unless contraindications exist (admitted with heart failure, etc.)

Fesoterodine (Toviaz®)

Susan Wilson, PharmD

shwilson@novanthealth.org

On Thursday, November 19, fesoterodine (Toviaz™) was reviewed for the Pharmacy and Therapeutics Committee. Fesoterodine is a new antimuscarinic agent for the treatment of overactive bladder symptoms. Fesoterodine is supplied as 4 mg and 8 mg tablets, to be dosed once daily. A therapeutic interchange was suggested and approved for all doses of fesoterodine to be automatically substituted to tolterodine ER 4 mg once daily.

Drug Ordered

Fesoterodine (Toviaz™) 4 mg once daily
Fesoterodine (Toviaz™) 8 mg once daily

Drug Dispensed

Tolterodine ER (Detrol LA®) 4 mg once daily
Tolterodine ER (Detrol LA®) 4 mg once daily

Pharmacy Resident Research Project—Sloan Hepfer, PharmD

kshepfer@novanthealth.org

Editorial Staff:

Micahel Nnadi, PharmD
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Director of Pharmacy

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Effect of Antipsychotic Medications on Length of Stay in Elderly Demented Patients

Acute delirium has been associated with increased length of stay in elderly demented patients. Antipsychotic medications are frequently used to treat acute delirium and/or agitation in this population in the inpatient hospital setting. The primary objective of our retrospective study is to determine if antipsychotic medications decrease the prolonged duration of hospitalization of acute delirious patients. We know that antipsychotics have adverse effects, especially in the elderly population. Thus, a secondary objective of fall incidence will be collected in order to assess the occurrence of this adverse event in patients with and without antipsychotic administration. To analyze the effect of antipsychotic medications on length of stay as compared to patients who did not receive antipsychotics we will use age, cognition, and severity of illness to control for confounding factors that may impact duration of hospitalization. This project has been approved by the Institutional Review Board (IRB) and results will be reported by April of 2010.

Proton Pump Inhibitors and Clopidogrel Drug Interaction

Recommendations from the Society of Cardiovascular Angiography and Interventions

It is well known in the cardiovascular community that the antiplatelet effect of clopidogrel varies from patient to patient, and that reduced platelet inhibition by clopidogrel is associated with an increased risk for cardiac events. Clopidogrel is a prodrug that must be metabolized to the active form in order to exert its antiplatelet effect. Intestinal absorption of the prodrug clopidogrel is limited by an intestinal efflux pump P-glycoprotein coded by the ABCB1 gene. Fifteen percent of the parent compound is bio-activated by various cytochrome P450 (CYP) isoforms (CYP 3A4, CYP 3A5, and CYP 2C19) into active metabolites. It is approved for use with aspirin in patients with Acute Coronary Syndrome (ACS) and Percutaneous Coronary Intervention (PCI). PPIs are frequently used to treat and prevent gastrointestinal (GI) reflux and peptic ulcer disease (PUD), especially when dual antiplatelet medications are used (recommended by recent guidelines for the majority of patients post myocardial infarction to minimize the risk of an adverse GI event due to the use of daily aspirin).

Data has been published suggesting that omeprazole interacts with and reduces the antiplatelet efficacy of clopidogrel. More recent data suggests that this may be a class effect and that other proton pump inhibitors may also interact with clopidogrel. Patients receiving proton pump inhibitors concurrently with clopidogrel have been shown to have an increased risk of heart attack, stroke, unstable angina, or repeat coronary procedure.

In May 2009, the clopidogrel prescribing information was updated to include information about Cytochrome P450 2C19 polymorphisms on the antiplatelet effect of clopidogrel and that the use of medications known to inhibit CYP 2C19 is not recommended. Our formulary proton pump inhibitor is pantoprazole (Protonix), which appears to have the weakest effect on CYP 2C19 enzyme.

No mechanism of interaction has been fully proven. Cytochrome P450 2C19 (CYP 2C19) is one of the enzymes involved in the activation of clopidogrel. Some PPIs inhibit CYP 2C19 metabolism, thus reducing conversion of clopidogrel to its active form. Another possible mechanism is that PPI therapy increases gastric pH, which might reduce the absorption of clopidogrel. Previous literature demonstrated that pantoprazole might not be affected based on a lower degree of CYP 2C19 inhibition.

The Society for Cardiovascular Angiography and Interventions (SCAI) recommends the use of an alternative drug such as H₂ receptor antagonists (H₂RA) such as famotidine (Pepcid) or antacids for GI symptoms in patients who take clopidogrel. Cimetidine should not be used as it is also a CYP 2C19 inhibitor. Prescribers should be advised to avoid combining PPIs with clopidogrel, when appropriate, until more evidence is available. For patients who require a PPI, pantoprazole is most likely the best choice.

Congratulations to Ryan Kammer PharmD, Jeremy Hodges RPh and Christina Roels PharmD for achieving their Board Certification in Pharmacotherapy. They join Amy Dooley, PharmD and Lisa Brennan, PharmD in this accomplishment.

Heparin Infusions—As of 12/15/2009 FMC, TMC and MPH are using heparin 25,000 units/250 ml (100 unit/ml) infusions. Also, a new protocol which is weight based and utilizes heparin levels (anti Xa levels) to monitor therapy instead of PTT has been implemented. This change has been made as heparin levels more accurately reflect the anticoagulant effect of heparin.