

NATIONAL PBM COMMUNICATION • November 15, 2010

ISMP Medication Safety Alert: Dronedaronone (Multaq®) Adverse Event Signal

- The ISMP (Institute for Safe Medication Practices) QuarterWatch™ monitors serious adverse events reported to the FDA through the MedWatch reporting system and recently reported the following:
 - Since approval of dronedaronone in 2009, 387 serious adverse events have been reported including: 24 deaths, 2 reports of disability, and 361 other serious adverse events.
 - 100 (26%) of the reports were related to new or worsening heart failure.
 - Reports of heart rhythm disturbances included: 18 bradycardia, 47 atrial tachycardia, and 13 ventricular tachycardia.
 - 33 reports were related to a potential drug interaction with warfarin.
 - There were also 15 cases of kidney failure or impairment.
- The report states that the adverse event risks with dronedaronone may have been underestimated and that the risk for worsening heart failure and arrhythmias, and potential for drug interactions, need to be taken into consideration and weighed against the limited clinical benefits.
- Dronedaronone (Multaq®) is approved to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent atrial fibrillation or atrial flutter, with a recent episode of atrial fibrillation/atrial flutter and associated cardiovascular risk factors (i.e., age > 70 years, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter ≥ 50mm or left ventricular ejection fraction < 40%), who are in sinus rhythm or who will be cardioverted.
- VA National **Dronedaronone Criteria for Use** are available at:
 - [VA National Dronedaronone Criteria for Use](#)
- Prescribing information for dronedaronone includes a **Boxed Warning** that dronedaronone is contraindicated in patients with New York Heart Association (NYHA) Class IV heart failure or NYHA Class II-III heart failure with recent decompensation requiring hospitalization or referral to a specialized heart failure clinic, based on data from the ANDROMEDA study that treatment with dronedaronone in this patient population resulted in more than a two-fold increase in mortality.
- Since the PBM's formulary review of dronedaronone, VAMedSAFE has been conducting a safety surveillance on patients prescribed dronedaronone and reports of heart failure exacerbation and new onset heart failure, as well as whether dronedaronone was prescribed in patients with a potential contraindication based on recommendations in the Boxed Warning.
 - During the evaluation period 8/1/2009-6/30/2010, of 533 patients prescribed dronedaronone, 25 appeared to have a potential contraindication (i.e., recent heart failure hospitalization or clinic visit for heart failure by database parameters). These data are currently being validated by chart review including the most recent quarterly data.
 - In addition to these ongoing monitoring parameters, VAMedSAFE is collecting data on bleeding events in patients prescribed concomitant warfarin, as well as thyroid and pulmonary events.
 - Adverse events reported via the VA Adverse Drug Event Reporting System (VA ADERS) are also being routinely monitored (refer to Appendix on the PBM INTRANet site under the link "VAMedSAFE Project Results [Select]"). Of the 17 patients with reported adverse events with dronedaronone as the primary suspect drug, 5 cases reported symptoms potentially related to heart failure (e.g., edema, increased weight, dyspnea, tachypnea, decreased exercise tolerance, orthopnea, paroxysmal nocturnal dyspnea).
 - VAMedSAFE is also working with the FDA and their Federal Sentinel Initiative to monitor adverse events with dronedaronone.
- It is recommended that dronedaronone be prescribed according to VA National Criteria for Use (refer to link above) and per the manufacturer's prescribing information.
- Providers should especially be aware of the potential for new or worsening heart failure or arrhythmias, kidney impairment, QT prolongation, drug interactions, and contraindications as listed in the Boxed Warning (refer to Criteria for Use and prescribing information).
- Report any adverse reactions experienced with the use of this medication to the VA ADERS program and FDA MedWatch.
- Refer to <http://www.ismp.org/QuarterWatch/2010Q1.pdf> for further details regarding the ISMP Medication Safety Alert.

ACTIONS

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives**: Forward this document to all appropriate providers who prescribe these medications (e.g., primary care providers, cardiologists, and clinic staff, including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D**: Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).