

MULTAQ® (dronedarone) FACT SHEET

- MULTAQ® (dronedarone) 400 mg Tablets is an anti-arrhythmic drug approved by the U.S. Food and Drug Administration (FDA) to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent atrial fibrillation (AF) or atrial flutter (AFL), with a recent episode of AF/AFL and associated cardiovascular risk factors, who are in sinus rhythm or who will be cardioverted. Associated cardiovascular risk factors include age over 70 years, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter ≥ 50 mm or left ventricular ejection fraction [LVEF] $< 40\%$.
- MULTAQ is the first drug approved in the United States that has shown a clinical benefit to reduce cardiovascular hospitalization in patients with AF/AFL. It is one of the major therapeutic innovations for atrial fibrillation in the last ten years.
- The FDA approval is based on a number of international, multi-center, randomized clinical trials involving nearly 6,300 AF/AFL patients. In these studies, patients were randomized and treated, including more than 3,200 who received MULTAQ.
 - The landmark ATHENA trial, which was published in the *New England Journal of Medicine* in February 2009, included more than 4,600 patients, with more than 2,300 receiving MULTAQ. The trial was conducted at 551 investigational sites in 37 countries, making it the largest study with an anti-arrhythmic drug for atrial fibrillation and atrial flutter.
 - MULTAQ, in addition to standard therapy, significantly reduced the risk of first cardiovascular hospitalization or death by 24 percent ($p < 0.001$) in patients with AF/AFL or a recent history of these conditions, when compared to placebo, meeting the study's primary endpoint. This reduction was generally consistent across study subgroups based on baseline characteristics or medications. Patients taking MULTAQ had higher rates of diarrhea, nausea, bradycardia, QT-interval prolongation and cutaneous rash than patients taking placebo.
- Initiation of MULTAQ treatment is contraindicated in patients with severe heart failure (NYHA class IV) or NYHA Class II – III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic. This unstable population corresponds to the population of the ANDROMEDA trial in which patients receiving dronedarone had a greater than two-fold increase in mortality compared to placebo.
- To ensure the use of Multaq® in the appropriate patient population, sanofi-aventis U.S. LLC also announced the launch of mPACT™ Multaq® Partnership for Appropriate Care and Treatment, the Risk Evaluation and Mitigation Strategy (REMS) developed by sanofi-aventis U.S. LLC. The mPACT™ Partnership was developed to assist healthcare professionals (HCPs) with the identification of appropriate patients and to ensure the safe use of Multaq® while minimizing risk. The risk mitigation program consists of a Communication Plan for HCPs, a medication guide for patients and post-marketing surveillance.
- MULTAQ is to be given twice daily as a 400 mg tablet and should be taken as one tablet with the morning and evening meals. Treatment with MULTAQ can be initiated in an outpatient setting. Most common adverse reactions are diarrhea, nausea, vomiting, abdominal pain, asthenia (weakness) and cutaneous rash.

Important Safety Information

WARNING: HEART FAILURE

MULTAQ is contraindicated in patients with NYHA Class IV heart failure, or NYHA Class II-III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic. In a placebo-controlled study in patients with severe heart failure requiring recent hospitalization or referral to a specialized heart failure clinic for worsening symptoms (the ANDROMEDA Study), patients given dronedarone had a greater than two-fold increase in mortality. Such patients should not be given dronedarone.

MULTAQ is also contraindicated in patients with second- or third-degree atrioventricular (AV) block or sick sinus syndrome (except when used in conjunction with a functioning pacemaker), bradycardia <50 bpm, QTc Bazett interval \geq 500 msec, and severe hepatic impairment.

MULTAQ should not be given to patients who are or may become pregnant (Category X) or nursing.

MULTAQ should not be coadministered with strong CYP 3A inhibitors or medicinal products that prolong the QT interval.

In patients with new or worsening heart failure, the suspension or discontinuation of MULTAQ should be considered.

Serum creatinine levels increase by about 0.1 mg/dL following MULTAQ treatment initiation. The elevation has a rapid onset, reaches a plateau after 7 days and is reversible after discontinuation.

Hypokalemia and hypomagnesemia may occur with concomitant administration of potassium-depleting diuretics. Potassium levels should be within the normal range pre and during administration of MULTAQ.

For full prescribing information, please visit <http://products.sanofi-aventis.us/Multaq/Multaq.pdf>