1. MULTAQ® HEALTHCARE PROFESSIONAL INFORMATION SHEET

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for AFib in patients in sinus rhythm with a history of paroxysmal or persistent AFib. Multaq is available in 400-mg tablets.

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of MULTAQ outweigh the risks.

**Boxed Warning**

**WARNING:**

**INCREASED RISK OF DEATH, STROKE AND HEART FAILURE IN PATIENTS WITH DECOMPENSATED HEART FAILURE OR PERMANENT ATRIAL FIBRILLATION**

MULTAQ is contraindicated in patients with symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure. MULTAQ doubles the risk of death in these patients.

MULTAQ is contraindicated in patients in atrial fibrillation (AFib) who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AFib, MULTAQ doubles the risk of death, stroke, and hospitalization for heart failure.

MULTAQ doubles the risk of death and is therefore contraindicated in the following populations:

- **Permanent atrial fibrillation:** Patients treated with MULTAQ should undergo monitoring of cardiac rhythm no less often than every 3 months. Cardiovert patients who are in AFib (if clinically indicated) or discontinue MULTAQ. MULTAQ offers no benefit in subjects in permanent AFib. In this population, MULTAQ was associated with an increased risk of stroke, particularly in the first two weeks of therapy. MULTAQ should only be initiated in patients in sinus rhythm who are receiving appropriate antithrombotic therapy.

- **Symptomatic heart failure with recent decompensation requiring hospitalization or NYHA Class IV heart failure**

For a complete list of contraindications, please refer to the prescribing information, including boxed WARNING.

In the postmarketing setting, the following REMS-related risks have been reported:

- **New onset or worsening heart failure:** In a placebo-controlled study in patients with permanent AFib, increased rates of heart failure were observed in patients with normal left ventricular function and no history of symptomatic heart failure, as well as those with a history of heart failure or left ventricular dysfunction. If heart failure develops or worsens and requires hospitalization, discontinue MULTAQ.

- **Hepatocellular liver injury, including acute liver failure requiring transplant:** Consider obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment. If hepatocellular injury is suspected, promptly discontinue MULTAQ and test serum enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase, as well as serum bilirubin, to establish whether there is liver injury. If liver injury is found, institute appropriate treatment and investigate the probable cause. Do not restart MULTAQ in patients without another explanation for the observed liver injury.
Please consider the following *Steps for Ensuring Appropriate Use* when prescribing MULTAQ for your patients:

1. **Appropriate Patient Selection**
   - Screen patients for severity and stability of heart failure; MULTAQ is contraindicated in patients with NYHA Class IV heart failure or symptomatic heart failure with recent decompensation requiring hospitalization because it doubles the risk of death.
   - MULTAQ is contraindicated in patients with permanent AFib that will not or cannot be cardioverted into normal sinus rhythm.
   - MULTAQ should only be initiated in patients in sinus rhythm who are receiving appropriate antithrombotic therapy. In a placebo-controlled study in patients with permanent AFib, MULTAQ was associated with an increased risk of stroke, particularly in the first two weeks of therapy.
   - STOP treatment with Class I or III antiarrhythmics (e.g., amiodarone, flecaïnidé, propafenone, quinidine, disopyramide, dofetilide, sotalol) or drugs that are strong inhibitors of CYP 3A (e.g., ketoconazole) before starting MULTAQ.
   - The dosage of certain cardiovascular medications may need to be adjusted and certain laboratory test changes may occur. These cardiovascular medications include statins, calcium-channel blockers, sirolimus, tacrolimus, beta-blockers, and other CYP 2D6 substrates, digoxin, dabigatran, and warfarin.

2. **Patient Monitoring**
   - Observe patients for new onset or worsening of heart failure. If heart failure develops or worsens and requires hospitalization, discontinue MULTAQ® (dronedarone).
   - Patients treated with dronedarone should undergo monitoring of cardiac rhythm no less often than every 3 months. Cardiovert patients who are in AFib (if clinically indicated) or discontinue MULTAQ. MULTAQ offers no benefit in patients in permanent AFib.
   - Monitor patients for signs and symptoms of liver injury. Consider obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment, but it is not known whether routine periodic monitoring of serum enzymes will prevent the development of severe liver injury.
   - Patients should be carefully evaluated clinically for pulmonary toxicity. If confirmed, treatment should be discontinued.
   - Renal function should be monitored periodically in patients treated with MULTAQ as increases in creatinine and renal failure have been reported in the postmarketing setting. In most cases, these effects appear to be reversible after discontinuation of MULTAQ.
3. Patient Counseling

- Advise patients to consult a physician if they develop signs or symptoms of heart failure, such as weight gain, dependent edema, or increasing shortness of breath.
- Advise patients to immediately report symptoms suggesting hepatic injury (such as anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching) to their physician.
- Advise patients that MULTAQ should not be taken with certain other medications and to consult with their physicians before starting any new drugs, as the dosage of certain cardiovascular medication may need to be adjusted.
- Refer patients to the Medication Guide and address any additional questions.

Please refer to the enclosed Prescribing Information for complete safety information before prescribing MULTAQ.

Serious Adverse Events

Health care professionals should report any serious adverse events thought to be associated with MULTAQ use to sanofi-aventis at 1-800-833-1610, option 2, or visit www.multaqgrams.com.

Alternatively, report this information to FDA’s MedWatch reporting system by phone (1-800-FDA-1088), facsimile (1-800-FDA-0178), online (https://www.accessdata.fda.gov/scripts/medwatch/), or mail using the MedWatch for FDA 3500, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

Additional Resources

For additional information, talk to your sanofi-aventis sales representative, call sanofi-aventis Medical Information Services department at 1-800-833-1610, option 1, or visit www.multaqgrams.com. Additionally, refer patients to the MULTAQ Medication Guide.