Indication

MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information for MULTAQ® (dronedarone)—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.

Please see additional Important Safety Information on pages 10 and 11, and for full Prescribing Information, including boxed WARNING, please click here or visit MULTAQ.com/hcp.
Why rhythm control matters in AFib management

AFib is a progressive disease with serious consequences\(^1,2\)

The chronic progressive nature of AFib may explain the need for early intervention\(^2\)

The AFib continuum of disease\(^3\)

- Diagnosis
  - Paroxysmal AFib
    - AFib episodes ≤7 days
    - Spontaneous termination
  - Persistent AFib
    - AFib episodes >7 days
    - No spontaneous termination
  - Permanent AFib
    - AFib that cannot be converted to SR


Paroxysmal and persistent AFib comprise the majority of cases\(^4\)

- 52% Paroxysmal\(^4\)
- 15% Persistent\(^4\)
- >50% of patients are still in paroxysmal AFib, but there is a narrow window of opportunity when active intervention can make a difference\(^4-6\)
Why rhythm control matters in AFib management

Fibrosis is a key indicator of structural damage associated with disease progression

Utah Stage* I (minimal)
<5% fibrosis of the left atrium

Utah Stage II (mild)
5%-20% fibrosis of the left atrium

Utah Stage III (moderate)
20%-35% fibrosis of the left atrium

Utah Stage IV (extensive)
>35% fibrosis of the left atrium

*Utah staging system classifies the degree of fibrosis in the atrium.

In an observational study, paroxysmal AFib was more prevalent in Utah stage I, whereas persistent AFib was more prevalent in Utah stage IV

AFib can exist before diagnosis—reinforcing the need for early action upon diagnosis
Through the lens of the 2014 AHA/ACC/HRS AFib Guidelines: Choose MULTAQ as first-line therapy

MULTAQ is recommended first line to maintain sinus rhythm in patients without structural heart disease or with coronary artery disease

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Important Safety Information for MULTAQ® (dronedarone)

- If hepatic injury is suspected, promptly discontinue MULTAQ and perform liver function tests 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.
- Larger increases in creatinine levels after MULTAQ initiation have been reported in the postmarketing setting. Monitor renal function periodically.
- MULTAQ increases exposure to digoxin. Consider discontinuing digoxin. If digoxin treatment is continued, halve the dose of digoxin, monitor serum levels closely, and observe for toxicity.
- MULTAQ can increase plasma concentrations of tacrolimus, sirolimus, and other CYP 3A substrates with a narrow therapeutic range when given orally. Monitor plasma concentrations and adjust dosage appropriately.
- Hypokalemia or hypomagnesemia may occur with concomitant administration of potassium-depleting diuretics. Potassium levels should be within the normal range prior to administration of MULTAQ and maintained in the normal range during administration of MULTAQ.
- Discontinue MULTAQ if QTc Bazett interval is ≥500 ms.
- Monitor INR after initiating MULTAQ in patients taking warfarin.

Monitoring considerations:

- No specific assessment of thyroid or lung function is required with MULTAQ.
- Patients treated with MULTAQ should undergo monitoring of cardiac rhythm no less often than every 3 months.
- Consider obtaining periodic liver enzymes, especially during first 6 months of treatment.
- Monitor renal function periodically.

(See additional monitoring considerations below)

MULTAQ 400 mg bid should be taken with full meals:

- To ensure a therapeutic dose, MULTAQ should be taken with full morning and evening meals.
- The absolute bioavailability of MULTAQ is nearly 4 times greater when taken with food.

Achieving steady state:

- After initial administration, steady state is reached within 4 to 8 days.

Perspectives from the 2014 AHA/ACC/HRS AFib Guidelines:

- “Drug-related proarrhythmia is most common during the initiation phase of drug therapy.”
- Data supporting the outpatient initiation of antiarrhythmic drug therapy are well-established for MULTAQ.

For patients with paroxysmal or persistent AFib new to rhythm control therapy:

Approved for outpatient initiation with no continuous ECG monitoring.

NO HOSPITAL ADMISSION REQUIRED
NO CONTINUOUS ECG MONITORING
NO LOADING DOSE OR TITRATION

Important Safety Information for MULTAQ® (dronedarone):

- If hepatic injury is suspected, promptly discontinue MULTAQ and perform liver function tests 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.
- Larger increases in creatinine levels after MULTAQ initiation have been reported in the postmarketing setting. Monitor renal function periodically.
- MULTAQ increases exposure to digoxin. Consider discontinuing digoxin. If digoxin treatment is continued, halve the dose of digoxin, monitor serum levels closely, and observe for toxicity.
- MULTAQ can increase plasma concentrations of tacrolimus, sirolimus, and other CYP 3A substrates with a narrow therapeutic range when given orally. Monitor plasma concentrations and adjust dosage appropriately.
- Hypokalemia or hypomagnesemia may occur with concomitant administration of potassium-depleting diuretics. Potassium levels should be within the normal range prior to administration of MULTAQ and maintained in the normal range during administration of MULTAQ.
- Discontinue MULTAQ if QTc Bazett interval is ≥500 ms.
- Monitor INR after initiating MULTAQ in patients taking warfarin.

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Based on the EURIDIS/ADONIS trials

MULTAQ reduced symptomatic AFib recurrence¹⁰

At 1 year, 62.3% of patients treated with MULTAQ were free of symptomatic AFib recurrence vs 54% of patients on placebo¹⁰

Reduced risk of first AFib recurrence¹⁰

- 25% RRR of first recurrence (symptomatic or asymptomatic)
- Absolute difference in recurrence rate of about 11% at 1 year (P<0.001)
- Majority of first recurrences were symptomatic

Prolonged time to first AFib recurrence¹⁰

- MULTAQ kept patients in sinus rhythm 2.2 times longer than placebo (116 days vs 53 days, respectively)

Important Safety Information for MULTAQ® (dronedarone)

- MULTAQ is contraindicated in patients with liver or lung toxicity related to the previous use of amiodarone
- MULTAQ is contraindicated in patients with severe hepatic impairment
- MULTAQ is 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 ≥500 ms or PR interval >280 ms

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For patients with paroxysmal or persistent AFib new to rhythm control therapy

Only MULTAQ is proven to reduce the risk of CV hospitalization

Based on the pivotal ATHENA trial

MULTAQ reduced the combined endpoint of CV hospitalization or mortality, entirely attributable to reduction in CV hospitalization ($P<0.0001$)

Data from a prospective, randomized, placebo-controlled, double-blind, multinational, multicenter, parallel-group trial (30-month maximum duration; N=4628; n=2301 in MULTAQ arm; n=2327 in placebo arm). Primary endpoint was time to first CV hospitalization or death from any cause (results entirely attributable to effect on CV hospitalization; $P<0.0001$). Secondary endpoints were CV hospitalization ($P<0.0001$) and all-cause mortality ($P=NS$).

Incidence of primary endpoint events was 31.6% with MULTAQ vs 39.2% with placebo (HR 0.76; 95% CI 0.68-0.83; $P<0.0001$)

Decreased risk of being hospitalized for AFib events

39% RRR in hospitalizations related to AFib and other supraventricular rhythm disorders (HR 0.61; 95% CI 0.53-0.71; $P<0.0001$)

- Incidence was 12.7% with MULTAQ vs 19.6% with placebo

- AFib hospitalization was a component of the secondary endpoint of CV hospitalization (26% RRR; HR 0.74; 95% CI 0.67-0.82; $P<0.0001$)
  - Incidence was 29.1% with MULTAQ vs 36.8% with placebo

*Relative risk reduction (RRR) observed over the study period (median 22-month treatment and follow-up; minimum 12 months, maximum 30 months).

Important Safety Information for MULTAQ® (dronedarone)

- 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

- 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. If heart failure develops or worsens and requires hospitalization, discontinue MULTAQ

Please see additional Important Safety Information on pages 10 and 11, and for full Prescribing Information, including boxed WARNING, please click here or visit MULTAQ.com/hcp.
### Adverse Events in the EURIDIS/ADONIS Trials

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N=409)</th>
<th>MULTAQ (N=828)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Death – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any cause</td>
<td>3 (0.7)</td>
<td>8 (1.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Sudden death</td>
<td>1 (0.2)</td>
<td>4 (0.5)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Stroke – no. (%)</strong></td>
<td>3 (0.7)</td>
<td>4 (0.5)</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>Pulmonary event – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>7 (1.7)</td>
<td>19 (2.3)</td>
<td>0.67</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>15 (3.7)</td>
<td>27 (3.3)</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>Endocrine event – no. / total no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>56/396 (14.1)</td>
<td>67/801 (8.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>14/396 (3.5)</td>
<td>44/801 (5.5)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Cardiac event – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia or conduction block</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any event</td>
<td>8 (2.0)</td>
<td>22 (2.7)</td>
<td>0.56</td>
</tr>
<tr>
<td>Serious event</td>
<td>3 (0.7)</td>
<td>8 (1.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Heart failure or shock</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any event</td>
<td>4 (1.0)</td>
<td>20 (2.4)</td>
<td>0.12</td>
</tr>
<tr>
<td>Serious event</td>
<td>3 (0.7)</td>
<td>13 (1.6)</td>
<td>0.29</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>2 (0.5)</td>
<td>6 (0.7)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Neurologic event – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia or other sleep disorder</td>
<td>6 (1.5)</td>
<td>12 (1.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Memory impairment</td>
<td>0</td>
<td>1 (0.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>1 (0.2)</td>
<td>0</td>
<td>0.33</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>4 (1.0)</td>
<td>11 (1.3)</td>
<td>0.78</td>
</tr>
<tr>
<td>Tremor</td>
<td>2 (0.5)</td>
<td>6 (0.7)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Gastrointestinal or hepatic event</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea – no. (%)</td>
<td>20 (4.9)</td>
<td>59 (7.1)</td>
<td>0.14</td>
</tr>
<tr>
<td>Nausea – no. (%)</td>
<td>14 (3.4)</td>
<td>36 (4.3)</td>
<td>0.54</td>
</tr>
<tr>
<td>Abnormality of liver function – no. / total no. (%)</td>
<td>55/405 (13.6)</td>
<td>100/822 (12.2)</td>
<td>0.52</td>
</tr>
<tr>
<td><strong>Dermatologic event – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Photosensitivity or skin discoloration</td>
<td>1 (0.2)</td>
<td>6 (0.7)</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevation of serum creatinine – no. (%)</td>
<td>1 (0.2)</td>
<td>20 (2.4)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

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For patients with paroxysmal or persistent AFib

**Adverse Events in the ATHENA Trial**

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N=2313)</th>
<th>MULTAQ 400 mg bid (N=2291)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE – no. (%)</td>
<td>1603 (69.3)</td>
<td>1649 (72.0)</td>
<td>0.048</td>
</tr>
<tr>
<td><strong>Cardiac events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>221 (9.6)</td>
<td>260 (11.3)</td>
<td>0.048</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>28 (1.2)</td>
<td>81 (3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QT-interval prolongation</td>
<td>14 (0.6)</td>
<td>40 (1.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Respiratory events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>83 (3.6)</td>
<td>83 (3.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>97 (4.2)</td>
<td>120 (5.2)</td>
<td>0.10</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>5 (0.2)</td>
<td>5 (0.2)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Gastrointestinal events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>144 (6.2)</td>
<td>223 (9.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nausea</td>
<td>72 (3.1)</td>
<td>122 (5.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal liver-function test</td>
<td>14 (0.6)</td>
<td>12 (0.5)</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>Endocrine events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>6 (0.3)</td>
<td>11 (0.5)</td>
<td>0.23</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>7 (0.3)</td>
<td>6 (0.3)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Neurologic events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>152 (6.6)</td>
<td>169 (7.4)</td>
<td>0.30</td>
</tr>
<tr>
<td>Headache</td>
<td>87 (3.8)</td>
<td>70 (3.1)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Skin-related events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>47 (2.0)</td>
<td>77 (3.4)</td>
<td>0.006</td>
</tr>
<tr>
<td>Urticaria</td>
<td>9 (0.4)</td>
<td>11 (0.5)</td>
<td>0.66</td>
</tr>
<tr>
<td>Serum creatinine increase</td>
<td>31 (1.3)</td>
<td>108 (4.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any serious TEAE</td>
<td>489 (21.1)</td>
<td>456 (19.9)</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Cardiac events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal events</strong></td>
<td></td>
<td></td>
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<tr>
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</tr>
<tr>
<td><strong>Neurologic events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Skin-related events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase in serum creatinine</td>
<td>1 (&lt;0.1)</td>
<td>5 (0.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>Premature discontinuation of study drug because of an adverse event</td>
<td>187 (8.1)</td>
<td>290 (12.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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

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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 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 ≥500 ms or PR interval >280 ms
- Who are or may become pregnant (Category X) or nursing. MULTAQ may cause fetal harm when administered to a pregnant woman
- With concomitant use of strong CYP 3A inhibitors, such as ketoconazole, itraconazole, voriconazole, cyclosporine, telithromycin, clarithromycin, nefazodone, ritonavir, or drugs or herbal products that prolong the QT interval and might increase the risk of Torsade de Pointes, such as phenothiazine antipsychotics, tricyclic antidepressants, certain oral macrolide antibiotics, and Class I and III antiarrhythmics
- With liver or lung toxicity related to the previous use of amiodarone
- With severe hepatic impairment
- With hypersensitivity to the active substance or to any of the excipients

Cardiovascular Death in NYHA Class IV or Decompensated 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.

Cardiovascular Death and Heart Failure in Permanent AFib
MULTAQ doubles the risk of cardiovascular death (largely arrhythmic) and heart failure events in patients with permanent AFib. 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.

Increased Risk of Stroke in Permanent AFib
In a placebo-controlled study in patients with permanent AFib, dronedarone 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.

New Onset or Worsening Heart Failure
New onset or worsening of heart failure has been reported during treatment with MULTAQ in the postmarketing setting. 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.

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. If heart failure develops or worsens and requires hospitalization, discontinue MULTAQ.

Liver Injury
Hepatocellular liver injury, including acute liver failure requiring transplant, has been reported in patients treated with MULTAQ in the postmarketing setting. Advise patients treated with MULTAQ to report immediately symptoms suggesting hepatic injury (such as anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching). Consider obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment. It is not known whether routine periodic monitoring of serum enzymes will prevent the development of severe liver injury. If hepatic 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 see additional Important Safety Information on page 11, and for full Prescribing Information, including boxed WARNING, please click here or visit MULTAQ.com/hcp.
Renal Impairment and Failure
If the QTc Bazett interval is ≥500 ms, discontinue MULTAQ. Greater effects have been observed for QTc (Bazett) prolongation. MULTAQ induces a moderate (average of about 10 ms but much higher at doses equivalent to recommended human doses) QT Interval Prolongation. Administration of MULTAQ may result in increased exposure to digoxin in patients taking MULTAQ. Consider discontinuing digoxin. If digoxin treatment is continued, halve the dose of digoxin, monitor serum levels closely, and observe for toxicity.

Hypokalemia and Hypomagnesemia with Potassium-Depleting Diuretics
Hypokalemia and hypomagnesemia may occur with concomitant administration of potassium-depleting diuretics. Potassium levels should be within the normal range prior to administration of MULTAQ and maintained in the normal range during administration of MULTAQ.

QT Interval Prolongation
MULTAQ induces a moderate (average of about 10 ms but much greater effects have been observed) QTc (Bazett) prolongation. If the QTc Bazett interval is ≥500 ms, discontinue MULTAQ.

Renal Impairment and Failure
Marked increase in serum creatinine, pre-renal azotemia and acute renal failure, often in the setting of heart failure or hypovolemia, have been reported in patients taking MULTAQ. In most cases, these effects appear to be reversible upon drug discontinuation and with appropriate medical treatment. Monitor renal function periodically.

Small increases in creatinine levels (about 0.1 mg/dL) following MULTAQ treatment initiation have been shown to be a result of inhibition of creatinine’s tubular secretion. The elevation has a rapid onset, reaches a plateau after 7 days and is reversible after discontinuation.

Women of Childbearing Potential
Premenopausal women who have not undergone a hysterectomy or oophorectomy must use effective contraception while using MULTAQ. Dronedarone caused fetal harm in animal studies at doses equivalent to recommended human doses. Counsel women of childbearing potential regarding appropriate contraceptive choices.

Drug-Drug Interactions
• Treatment with Class I or III antiarrhythmics or drugs that are strong inhibitors of CYP 3A must be stopped before starting MULTAQ (see Contraindications).
• Patients should be instructed to avoid grapefruit juice beverages while taking MULTAQ.
• Calcium channel blockers with depressant effects and beta-blockers could increase the bradycardia effects of MULTAQ on conduction.
• In the ANDROMEDA (patients with recently decompensated heart failure) and PALLAS (patients with permanent AFib) trials, baseline use of digoxin was associated with an increased risk of arrhythmic or sudden death in MULTAQ-treated patients compared to placebo. In patients not taking digoxin, no difference in risk of sudden death was observed in the MULTAQ vs placebo groups.

Digoxin can potentiate the electrophysiologic effects of MULTAQ (such as decreased AV-node conduction). MULTAQ increases exposure to digoxin. Consider discontinuing digoxin. If digoxin treatment is continued, halve the dose of digoxin, monitor serum levels closely, and observe for toxicity.

• Postmarketing cases of increased INR with or without bleeding events have been reported in warfarin-treated patients initiated with MULTAQ. Monitor INR after initiating MULTAQ in patients taking warfarin.

• Statins: Avoid simvastatin doses greater than 10 mg daily. Follow statin label recommendations for use with CYP 3A and P-gp inhibitors such as MULTAQ.

Adverse Reactions
In studies, the most common adverse reactions observed with MULTAQ were diarrhea, nausea, abdominal pain, vomiting, and asthenia.

References:

Please see additional Important Safety Information on page 10, and for full Prescribing Information, including boxed WARNING, please click here or visit MULTAQ.com/hcp.
Indication
MULTAQ is an antiarrhythmic drug indicated to reduce the risk of hospitalization for atrial fibrillation (AFib) in patients in sinus rhythm with a history of paroxysmal or persistent AFib.

Important Safety Information for MULTAQ® (dronedarone)—Boxed WARNING
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.

Please see additional Important Safety Information on pages 10 and 11, and for full Prescribing Information, including boxed WARNING, please click here or visit MULTAQ.com/hcp.

For patients with paroxysmal or persistent AFib
Start with MULTAQ in patients new to rhythm control therapy

Recommended first line in the 2014 AHA/ACC/HRS AFib Guidelines
For maintenance of sinus rhythm in patients without structural heart disease or with coronary artery disease

Approved for initiation out of the hospital
No loading dose or titration required
MULTAQ 400 mg bid should be taken with full morning and evening meals

Proven to reduce AFib recurrence
62.3% of patients free of symptomatic AFib recurrence at 1 year
Kept patients in sinus rhythm 2.2 times longer than placebo

Proven to reduce the risk of CV hospitalization
Decreased risk of CV hospitalization or mortality, entirely attributable to risk of CV hospitalization (24% RRR)

Most common reasons for discontinuation
GI disorders (~3%)
QT prolongation (1.5%)

More than 4.4 million prescriptions filled to date
More than 5 years of treatment experience

MULTAQ (dronedarone) 400 mg Tablets

Visit MULTAQ.com/hcp for more information.

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