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FDA Drug Safety Communication: Severe liver injury associated with the use of dronedarone (marketed as Multaq)

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[1-14-2011] The U.S. Food and Drug Administration (FDA) is alerting healthcare professionals and patients about cases of rare, but severe liver injury, including two cases of acute liver failure leading to liver transplant in patients treated with the heart medication dronedarone (Multaq).

Dronedarone is a drug used to treat abnormal heart rhythm in patients who have had an abnormal heart rhythm (atrial fibrillation or atrial flutter) during the past 6 months. Dronedarone can reduce the risk of being hospitalized for these heart problems. Since dronedarone's approval in July 2009 through October 2010, around 492,000 dronedarone prescriptions were dispensed and around 147,000 patients filled dronedarone prescriptions at outpatient retail pharmacies in the United States.¹ Additional usage can occur in the hospital setting.

Dronedarone was approved with a Risk Evaluation and Mitigation Strategy (REMS) with a goal of preventing its use in patients with severe heart failure or who have recently been in the hospital for heart failure. In a study of patients with these conditions, patients given dronedarone had a greater than two-fold increase in risk of death.

Information about the potential risk of liver injury from dronedarone is being added to the WARNINGS AND PRECAUTIONS and ADVERSE REACTIONS sections of the dronedarone labels.

Today's communication is in keeping with FDA's commitment to inform the public about its ongoing safety review of drugs. FDA is continuing to review reports of possible adverse events and drug interactions with dronedarone submitted to our Adverse Event Reporting System.

[Additional Information for Patients](#)

- Contact your healthcare professional if you develop itching, yellow eyes or skin, dark urine, loss of appetite, or light-colored stools. These may be signs of liver injury.
- Talk to your healthcare professional about any concerns you have with this medication.
- Do not stop taking dronedarone unless told to do so by your healthcare professional.
- Report any side effects you experience to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.
- Read the Medication Guide when picking up a prescription for dronedarone. It will help you understand the potential risks and benefits of this medication.

[Additional Information for HCPs](#)

- Advise patients to contact a healthcare professional immediately if they experience signs and symptoms of hepatic injury or toxicity (anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching) while taking dronedarone.
- Consider obtaining periodic hepatic serum enzymes, especially during the first 6 months of treatment. However, it is not known whether routine periodic monitoring of serum liver enzymes (ALT, AST, and alkaline phosphatase) and bilirubin in patients taking dronedarone will prevent the development of severe liver injury.
- If hepatic injury is suspected, dronedarone should be promptly discontinued and testing of serum liver enzymes and bilirubin should be performed. If hepatic injury is found, appropriate treatment should be initiated.
- Dronedarone should not be restarted in patients who experience hepatic injury without another explanation for the observed liver injury.
- Report adverse events involving dronedarone to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

[Data Summary](#)

FDA has received several case reports of hepatocellular liver injury and hepatic failure in patients treated with dronedarone, including two post-marketing reports of acute hepatic failure requiring transplantation. Because these reactions are reported voluntarily from a treatment population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The two cases of acute hepatic failure requiring transplantation occurred at 4.5 and 6 months after initiation of dronedarone in patients with previously normal hepatic serum enzymes. Both patients were female and approximately 70 years of age. In the first case, the patient had underlying intermittent atrial fibrillation, arterial hypertension and stable coronary artery disease. She was treated with dronedarone for 4.5 months. Two weeks prior to hospitalization she reported increased exhaustion and tiredness. One week prior to admission she discontinued dronedarone, and at the time of admission she was noted to have jaundice, coagulopathy, transaminitis and hyperbilirubinemia, which progressed to hepatic encephalopathy over the next nine days. A pre-transplant workup did not reveal another etiology of liver failure. In the second case, the patient had a medical history of paroxysmal atrial fibrillation and Sjogren's syndrome. Following 6 months of treatment with dronedarone she developed weakness, abdominal pain, coagulopathy, transaminitis and hyperbilirubinemia. She was transplanted 1 month later; no alternative etiology for liver failure was identified in the transplant work-up. In both cases, the explanted liver showed evidence of extensive hepatocellular necrosis.

Multaq (dronedarone) is approved to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent atrial fibrillation

(AF) or atrial flutter (AFL), with a recent history of AF/AFL and associated cardiovascular risk factors (age >70, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter \geq 50 mm or left ventricular ejection fraction <40%) who are in sinus rhythm or who will be cardioverted.

Dronedaronone 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 dronedaronone had a greater than two-fold increase in mortality. Such patients should not be given dronedaronone.

1. SDI, Vector One[®]: National (VONA) and Total Patient Tracker (TPT). July 2009-October 2010. Data extracted 12-14-10.

Related Information

- [FDA Drug Safety Podcast for Healthcare Professionals: Severe liver injury associated with the use of dronedaronone \(marketed as Multaq\)](#)¹ 1/20/2011
- [Multaq \(dronedaronone\) Information](#)²

Contact Us

- **Report a Serious Problem**

- 1-800-332-1088
- 1-800-FDA-0178 Fax
[MedWatch Online](#)³

Regular Mail: Use postage-paid [FDA Form 3500](#)⁴

Mail to: MedWatch 5600 Fishers Lane
Rockville, MD 20857

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