2. DEAR HEALTHCARE PROFESSIONAL LETTERS
December 2011

IMPORTANT DRUG WARNING

Increased Risk of Death, Stroke and Heart Failure in Patients with Permanent Atrial Fibrillation treated with Multaq (Dronedarone)

Dear Healthcare Provider:

In August 2011, Sanofi communicated preliminary information on the premature termination of the PALLAS (Permanent Atrial fibrillation outcome Study using Dronedarone on top of standard therapy) study due to increased risk of CV death, stroke, and heart failure events.

Following adjudication and final analysis of the PALLAS data and subsequent update and FDA-approval of the United States Prescribing Information (USPI), Sanofi would like to provide you with highlights of the important updates to the Multaq USPI pertaining to PALLAS and permanent atrial fibrillation (AF).

In addition to an update to the heart failure contraindication, the boxed warning for Multaq has been expanded to include permanent AF (AF patients who will not or cannot be cardioverted into normal sinus rhythm). The boxed warning now reads as follows:

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

The following has also been added to the WARNINGS AND PRECAUTIONS section of the Multaq USPI:

5 WARNING AND PRECAUTIONS

5.2 Cardiovascular Death and Heart Failure in Permanent AF
MULTAQ doubles the risk of cardiovascular death (largely arrhythmic) and heart failure events in patients with permanent AF. Patients treated with dronedarone
should undergo monitoring of cardiac rhythm no less often than every 3 months. Cardiovert patients who are in atrial fibrillation (if clinically indicated) or discontinue MULTAQ. MULTAQ offers no benefit in subjects in permanent AF.

5.3 Increased Risk of Stroke in Permanent AF
In a placebo-controlled study in patients with permanent atrial fibrillation, 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.

Additionally, the indication for Multaq has been updated to help ensure its appropriate use in paroxysmal or persistent atrial fibrillation (i.e. non-permanent AF patients). Multaq is indicated to reduce the risk of hospitalization for atrial fibrillation in patients in sinus rhythm with a history of paroxysmal or persistent atrial fibrillation (AF).

In accordance with these changes, the Multaq Medication Guide has been updated to include this information. We encourage you to discuss the new important safety information outlined in this letter and the updated Multaq USPI and Medication Guide with your patients (the link to the current Prescribing Information, including Medication Guide, has been provided below for your review).

Also of note, Sanofi is collaborating with the FDA to appropriately update the Multaq Risk Evaluation and Mitigation Strategy (REMS). You will be notified of the changes to the Multaq REMS program once it is FDA-approved.

Please note the information above does not contain all changes to the Multaq USPI. Please refer to the full Prescribing Information for Multaq for complete details.

For additional information, please contact Sanofi Medical Information Services at 1-800-633-1610 (option 1). Healthcare professionals should report adverse events suspected to be associated with the use of Multaq to Sanofi at 1-800-633-1610 (option 2).

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

Sincerely,

[Signature]

Paul H. Chew, MD
US Chief Science Officer/Chief Medical Officer
sanofi-aventis U.S.

Click here for full Prescribing Information, including Boxed Warning.
This letter was prepared with the guidance of FDA.