



sanofi aventis

Because health matters

26th September 2011

Information on restriction of use of Multaq (dronedarone)

Dear Healthcare Professional

Summary

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has completed its assessment of the benefits and risks of treatment with Multaq (dronedarone). As a result, the Multaq Summary of Product Characteristics (SmPC) has been modified to include the following restrictions on use, contraindications and warnings:

- Multaq is now only indicated in adult clinically stable patients with paroxysmal or persistent atrial fibrillation (AF) for the maintenance of sinus rhythm after successful cardioversion.
- Due to its safety profile, Multaq should only be prescribed after alternative treatment options have been considered. Treatment with Multaq should be initiated and monitored only under specialist supervision.
- Multaq is now contraindicated in patients with:
 - Unstable haemodynamic conditions
 - History of, or current heart failure or left ventricular systolic dysfunction
 - Permanent AF (AF duration \geq 6 months or unknown, and attempts to restore sinus rhythm no longer considered by the physician)
 - Liver and lung toxicity related to the previous use of amiodarone
- Patients taking Multaq should be carefully monitored during treatment by regular assessment of cardiac, hepatic and pulmonary function (see the section below for further details).
- If the patient develops any of conditions which would lead to a contraindication (as mentioned in the prescribing information) treatment with Multaq should be stopped.
- Patients currently taking Multaq should have their treatment reviewed at the next routine appointment to ensure that they remain eligible for Multaq treatment according to the revised prescribing information.

The communication of this information has been agreed with the European Medicines Agency and National Competent Authorities.

Further information

The CHMP initiated a review of the risks and benefits of treatment with Multaq after cases of liver injury, including two cases of liver failure requiring transplantation, were reported in patients receiving dronedarone. The review was extended to include cardiovascular safety following premature termination of the PALLAS study, and pulmonary safety after case reports of pulmonary injury.

The PALLAS study was undertaken to assess clinical benefit of dronedarone in patients with permanent atrial fibrillation and additional risk factors. The study was prematurely terminated due to a significant excess of cardiac-related deaths as well as cardiovascular hospitalisations and stroke in the dronedarone group.

The CHMP considered that the benefits of treatment continue to outweigh the risks in a restricted patient population under strict monitoring.

Prescribers should adhere to the prescribing information regarding contraindications and warnings, in particular to be aware of the potential for interactions with and need for dose adjustments when Multaq is used with other medicinal products, including anti-coagulants and digoxin.

Prescribers should also note the following new monitoring requirements for safe use of Multaq:

Cardiovascular monitoring

- Regular cardiac examinations including an ECG at least every 6 months should be performed in patients receiving Multaq. If AF reoccurs discontinuation of dronedarone should be considered.
- If patients develop permanent AF, treatment with Multaq should be discontinued.
- Patients should be carefully evaluated for symptoms of cardiac heart failure during treatment.
- Patients should be appropriately anti-coagulated as per clinical AF guidelines. International Normalized Ratio (INR) should be closely monitored after initiating dronedarone in patients taking vitamin K antagonists as per the label for these products.

Hepatic monitoring

- Liver function tests should be performed prior to initiation of treatment with dronedarone, after one week and after one month following initiation of treatment and then repeated monthly for six months, at months 9 and 12, and periodically thereafter.

Renal monitoring

- Plasma creatinine values should be measured prior to and 7 days after initiation of dronedarone.

Pulmonary monitoring

- Cases of interstitial lung disease including pneumonitis and pulmonary fibrosis have been reported in association with use of Multaq. Onset of dyspnoea or non-productive cough may be related to pulmonary toxicity. If pulmonary toxicity is suspected during treatment, relevant pulmonary examinations should be considered and treatment discontinued if pulmonary toxicity is confirmed.

Patients should be instructed to seek medical advice in case of occurrence of new cardiac or pulmonary symptoms or signs of hepatic impairment.

For complete information on all SmPC changes, please read carefully the attached revised SmPC.

Call for reporting:

Healthcare professionals should report any adverse reactions suspected to be associated with the use of Multaq to the Irish Medicines Board using the on-line reporting function on the IMB website (www.imb.ie) or alternatively by contacting the IMB at 01 6764971.

In addition, this information may be reported to sanofi-aventis Ireland Ltd., please phone 01-4035600.

Communication information

Updated educational materials will be distributed when available.

If you have any questions or require additional information, please contact our Medical Information Department at 01-4035600 or email IEmedinfo@sanofi-aventis.com

Sincerely,



Dr. Velichka Valcheva

Medical Director

Sanofi-aventis Ireland