IRISH MEDICINES BOARD

Multaq (dronedarone) - Restriction of use and new monitoring requirements

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has completed its benefit-risk assessment of Multaq (see IMB Drug Safety Newsletters February and August 2011). As a result of the emergence of safety issues in the post marketing period (hepatic, lung, and the negative inotropic effect), new restrictions for the use of Multaq have been introduced to maintain a positive benefit-risk balance.

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. Multaq should only be prescribed after alternative treatment options have been considered. Treatment should only be initiated and monitored by specialists to ensure that the benefit-risk balance is positive for patients at the time of initiation of Multaq and that patients remain eligible for treatment according to the new restrictions for use.

The following additional restrictions will be included in the Summary of Product Characteristics (SPC). A Direct Healthcare Professional Communication is available on www.imb.ie

Updates to Contraindications and Warnings

- 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 ≥ 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 (section below).
- 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. If patients develop any conditions which would lead to a contraindication, treatment with Multaq should be stopped.
- Prescribers should adhere to the prescribing information regarding contraindications and warnings, in particular to be aware of the potential for interactions and need for dose adjustments when Multaq is used with other medicinal products, including anti-coagulants and digoxin.

Updates to Monitoring Requirements

Cardiovascular monitoring

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

Hepatic monitoring

- Liver function tests should be performed prior to initiation of Multaq, 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 seven days after initiation of Multaq.

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.

Suspected adverse reactions associated with the use of Multaq should be reported to the IMB via the usual routes.

Key Message

- 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.
- Multaq should only be prescribed after alternative treatment options have been considered. Treatment with Multaq should be initiated and monitored only under specialist supervision.
- Prescribers should strictly adhere to the Multaq prescribing information regarding indication, contraindications and warnings.
- Prescribers should follow the new monitoring requirements for safe use of Multaq.