



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Questions and answers on the possible risk of liver injury with Multaq (dronedarone)

The European Medicines Agency (EMA) has become aware of two cases of serious liver injury in patients taking Multaq, for which a causal relationship with the medicine could not be excluded. As a precaution, the EMA's Committee for Medicinal Products for Human Use (CHMP) has recommended changes to the medicine's product information to help manage the possible risk of severe liver complications.

### What is Multaq?

Multaq is a medicine that contains the active substance dronedarone (400 mg). It is used in adults who have had atrial fibrillation in the past or who currently have non-permanent fibrillation. Atrial fibrillation happens when the atria (the upper chambers of the heart) contract irregularly and rapidly. Multaq is used to prevent the fibrillation coming back or to lower the heart rate.

The active substance in Multaq, dronedarone, is an anti-arrhythmic medicine. It works mainly by blocking channels through which charged particles of potassium move in and out of the muscle cells, causing the excessive electrical activity that leads to atrial fibrillation and rapid heart rate.

Multaq has been authorised in the European Union since 26 November 2009 and is marketed in 16 Member States<sup>1</sup> as well as Norway.

### What is the problem with Multaq?

As part of its routine monitoring of Multaq, the CHMP has become aware of reports of severe liver injury in patients treated with the medicine. These include two cases of liver failure requiring a transplant, reported in December 2010. The two cases occurred 4.5 and 6 months after starting treatment in patients with normal liver function before treatment.

The new reports triggered an analysis of all the available data on the potential risk of liver injury with Multaq.

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<sup>1</sup> Multaq is marketed in Austria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Ireland, Italy, Malta, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.



## **What are the conclusions of the CHMP?**

The Committee noted that although the two patients requiring a liver transplant were also taking other medications, a causal relationship with Multaq could not be excluded. Therefore, the CHMP decided that there was a need for an urgent regulatory action to help manage the possible risk of severe liver complications with the medicine. The Committee recommended that warnings and precautions be introduced into the medicine's prescribing information, to ensure that patients' liver function is tested before initiation of treatment, closely monitored during treatment, and treatment is stopped if there are signs of potential liver damage.

The Committee also agreed that the company should provide a letter to healthcare professionals explaining the changes in recommendations for use of Multaq.

## **What are the recommendations for prescribers?**

- Before starting treatment with Multaq, doctors should perform liver function tests. Tests should be repeated monthly for six months, at months 9 and 12, and periodically thereafter.
- Doctors should contact patients who are currently receiving Multaq within the next month so that liver function tests can be performed. Thereafter, they should carry out further tests as described above depending on when treatment was started.
- Doctors should stop treatment with Multaq in patients with raised levels of the liver enzyme alanine aminotransferase (more than three times above the upper limit of normal). Appropriate investigation and close observation of patients should continue until the enzyme levels return to normal.

## **What are the recommendations for patients?**

- Patients are advised to immediately report to their doctor any symptoms that could indicate liver injury (such as sustained new-onset abdominal pain, loss of appetite, nausea, vomiting, fever, malaise, tiredness, jaundice, dark urine or itching).
- Patients who have any questions should speak to their doctor or pharmacist.

## **What will happen next?**

The product information for Multaq will be updated shortly. The current European public assessment report for Multaq can be found on the Agency's website: [ema.europa.eu/Find\\_medicine/Human\\_medicines/European\\_Public\\_Assessment\\_Reports](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports).