

London, 18 October 2007  
Doc. Ref. EMEA/471052/2007

## **QUESTIONS AND ANSWERS ON THE RECOMMENDATION TO WITHDRAW THE MARKETING AUTHORISATIONS FOR CLOBUTINOL-CONTAINING MEDICINES**

The European Medicines Agency (EMA) has completed a review of the safety of clobutinol. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of medicines containing clobutinol no longer outweigh their risks, and that all marketing authorisations for these products should be withdrawn throughout Europe.

### **What is clobutinol?**

Clobutinol is a cough suppressant. It is used for the short-term treatment of irritable, non-productive cough (a 'dry' cough where the patient does not cough up any phlegm or mucus).

Medicines containing clobutinol have been available since 1961 and are authorised in a number of Member States<sup>1</sup>. They include tablets, oral solutions, syrups and solutions for injection, and are available over-the-counter (without a prescription) in many Member States. Clobutinol is available as generic and branded medicines, most of which were marketed by Boehringer Ingelheim under the trade name Silomat.

### **Why was clobutinol reviewed?**

In August 2007, the German medicines regulatory authority suspended the marketing authorisation for clobutinol-containing medicines, because of concerns over the effect that clobutinol can have on the heart. As a result, these medicines were taken off the market in Germany. At the same time, Boehringer Ingelheim decided to withdraw its clobutinol-containing products voluntarily from all markets worldwide, instructing patients to stop taking its clobutinol-containing medicines and to return them to their pharmacist.

As required by Article 107 of Directive 2001/83/EC as amended, the German authority informed the CHMP of its action so that the Committee could prepare an opinion on whether the marketing authorisations for products containing clobutinol should be maintained, changed, suspended or withdrawn across the European Union (EU).

### **Why did the German authority suspend the authorisation for clobutinol?**

The German authority acted after being informed about new preliminary results of a study that is being performed by Boehringer Ingelheim in healthy volunteers. These results showed that the use of clobutinol was linked to side effects affecting the heart: it caused the 'QT interval' (part of the heartbeat) to last for longer than normal. This side effect, called 'QT prolongation', is known to be linked to fainting and disruption of the heart rhythm.

The German authority reviewed the safety of clobutinol and concluded that the benefits of the medicine did not outweigh its risks. It therefore suspended the medicine's marketing authorisations on 31 August 2007, meaning that the medicine could no longer be sold on the German market.

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<sup>1</sup> Clobutinol-containing medicines are available in Austria, Belgium, the Czech Republic, Germany, Greece, Finland and France.

**Which data has the CHMP reviewed?**

In the current review, the CHMP reviewed all available information on the safety of clobutinol, especially its side effects affecting the heart. This information came from Boehringer Ingelheim and the other companies that market clobutinol-containing products in the EU, as well as from the published scientific literature. It included the findings from the study that triggered the German authority's action, as well as results from laboratory studies and details on individual cases of heart problems in patients taking clobutinol.

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

Based on the information provided, the CHMP has concluded that:

- the new findings show that the use of clobutinol is linked to a clear risk of QT prolongation;
- this risk increases when patients take higher doses of the medicine.

The Committee also noted that clobutinol-containing medicines are usually taken by patients who are not being monitored for side effects affecting the heart and that they are used to treat the symptoms of a common complaint for which alternative treatments are available.

In the light of these findings, the CHMP concluded that the benefits of clobutinol no longer outweigh its risks. Therefore, the Committee recommended that the marketing authorisations of medicines containing clobutinol be withdrawn in all EU markets.

**What are the recommendations for patients and prescribers?**

- Patients who are currently taking clobutinol should consult their doctor or pharmacist to discuss which other treatment they can use. The risk linked to clobutinol is temporary, so there is no risk in patients who have taken the medicine in the past.
- Prescribers should not issue any new prescriptions for clobutinol and should switch patients currently taking the medicine to an alternative treatment if necessary.
- Patients who have any questions should speak to their doctor or pharmacist.

A European Commission Decision on this opinion will be issued in due course.