25 March 2010
EMA/179698/2010

Questions and answers on the precautionary recall of batches of clopidogrel-containing medicines

Recall triggered because of Good Manufacturing Practice (GMP) failure in Glochem Industries Ltd factory

The European Medicines Agency has completed a review of eight generic clopidogrel-containing medicines at the request of the European Commission, following concerns regarding a failure in good manufacturing practice (GMP) at the manufacturing site of the active substance used in the medicines. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded[1] that, as a precautionary measure, there is a need to recall all batches of the medicines containing clopidogrel that was manufactured in the Glochem Industries Limited factory in Visakhapatnam (India).

What is clopidogrel?

Clopidogrel is an antiplatelet medicine that is used to prevent problems with blood clots such as heart attacks or strokes. Clopidogrel-containing medicines are available in the European Union (EU) under the trade names Plavix and Iscover, and as generic medicines.

Which clopidogrel-containing medicines were reviewed?

The CHMP reviewed eight generic clopidogrel-containing medicines, which had received a centralised marketing authorisation. They are all licensed to the same company, Acino Pharma GmbH, and they all contain clopidogrel that is made in the same factory. The medicines are:

Clopidogrel Acino 75 mg tablets
Clopidogrel Acino Pharma 75 mg tablets
Clopidogrel A1 Pharma 75 mg tablets
Clopidogrel Acino Pharma GmbH 75 mg tablets
Clopidogrel Hexal 75 mg tablets
Clopidogrel Sandoz 75 mg tablets
Clopidogrel Ratiopharm 75 mg tablets
Clopidogrel Ratiopharm GmbH 75 mg tablets

[1] Outcome of a procedure under Article 20 of Regulation (EC) No 726/2004

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

Why were those medicines reviewed?

The CHMP was informed by the German medicines regulatory authorities of the results of an inspection of the active substance manufacturing site where the clopidogrel used in all eight medicines was made, Glochem Industries Ltd. in Visakhapatnam (India). The inspection identified failings in good manufacturing practices (GMP). GMP is the set of rules that all companies involved in the manufacture of medicines and substances used in medicines must follow to ensure that their production processes, premises and equipment consistently deliver products of adequate quality. The inspectors notified the CHMP that the site was not GMP compliant.

Consequently, the European Commission asked the CHMP to assess the impact of the GMP findings on the quality of these eight clopidogrel-containing medicines, and to issue an opinion on measures necessary to ensure quality and on whether the marketing authorisations should be maintained, varied, suspended or withdrawn across the EU.

Which data has the CHMP reviewed?

The Committee looked at the report from the inspection of the manufacturing site and at documentation presented by the marketing authorisation holder. The CHMP also invited the company to answer the Committee's questions during an 'oral explanation' during its March 2010 meeting.

What are the conclusions of the CHMP?

The Committee concluded that the processes used to manufacture the active substance at the Glochem Visakhapatnam facility could not be trusted. This meant that the Committee did not have sufficient confidence in the quality of the active substance, and this led to a lack of confidence in the quality of the medicines.

As a precautionary measure, the CHMP recommended that all batches containing clopidogrel made at this site be recalled from the entire supply chain including stock already dispatched to pharmacies.

The Committee also recommended that the site in question be removed from the list of sites allowed to supply clopidogrel active substance to Acino Pharma GmbH for their generic medicines.

What are the recommendations for patients and prescribers?

- No consequences are expected either for patients or prescribers. This measure is precautionary.
- There are other clopidogrel-containing medicines, both branded and generic, available in the EU to ensure adequate supply.
- The marketing authorisation holder for the eight generic medicines has now changed its supplier and future batches will be produced using clopidogrel from a site that is GMP compliant.
- 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.