European Medicines Agency

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Questions and answers on the withdrawal of the marketing authorisation application for Clopidogrel Teva Pharma

clopidogrel

On 22 April 2009, Teva Pharma B.V. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wished to withdraw its application for a marketing authorisation for Clopidogrel Teva Pharma, for the prevention of atherothrombotic events in patients who have myocardial infarction, ischaemic stroke or established peripheral arterial disease.

What is Clopidogrel Teva Pharma?
Clopidogrel Teva Pharma is a medicine that contains the active substance clopidogrel. It was to be available as tablets (75 mg).
Clopidogrel Teva Pharma was developed as a 'generic medicine'. This means that Clopidogrel Teva Pharma was intended to be similar to a 'reference medicine' already authorised in the European Union (EU) called Plavix. For more information on generic medicines, see the question-and-answer document here.

What was Clopidogrel Teva Pharma expected to be used for?
Clopidogrel Teva Pharma was expected to be used in adults to prevent atherothrombotic events (problems caused by blood clots and hardening of the arteries). It was to be used in patients who had recently had a myocardial infarction (heart attack) or an ischaemic stroke (non-bleeding stroke), or in patients with peripheral arterial disease (problems with blood flow in the arteries).

How is Clopidogrel Teva Pharma expected to work?
Clopidogrel Teva Pharma is expected to work in the same way as the reference medicine, Plavix. The active substance in Clopidogrel Teva Pharma and in Plavix, clopidogrel, is an inhibitor of platelet aggregation. This means that it helps to prevent blood clots from forming. When the blood clots, this is due to special cells in the blood called platelets sticking together (aggregating). Clopidogrel stops the platelets aggregating by blocking a substance called ADP from attaching to a special receptor on their surface. This stops the platelets becoming 'sticky'. This reduces the risk of a blood clot forming and helps prevent another heart attack or stroke.

What documentation did the company present to support its application to the CHMP?
Because Clopidogrel Teva Pharma was developed as a generic medicine, the company presented the results of studies carried out to investigate whether it is 'bioequivalent' to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

How far into the evaluation was the application when it was withdrawn?
The application was at day 177 when the company withdrew. After the CHMP had assessed the responses from the company to a list of questions, there were still some unresolved issues outstanding. The CHMP normally takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions at day 120, which is sent to the company. Once the company has supplied responses to the questions, the CHMP reviews them and may, before

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giving an opinion, ask any remaining questions at day 180. Following the CHMP's opinion, it usually takes around two months for the European Commission to grant a licence.

What was the recommendation of the CHMP at that time?
Based on the review of the data and the company's response to the CHMP lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Clopidogrel Teva Pharma could not have been approved for the prevention of atherothrombotic events in patients who have had myocardial infarction, ischaemic stroke or who have established peripheral arterial disease.

What were the main concerns of the CHMP?
The CHMP concluded that the studies presented did not provide enough evidence to show that Clopidogrel Teva Pharma was bioequivalent to the reference medicine Plavix. At this point in time, the CHMP was of the opinion that Clopidogrel Teva Pharma could not be considered a generic medicine of Plavix, the reference medicinal product.

What were the reasons given by the company for withdrawing the application?
The letter from the company notifying the Agency of the withdrawal of the application is available here.