European Medicines Agency

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Questions and answers on the withdrawal of the marketing authorisation application for Mersarex *iclaprim*

On 21 October 2009, Arpida A/S officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Mersarex, for the treatment of adults with complicated skin and soft tissue infections.

What is Mersarex?
Mersarex is a concentrate for solution for infusion (drip into a vein). It contains the active substance iclaprim.

What was Mersarex expected to be used for?
Mersarex was expected to be used to treat complicated infections of the skin and the 'soft tissues' below the skin. Complicated means that the infection is difficult to treat, because it has spread to the deep tissues below the skin, treatment with surgery might be needed, or the patient has other conditions that might affect the response to treatment.

How was Mersarex expected to work?
The active substance in Mersarex, iclaprim, is an antibiotic of the group 'dihydrofolate reductase inhibitors'. It was expected to work by blocking the action of a bacterial protein called dihydrofolate reductase. Bacteria need this protein to produce the active form of folic acid, which they need to multiply. By blocking the action of dihydrofolate reductase, the medicine was expected to slow down the growth and spread of the bacteria.

What documentation did the company present to support its application to the CHMP?
The effects of Mersarex were first tested in experimental models before being studied in humans. The company presented results from two main studies involving 991 adults with complicated infections of the skin and soft tissues. Around half of the patients were treated with Mersarex, while the others were treated with linezolid (another antibiotic). The study looked at whether Mersarex given for up to 14 days was as good as linezolid. The main measure of effectiveness was the number of patients who were cured.

How far into the evaluation was the application when it was withdrawn?
The application was at day 181 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.
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 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 issue a decision on this opinion.

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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 Mersarex could not have been approved for the treatment of complicated infections of the skin and the soft tissues.

What were the main concerns of the CHMP?
The CHMP was of the opinion that the results did not show that Mersarex was as good as the comparator medicine and that there were insufficient data from clinical studies to justify the dosage proposed by the company. There were also concerns that the medicine may cause side effects affecting the heart (such as QTc interval prolongation, an alteration of the electrical activity of the heart) and the liver. The CHMP also noted that some bacteria already show a level of resistance to the antibiotic even before it is in general use.

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

What are the consequences of the withdrawal for patients in clinical trials or compassionate use programmes using Mersarex?
The company informed the CHMP that there are no patients currently using Mersarex in clinical trials or compassionate use programmes.