European Medicines Agency

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Questions and answers on the withdrawal of the marketing application for Vibativ

International non-proprietary name (INN): ***telavancin***

On 20 October 2008, Astellas Pharma Europe B. V. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Vibativ, for the treatment of complicated skin and soft tissue infections in adults.

What is Vibativ?
Vibativ is a powder to be made up into a solution for infusion (drip into a vein). It contains the active substance telavancin.

What was Vibativ expected to be used for?
Vibativ was expected to be used to treat adults with 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.
Vibativ was to be used only when the infection was known or thought to be caused by types of bacteria that are classified as 'Gram-positive'. These include *Staphylococcus aureus* (including 'methicillin-resistant' forms known as 'MRSA') and *Streptococcus pyogenes*.

How is Vibativ expected to work?
The active substance in Vibativ, telavancin, is an antibiotic that belongs to the group 'glycopeptides'. It is expected to work in two ways, both by stopping the bacteria making their cell walls and by disrupting their cell membranes. Together, the cell wall and membrane form a barrier between the bacterial cell contents and the external environment. By disrupting this barrier, telavancin is expected to kill the bacteria that are causing the infection.

What documentation did the company present to support its application to the CHMP?
The effects of Vibativ were first tested in experimental models before being studied in humans. Vibativ was compared with vancomycin (another antibiotic) in two main studies involving a total of 2,079 adults with complicated skin and soft tissue infections due to Gram-positive bacteria. The studies were carried out at sites where infection with MRSA is common. The antibiotics were given for up to 14 days. The main measure of effectiveness was the number of patients whose infection had been cured after the end of treatment.

How far into the evaluation was the application when it was withdrawn?
The application was at day 201 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 responses to the CHMP list of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Vibativ could not have been approved for the treatment of complicated skin and soft tissue infections in adults.

What were the main concerns of the CHMP?
The CHMP was concerned that there was no additional benefit of Vibativ over vancomycin, and could cause more kidney damage than vancomycin. The Committee was also concerned that Vibativ may cause 'QTc prolongation' (an alteration of the electrical activity of the heart). The CHMP also had concerns regarding the production of the medicine, its stability and the possible presence of impurities. At that point in time, the CHMP was of the opinion that the benefits of Vibativ in the treatment of complicated skin and soft tissue infections in adults did not outweigh its risks. Hence, the CHMP recommended that Vibativ be refused marketing authorisation.

What were the reasons given by the company to withdraw the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

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