European Medicines Agency

London, 24 September 2009
Doc. Ref. EMEA/554626/2009
EMEA/H/C/1025

Questions and answers on the withdrawal of the marketing authorisation application for Ramvocid *oritavancin*

On 20 August 2009, Targanta Netherlands 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 Ramvocid, for the treatment of complicated skin and soft tissue infections caused by Gram-positive bacteria.

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

What was Ramvocid expected to be used for?
Ramvocid 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.
Ramvocid was to be used when the infection was caused by a group of bacteria known as 'Gram-positive' bacteria. These include *Staphylococcus aureus* (including 'methicillin-resistant' forms known as 'MRSA') and *Streptococcus pyogenes*.

How is Ramvocid expected to work?
The active substance in Ramvocid, oritavancin, is an antibiotic that belongs to the group 'lipoglycopeptides'. 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, oritavancin 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 Ramvocid were first tested in experimental models before being studied in humans. The company presented results from one main study involving 1,267 patients with complicated skin and soft tissue infections. Patients were given either Ramvocid for seven days or vancomycin with or without cephalexin (other antibiotic medicines) for between 10 and 14 days. The main measure of effectiveness was the number of patients who were cured after treatment.

How far into the evaluation was the application when it was withdrawn?
The application was at day 180 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 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.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 71 29
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

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 Ramvocid could not have been approved for the treatment of complicated skin and soft tissue infections caused by Gram-positive bacteria.

What were the main concerns of the CHMP?
The CHMP was concerned that the company had not provided enough evidence to support the use of Ramvocid to treat complicated skin and soft tissue infections at the dose proposed, particularly in patients with MRSA. The Committee was also concerned over the way the company had measured the levels of impurities in the medicine.

What were the reasons given by the company for withdrawing the application?
The letter from the company notifying the European Medicines Agency 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 Ramvocid?
The company informed the CHMP that, at the time of the withdrawal, there were no patients in clinical trials or compassionate use programmes for Ramvocid.