18 February 2010
EMA/83783/2010
EMEA/H/C/883

Questions and answers

Refusal of the marketing authorisation for Zeftera[1] (ceftobiprole)

On 18 February 2010, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Zeftera, intended for the treatment of adults with complicated skin and soft-tissue infections.

The company that applied for the authorisation is Janssen-Cilag International N.V. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Zeftera?

Zeftera is a powder that is made up into a solution for infusion (drip into a vein). It contains the active substance ceftobiprole.

What was Zeftera expected to be used for?

Zeftera 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.

How is Zeftera expected to work?

The active substance in Zeftera, ceftobiprole, is an antibiotic that belongs to the group 'cephalosporins'. It works by attaching to certain types of protein on the surface of the bacteria cells. This prevents the bacteria from building the walls that surround their cells, which kills the bacteria.

[1] Previously known as Zevtera.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8668
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

Ceftobiprole is active against several types of bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA).

What did the company present to support its application?

The effects of Zeftera were first tested in experimental models before being studied in humans.

The company presented results of two main studies involving adults with complicated skin and soft tissue infections. The first study compared Zeftera with vancomycin (another antibiotic active against MRSA) in 784 patients, and the second compared it with the combination of vancomycin and ceftazidime (another cephalosporin antibiotic) in 828 patients. In both studies, the main measure of effectiveness was the number of patients whose infection had been cured at the end of treatment.

What were the CHMP's main concerns that led to the refusal?

In November 2008, the CHMP gave a positive opinion on Zeftera, recommending that it be granted marketing authorisation. However, the Committee later received information about an inspection of study sites by the Food and Drug Administration (FDA) in the United States of America that identified concerns over the way the main clinical studies were conducted. The Committee therefore requested that the European Commission stop the authorisation process for the medicine while further inspections were carried out.

These subsequent inspections showed that the studies had not been conducted in compliance with 'good clinical practice' (GCP) in some sites. Although the study results suggested that the medicine was beneficial to patients, the CHMP was concerned about how reliable the results were. The Committee therefore recommended that, in light of the uncertainty surrounding the results, the medicine should not be granted marketing authorisation.

What consequences does this refusal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that that there are no consequences for patients in clinical trials with Zeftera and that there are no compassionate use programmes in progress with Zeftera. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.