EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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 treatment of complicated skin and soft-tissue infections in adults. The company that applied for authorisation is Janssen-Cilag International N.V.

The applicant requested a re-examination of the opinion. After considering the grounds for this request, the CHMP re-examined the opinion, and confirmed the refusal of the marketing authorisation on 24 June 2010.

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.

[1] Previously known as Zevtera.

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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.

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 led the Committee to stop the medicine's authorisation process.

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.

During the re-examination the Committee looked at further analyses on the data from the studies and inspections. Due to continuing concerns over the reliability of the study results, the CHMP refusal was confirmed after re-examination.

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

The company informed the CHMP 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.