European Medicines Agency

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Questions and answers on the withdrawal of the marketing authorisation application for Factive
gemifloxacin

On 17 June 2009, Menarini International Operations Luxembourg S.A. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Factive, for the treatment of the bacterial infections, community-acquired pneumonia and acute exacerbation of chronic bronchitis.

What is Factive?
Factive is a medicine that contains the active substance gemifloxacin. It was to be available as tablets.

What was Factive expected to be used for?
Factive was expected to be used to treat the following bacterial infections in adults:
- mild or moderate community-acquired pneumonia (an infection of the lungs that is caught outside of hospital);
- acute exacerbation (flare-up) of chronic bronchitis (inflammation of the airways in the lungs).

How is Factive expected to work?
The active substance in Factive, gemifloxacin, is an antibiotic belonging to the class 'fluoroquinolones'. It is expected to work by blocking the action of two bacterial enzymes called DNA gyrase and topoisomerase IV, which are needed to make and repair bacterial DNA. When these enzymes are blocked, the bacteria cannot multiply and they eventually die.

What documentation did the company present to support its application to the CHMP?
The effects of Factive were first tested in experimental models before being studied in humans.
In four main studies, 1,874 adults with mild to moderate community-acquired pneumonia were treated for at least seven days with Factive or other antibiotics. In another study of patients with community-acquired pneumonia, 510 adults were given Factive either as a five- or seven-day treatment.
In three other main studies, 1,652 adults with acute exacerbation of chronic bronchitis were treated with Factive for five days or with other antibiotics. The main measures of effectiveness for the studies were based on the number of patients who got better after treatment.

How far into the evaluation was the application when it was withdrawn?
The application was at day 196 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.

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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 Factive could not have been approved for the treatment of community acquired pneumonia and acute exacerbation of chronic bronchitis caused by bacterial infection.

What were the main concerns of the CHMP?
The CHMP was concerned that Factive may be more genotoxic (harmful to the DNA, the genetic material in cells) and that it may therefore cause more damage to the DNA than other fluoroquinolones.
The Committee was also concerned there was not enough evidence of effectiveness of Factive in patients with moderate community-acquired pneumonia when given as a five-day treatment. The seven-day treatment was not considered acceptable because of the risk of side effects.
The Committee also noted that the information presented did not support the use of Factive for chronic bronchitis because no studies were carried out to investigate whether Factive was better than other treatments for this type of infection and because there were problems with the studies that were performed.
Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Factive in the treatment of community-acquired pneumonia and acute exacerbation of chronic bronchitis caused by bacterial infection did not outweigh its risks.

What were the reasons given by the company for withdrawing 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 withdrawal for patients in clinical trials or compassionate use programmes using Factive?
The company informed the CHMP that there are no clinical trials or compassionate use programmes with Factive in Europe.