European Medicines Agency

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Questions and answers on recommendation for the refusal of the marketing authorisation for Cayston

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

On 19 March 2009, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Cayston 75 mg powder and solvent for nebuliser solution, intended for the treatment of chronic airway infections caused by Pseudomonas aeruginosa (P. aeruginosa) bacteria in adults with cystic fibrosis. The company that applied for authorisation is Gilead Sciences International Limited. They may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Cayston?
Cayston is a powder and solvent that are made up into a nebuliser solution. It contains the active substance aztreonam.

What was Cayston expected to be used for?
Cayston was expected to be used to treat chronic (long-term) airway infections caused by *P. aeruginosa* bacteria in adults with cystic fibrosis. Cystic fibrosis is an inherited disease that affects the glands in the lungs, gut and pancreas that secrete fluids such as mucus and digestive juices.
Cayston was to be used to improve the patient's lung function and to reduce respiratory (breathing) symptoms.
Cayston was expected to be used with a nebuliser (a special machine that changes the solution into an aerosol that the patient can breathe in).

How is Cayston expected to work?
In cystic fibrosis, the patient's lungs produce too much thick mucus which is not cleared away. The excess mucus encourages the growth of bacteria. In patients with cystic fibrosis, P. aeruginosa infections usually start in the first 10 years of life and can cause long-term lung problems.
The active substance in Cayston, aztreonam, is an antibiotic that belongs to the group 'beta-lactams'. It works by attaching to certain types of protein on the surface of the P. aeruginosa cells. This prevents the bacteria from building the walls that surround their cells, which kills the bacteria.
Aztreonam has been available as an injection since the 1980's. In Cayston, the aztreonam is available as a lysine salt. This makes it possible for the antibiotic to be given directly into the lungs without causing irritation.

What documentation did the company present to support its application to the CHMP?
The effects of Cayston were first tested in experimental models before being studied in humans. Cayston was compared with placebo (a dummy treatment) in two main studies involving a total of 375 patients with cystic fibrosis. The average age of the patients was about 26 years and they were treated for four weeks. In one study, the main measure of effectiveness was how long it took before the patient needed to use another antibiotic because of respiratory symptoms. In the other study, the main measure of effectiveness was the reduction in respiratory symptoms.

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What were the major concerns that led the CHMP to recommend the refusal of the marketing authorisation?
The CHMP was concerned that there was insufficient evidence of the medicine's long-term benefits and after repeated courses of treatment in different age groups. In addition, there was insufficient long-term data on the medicine's safety and the risk of bacterial resistance.
At that point in time, the CHMP was of the opinion that the benefits of Cayston in the treatment of chronic airway infections due to P. aeruginosa in adults with cystic fibrosis did not outweigh its risks. The Committee also decided that not all criteria for granting a conditional marketing authorisation were met. Hence, the CHMP recommended that Cayston be refused marketing authorisation.

What are the consequences of the refusal for patients in clinical trials or compassionate use programmes using Cayston?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate use programmes with Cayston. If you are in a clinical trial or compassionate use programme and need more information about your treatment, contact the doctor who is giving it to you.