European Medicines Agency

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QUESTIONS AND ANSWERS ON RECOMMENDATION FOR THE REFUSAL OF THE MARKETING AUTHORISATION
for
CIMZIA

International non-proprietary name (INN): ***certolizumab pegol***

On 15 November 2007, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product CIMZIA 200 mg powder and solvent for solution for injection, intended for the treatment of severe, active Crohn's disease. The company that applied for authorisation is UCB Pharma SA. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is CIMZIA?
CIMZIA is a powder and solvent that are made up into a solution for injection under the skin. It contains the active substance certolizumab pegol.

What was CIMZIA expected to be used for?
CIMZIA was expected to be used to treat severe, active Crohn's disease (a disease causing inflammation of the digestive tract). It was to be used in patients who had not responded to a full and adequate course of therapy with a corticosteroid or an immunosuppressant medicine (a medicine that reduces the activity of the immune system) or who cannot take these therapies.

How is CIMZIA expected to work?
The active substance in CIMZIA, certolizumab pegol, is an immunosuppressant medicine. It includes certolizumab, which is part of a monoclonal antibody. A monoclonal antibody is an antibody (a type of protein) that has been designed to recognise and bind to a specific structure (called an antigen) that is found in the body. Certolizumab has been designed to bind to a chemical messenger in the body called tumour necrosis factor-alpha (TNF-alpha). This messenger is involved in causing inflammation and is found at high levels in patients with active Crohn's disease. By blocking TNF-alpha, certolizumab was expected to improve the inflammation and other symptoms of the disease.
In CIMZIA, certolizumab has been 'pegylated' (attached to a chemical called polyethylene glycol). This decreases the rate at which the substance is removed from the body and allows the medicine to be given less often.

What documentation did the company present to support its application to the CHMP?
The effects of CIMZIA were first tested in experimental models before being studied in humans.
The effectiveness of adding CIMZIA to existing treatment was compared with that of placebo (a dummy treatment) in two main studies involving adults with moderate to severe Crohn's disease.
The first study looked at the reduction of symptoms during 'induction treatment' in 660 patients who had not received CIMZIA before. The main measure of effectiveness was the proportion of patients whose symptoms had improved or disappeared after six and 26 weeks.
The second study looked at the maintenance of the medicine's effects in 428 patients who had responded to an initial six-week course of CIMZIA. The main measure of effectiveness was the proportion of the patients whose were still responding to treatment after 26 weeks.

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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 to show a benefit of CIMZIA. In the study of induction treatment, CIMZIA showed only marginal effectiveness, which was too low to be relevant for patients. In addition, the study of maintenance treatment did not last long enough to give meaningful information on the medicine's long-term effects.

The Committee was also concerned over CIMZIA's safety: although generally comparable with the safety of other medicines in the same class, there was also some concern over a possible increased risk of bleeding in patients receiving CIMZIA. In addition, the Committee was concerned that the company had not demonstrated that it would have been able to monitor the quality of the medicine to an acceptable level.

Therefore, at that point in time, the CHMP was of the opinion that the benefits of CIMZIA in the treatment of severe, active Crohn's disease did not outweigh its risks. Hence, the CHMP recommended that CIMZIA be refused marketing authorisation.

What are the consequences of the refusal for patients in clinical trials or compassionate use programmes using CIMZIA?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate use programmes with CIMZIA. 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.