European Medicines Agency

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

International non-proprietary name (INN): ***interferon beta-1a***

On 19 February 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 Biferonex 6 million-international-unit solution for injection, intended for the treatment of relapsing-remitting multiple sclerosis. The company that applied for authorisation is BioPartners GmbH. They may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Biferonex?
Biferonex is a solution for injection containing the active substance interferon beta-1a. It was to be available in a pre-filled syringe.

What was Biferonex expected to be used for?
Biferonex was expected to be used to treat adults with relapsing-remitting multiple sclerosis. Multiple sclerosis is a disease of the nerves, in which inflammation destroys the protective sheath around the nerves. Relapsing-remitting means that the patient has attacks (relapses) followed by periods with milder symptoms (remission). Biferonex was intended for patients who had experienced two or more attacks in the previous two years.

How is Biferonex expected to work?
The active substance in Biferonex, interferon beta-1a, belongs to the group 'interferons'. Interferons are natural substances produced by the body to help it fight against attacks such as infections caused by viruses. The exact way that Biferonex was expected to work in multiple sclerosis is not clear, but it was thought to modulate the activity of the immune system (the body's natural defences) and prevent relapses of multiple sclerosis.
Interferon beta-1a is produced by a method known as 'recombinant DNA technology': it is made by a cell that has received a gene (DNA), which makes it able to produce interferon beta-1a. The interferon beta-1a in Biferonex acts in the same way as naturally produced interferon beta.
Biferonex contains the same active substance as other medicines, Avonex and Rebif, that have been authorised in the European Union since 1997 and 1998, respectively. However, Biferonex is made in such a way that it does not contain the human blood protein, albumin.

What documentation did the company present to support its application to the CHMP?
The effects of Biferonex were first tested in experimental models before being studied in humans.
The company presented the results of one main study, in which Biferonex was compared with placebo (a dummy treatment) in 339 adults with relapsing-remitting multiple sclerosis. Each patient received either Biferonex or placebo for two years. The main measure of effectiveness was the reduction in the number of attacks.
The company also used information relating to Avonex, and information from the published literature on medicines containing interferon beta.

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What were the major concerns that led the CHMP to recommend the refusal of the marketing authorisation?

The Committee noted that there were differences between the active substance in Biferonex and other interferon beta-containing medicines available on the market. It therefore concluded that the use of published studies of these interferon beta-containing medicines to support the use of Biferonex was not justified and that studies on Biferonex itself were required.

The CHMP was also of the opinion that the results of the clinical study of Biferonex did not show enough evidence that the medicine was effective. Based on the information presented to the Committee, it is not clear whether this is due to the way the study was designed, the way the results were analysed, or to the medicine itself.

At that point in time, the CHMP was of the opinion that the benefits of Biferonex in the treatment of patients with relapsing-remitting multiple sclerosis did not outweigh its risks. Hence, the CHMP recommended that Biferonex be refused marketing authorisation.

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

The company informed the CHMP that there are no ongoing clinical trials or compassionate use programmes with Biferonex.