European Medicines Agency

London, 28 June 2006
Doc. Ref. EMEA/190896/2006

QUESTIONS AND ANSWERS ON RECOMMENDATION FOR REFUSAL OF MARKETING APPLICATION for ALPHEON

International Non-proprietary Name (INN): ***interferon alfa-2a***

On 28 June 2006 the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Alpheon 6 million IU/ml solution for injection intended for the treatment of hepatitis C. 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 Alpheon?
Alpheon is a solution for injection that contains the active substance interferon alfa-2a.
Alpheon was developed as a 'biosimilar' medicine. This means that Alpheon was intended to be similar to a biological medicine already authorised in the EU which contains the same active substance (also known as the 'reference medicine'), Roferon-A.

What was Alpheon expected to be used for?
Alpheon was expected to be used to treat adult patients who have chronic (long-term) hepatitis C (a disease of the liver due to an infection by a virus). The patients must have signs of liver damage: their liver tissues show some damage when observed with a microscope, and they have higher than normal levels of a liver enzyme (ALT) in their blood. They must also show signs of being infected by the hepatitis C virus. Alpheon was to be used with an antiviral medicine, ribavirin, except when patients could not take ribavirin.

How is Alpheon expected to work?
Interferons are natural substances produced by the body to help it fight against attacks such as infections caused by viruses. The interferon in Alpheon, interferon alfa-2a, is made by a method known as 'recombinant DNA technology': it is made by a yeast that has received a gene (DNA) that makes it able to produce it.

What documentation has been presented by the company to support the application to the CHMP?
The company that makes Alpheon presented information showing that Alpheon had been compared to Roferon-A (structure of the active substance, composition and purity of the medicine, the way it works, safety and effectiveness in hepatitis C). The study in patients with hepatitis C compared the efficacy of Alpheon with that of the reference medicine in 455 patients. The study measured how many patients responded (no sign of virus in their blood) after 12 out of the 48 weeks of treatment and 6 months after stopping treatment.

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What were the major concerns which led the CHMP to recommend the refusal of the marketing authorisation?
The CHMP had major concerns regarding the comparability of Alpheon and Roferon-A, because of differences identified between the two medicines (such as impurities). They also had concerns that there was not enough data on the stability of the active substance and of the medicine that was going to be marketed. Also, the process used for making the finished medicine had not been adequately validated.

The number of patients with hepatitis C responding to treatment with Alpheon and Roferon-A was similar in the clinical study. However, some differences were seen between the two medicines: more patients experienced a return of the disease after treatment with Alpheon was stopped than with the reference medicine, and there were more side effects with Alpheon. In addition, the test used in the study to investigate the potential for the medicine to trigger an immunological response (when the body makes special proteins, called antibodies, against the medicine) had not been sufficiently validated.

At this point in time, the CHMP was of the opinion that Alpheon could not be considered as a biosimilar medicine of Roferon-A, the reference medicinal product. Hence, the CHMP recommended that Alpheon be refused marketing authorisation.

What are the consequences of the refusal for patients undergoing clinical trials/compassionate use programmes with Alpheon?
There are no ongoing clinical trials or compassionate use programmes with Alpheon in the European Union.