European Medicines Agency

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Questions and answers on the withdrawal of the marketing application for Cylatron

International non-proprietary name (INN): ***peginterferon alfa-2b***

On 11 March 2009, SP Europe officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Cylatron for the adjuvant treatment of stage III melanoma.

What is Cylatron?
Cylatron is a powder and solvent that is made up into a solution for injection. It contains the active substance peginterferon alfa-2b.

What was Cylatron expected to be used for?
Cylatron was expected to be used in adults with stage III (advanced) melanoma as an add-on treatment after surgery, to prevent the disease from coming back. Melanoma is a type of skin cancer affecting cells called melanocytes. 'Stage III' means that some cancer cells have spread to the lymph nodes (part of the lymphatic system that drains fluids from the body's tissues). Cylatron was expected to be given to patients whose lymph nodes contained melanoma cells as visible under a microscope, but not when the cancer had caused the lymph nodes to become large enough to be felt through the skin.

How is Cylatron expected to work?
The active substance in Cylatron, peginterferon alfa-2b, belongs to the group 'interferons'. It consists of a substance called interferon alfa-2b, which has been 'pegylated' (coated with 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.
In melanoma, interferon alfa-2b is thought to work by suppressing the growth and multiplication of cancerous cells, by causing these cells to die and by stimulating the immune system (the body's natural defences) to attack and kill the cancer cells.
Peginterferon alfa-2b has been authorised in the European Union (EU) since May 2000 as PegIntron and ViraferonPeg for the treatment hepatitis C. Unpegylated interferon alfa-2b has also been authorised in the EU since March 2000 as IntronA. IntronA is authorised for the treatment of malignant melanoma after surgery, along with other diseases.

What documentation did the company present to support its application to the CHMP?
The effects of Cylatron were first tested in experimental models before being studied in humans. Cylatron was studied in one main study involving 1,256 adults with stage III melanoma. Patients were either given Cylatron for up to five years or received no treatment. When the study began, all of the patients had recently had surgery to remove lymph nodes containing melanoma cells. The main measure of effectiveness was the how long the patients survived until the disease came back.

How far into the evaluation was the application when it was withdrawn?
The application was at day 194 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

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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 grant a licence.

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 list of questions at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Cylatron could not have been approved for adjuvant treatment of stage III melanoma.

What were the main concerns of the CHMP?
The CHMP had concerns over side effects of Cylatron, particularly fatigue (tiredness) and depression. It was also concerned that, although the medicine showed some effects in delaying the return of the cancer, it had not been shown to be effective in increasing how long the patients survived.

What were the reasons given by the company to withdraw 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 undergoing clinical trials or compassionate use programmes with Cylatron?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate programmes with Cylatron. 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.

What is happening with PegIntron and ViraferonPeg for the treatment of hepatitis C and with IntronA for the treatment of malignant melanoma?
This withdrawal of application has no consequences on the use of PegIntron, ViraferonPeg and IntronA in their authorised indications, for which the balance of benefits and risks remains unchanged.