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Questions and answers

Withdrawal of the marketing authorisation application for Ratioepo[1] (epoetin theta)

On 25 February 2010, ratiopharm GmbH officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Ratioepo, for the treatment of symptomatic anaemia in adults with chronic renal failure or non-myeloid cancer.

What is Ratioepo?

Ratioepo is a solution for injection. It was expected to be available in pre-filled syringes containing between 1,000 and 30,000 international units (IU) of the active substance, epoetin theta.

What was Ratioepo expected to be used for?

Ratioepo was expected to be used to treat anaemia (low red blood cell counts) that is causing symptoms. It was to be used in adults with chronic renal failure (long-term, progressive decrease in the ability of the kidneys to work properly) and in adults with non-myeloid cancer (cancer not originating in the bone marrow) who are receiving chemotherapy (medicines to treat cancer).

How is Ratioepo expected to work?

A hormone called erythropoietin stimulates the production of red blood cells from the bone marrow. Erythropoietin is produced by the kidneys. In patients receiving chemotherapy or with kidney problems, anaemia can be caused by a lack of erythropoietin, or by the body not responding enough to the erythropoietin it has naturally. In these cases, erythropoietin is used to replace the missing hormone or to increase red blood cell counts. Erythropoietin is also used before surgery to increase the number of red blood cells to help patients to produce more blood for self-donation.

[1] This withdrawal of application does not affect Eporatio and Biopin, which were part of the same multiple application

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The active substance in Ratioepo, epoetin theta, is a copy of human erythropoietin and works in exactly the same way as the natural hormone to stimulate red blood cell production. It 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 epoetin theta.

What did the company present to support its application?

The effects of Ratioepo were first tested in experimental models before being studied in humans.

The company presented results from four main studies in 842 chronic renal failure patients and three main studies in 586 non-myeloid cancer patients receiving chemotherapy.

In the four renal failure studies, patients were given either Ratioepo (under the skin or into a vein) or epoetin beta (another erythropoietin-like medicine used for anaemia). The main measure of effectiveness in two of these studies was based on whether increasing the dose of Ratioepo from 20 or 40 IU per kg body weight to 120 IU per kg body weight led to improvements in haemoglobin levels during the correction phase. Haemoglobin is the protein found in red blood cells that carries oxygen around the body The other two studies compared Ratioepo with epoetin beta during the maintenance phase. The main measure of effectiveness was the average change in haemoglobin levels from 15 to 26 weeks after treatment.

In the cancer studies, the main measure of effectiveness was the number of patients receiving either Ratioepo or placebo (a dummy treatment) with an increase in haemoglobin of 2 g/dl over 12 or 16 weeks.

How far into the evaluation was the application when it was withdrawn?

The evaluation had finished and the CHMP had given a positive opinion. The company withdrew before the European Commission had issued a decision on this opinion.

What was the recommendation of the CHMP at that time?

The CHMP had given a positive opinion for Ratioepo and two other identical epoetin theta containing medicines Eporatio and Biopoin. The Committee concluded that the benefits of these medicines were greater than their risks and recommended that they be given marketing authorisation.

The European Commission had not yet made a final decision on the CHMP's recommendation for Ratioepo but had questioned the company's plan to market multiple epoetin theta-containing medicines.

What were the reasons given by the company for withdrawing the application?

The company withdrew the application for Ratioepo for administrative reasons. The letter from the company notifying the Agency of the withdrawal of the application is available here.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

There are no clinical trials or compassionate use programmes using Ratioepo. Patients who need treatment with Ratioepo will be able to receive either Eporatio or Biopoin, both of which are identical to Ratioepo and are not affected by this withdrawal.