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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Firazyr (icatibant)

On 14 February 2014, Shire Orphan Therapies GmbH officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application to extend the use of Firazyr in the treatment of angioedema caused by medicines called angiotensin-converting enzyme inhibitors.

What is Firazyr?

Firazyr is a solution for injection that contains the active substance icatibant. It has been authorised since July 2008 for treating the symptoms of attacks of hereditary angioedema in adults. Patients with angioedema have attacks of swelling that can occur anywhere in the body, such as in the face or limbs, or around the gut, causing discomfort and pain. Hereditary angioedema is angioedema caused by abnormalities in the genes responsible for the production of a protein called 'C1 esterase inhibitor'. Firazyr is used when these genetic abnormalities result in low levels of functional C1 esterase inhibitor.

Firazyr was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 17 February 2003 for the treatment of angioedema. For more information, see here.

What was Firazyr expected to be used for?

Firazyr was also expected to be used for the treatment of angioedema caused by medicines called angiotensin-converting enzyme inhibitors (ACE-I).

How is Firazyr expected to work?

In angioedema caused by ACE-I, Firazyr is expected to work in the same way as it does in its existing indication.

Patients with angioedema have high levels of a substance called bradykinin, which is involved in causing inflammation and swelling. The active substance in Firazyr, icatibant, blocks the receptors that

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bradykinin normally attaches itself to. This blocks the activity of bradykinin, helping to relieve the symptoms of the disease.

What did the company present to support its application?

The applicant presented data from one main study involving 27 patients with an angioedema attack caused by ACE-I. In the study, patients were given either Firazyr or standard therapy with two medicines called a corticosteroid and an antihistamine. The main measure of effectiveness was the time needed for the patient's symptoms to resolve.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the initial documentation provided by the company and formulated lists of questions. The CHMP was assessing the company's responses to the questions at the time of the withdrawal.

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 lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Firazyr could not have been approved for the treatment of ACE-I induced angioedema.

Following an inspection of one of the study sites, the CHMP had concerns over the way the study was conducted. In particular, important study documentation confirming which treatment each patient received was missing. In addition, the CHMP was concerned that the investigators may have become aware of which treatment patients received, which could have affected the reliability of the data. Finally, some of the data included in the results had not been collected in accordance with the study design.

Therefore, at the time of the withdrawal, the results of the study were not considered to be reliable and the CHMP concluded that the medicine could not have been approved on the basis of the data presented by the company.

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

In its letter notifying the Agency of the withdrawal of application, the company stated that its decision to withdraw the application was based on the CHMP's view that the data provided so far were not sufficient to address the CHMP's concerns and that more data would be needed.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials?

The company informed the CHMP that the currently ongoing clinical study with Firazyr in ACE-I induced angioedema will continue.

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with Firazyr for the treatment of hereditary angioedema?

There are no consequences on the use of Firazyr in its authorised indication.

The full European Public Assessment Report for Firazyr can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.