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Questions and answers

Withdrawal of the marketing authorisation application for Ruvise (imatinib)

On 17 January 2013 Novartis Europharm Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Ruvise, for the treatment of pulmonary arterial hypertension.

What is Ruvise?

Ruvise is a medicine that contains the active substance imatinib. It was to be available as tablets (100 mg and 400 mg). Medicines containing imatinib are currently approved in the European Union (EU) for the treatment of different types of cancers.

What was Ruvise expected to be used for?

Ruvise was expected to be used as an add-on treatment in adults with pulmonary arterial hypertension (PAH, high blood pressure in the arteries of the lungs) to improve exercise capacity (the ability to carry out physical activity). It was expected to be used in patients who still have symptoms despite being treated with at least two medicines specific for PAH.

Treatment with Ruvise was only to be started in patients who do not show a rapid progression of their disease.

How is Ruvise expected to work?

Imatinib is a tyrosine-kinase inhibitor. This means that it blocks some specific enzymes known as tyrosine kinases, which are involved in stimulating cells to divide. In the blood vessel cells in the lungs, this action of the tyrosine kinases contributes to the narrowing of blood vessels leading to high blood pressure. By blocking this action, Ruvise is expected to make it easier for the blood to flow through the arteries of the lungs, thereby lowering the high blood pressure in the lungs.

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What did the company present to support its application?

The applicant presented data from one main study involving 202 patients with PAH. In the study, patients were given either imatinib or placebo (a dummy treatment), added to two or more PAH medicines, for 24 weeks. The main measure of effectiveness was the distance that patients could walk during a six-minute walk test.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated two rounds of questions. After the CHMP had assessed the company's responses to the last round of questions, there were still some unresolved issues.

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 Ruvise could not be approved for the treatment of PAH.

The Committee was concerned that a beneficial effect of imatinib in PAH had not been sufficiently demonstrated. Data showed only a limited and variable improvement in the distance that patients could walk during the walk test. Furthermore, imatinib-treated PAH patients had a higher risk of serious side effects, often leading to hospitalisation during early treatment, and long-term follow-up showed no significant improvement in terms of survival or delaying the worsening of symptoms.

In view of the serious side effects observed in some PAH patients, the CHMP considered that more data were needed to identify which patients were at particular risk. The Committee also noted the higher unexplained risk of subdural haemorrhage (a type of bleeding in the brain).

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Ruvise did not outweigh its risks in the PAH population.

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

In its official letter, the company stated that its decision to withdraw the application was based on the fact that the additional data required to address CHMP's questions could not be made available within the regulatory timeframe.

The withdrawal letter is available here.

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

The company informed the CHMP that on-going PAH extension studies are continuing. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

This withdrawal has no impact on the use of other imatinib containing medicines in cancer.