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Questions and answers

Withdrawal of the marketing authorisation application for Raxone (idebenone)

On 21 March 2013, Santhera Pharmaceuticals (Deutschland) GmbH officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Raxone, for the treatment of Leber's hereditary optic neuropathy (LHON).

What is Raxone?

Raxone is a medicine that contains the active substance idebenone. It was to be available as 150 mg tablets.

What was Raxone expected to be used for?

Raxone was expected to be used for the treatment of LHON, which is an inherited disease characterised by progressive loss of sight.

Raxone was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 15 February 2007 for the treatment of LHON.

How is Raxone expected to work?

The active substance in Raxone, idebenone, acts on structures inside cells known as mitochondria, which produce the energy necessary for cells to function. Patients affected by LHON have mutations (defects) in the genetic material of mitochondria. This means that mitochondria do not work properly to generate energy, and produce toxic forms of oxygen (free radicals) that damage nerve cells in the eye that are needed for vision. The way idebenone works in LHON is not fully understood but it is thought to reduce the formation of free radicals and to help improve production of energy, thereby preventing the cellular damage and the loss of sight seen in LHON.

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What did the company present to support its application?

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

The company presented the results from one main study with Raxone involving 85 patients with LHON whose symptoms started in the previous five years. In the study, patients received Raxone or placebo (a dummy treatment) for six months. The main measure of effectiveness was the change in vision after six months of treatment measured using a standard eye test with a letter chart.

How far into the evaluation was the application when it was withdrawn?

The evaluation had finished and the CHMP had given a negative opinion. The company had requested a re-examination of the negative opinion, but withdrew before this re-examination had started.

What was the recommendation of the CHMP at that time?

Based on the review of the data, at the time of the withdrawal, the CHMP had given a negative opinion recommending that the marketing authorisation be refused for Raxone for the treatment of Leber's hereditary optic neuropathy (LHON).

At the time of the negative opinion, the CHMP was concerned that in patients with LHON whose symptoms started in the previous five years, taking Raxone for six months did not lead to a significant improvement in vision compared with placebo (patients taking Raxone were able to distinguish three more letters on the letter chart compared with patients taking placebo). The CHMP did not consider this benefit to be significant.

Based on the same study, the company later proposed to restrict the use of Raxone to patients with LHON whose symptoms started in the previous year. These patients showed an improvement of 17 letters on the letter chart compared with placebo. However, the CHMP concluded that the new sub-group of patients proposed for treatment was not well represented in the study (28 patients) and the reliability of the results is questionable. Given the small size of this sub-group, the CHMP considered that a spontaneous improvement could not be ruled out.

In addition, the CHMP considered that the data supporting the mode of action for idebenone in LHON are not sufficient.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Raxone did not outweigh its risks.

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 state that it was withdrawing the application for strategic reasons.

The withdrawal letter is available here.

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

The company informed the CHMP that there are no ongoing clinical trials. Patients in compassionate use programmes can continue using Raxone.

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