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Questions and answers

Refusal of the marketing authorisation for Raxone (idebenone)

On 17 January 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Raxone, intended for the treatment of patients with Leber's hereditary optic neuropathy (LHON).

The company that applied for authorisation is Santhera Pharmaceuticals (Deutschland) GmbH. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

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 the cells that are needed for vision. The way idebenone works in LHON is not fully understood but it is thought to reduce

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the formation of free radicals and help to improve production of energy, thereby preventing the cellular damage and loss of sight seen in LHON.

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.

What were the CHMP's main concerns that led to the refusal?

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 any 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 that point in time, the CHMP was of the opinion that the benefits of Raxone did not outweigh its risks and recommended that it be refused marketing authorisation.

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

The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate use programmes with Raxone.

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.

The summary of the opinion of the Committee for Orphan Medicinal Products for Raxone can be found on the Agency's website ema.europa.eu/Find medicine/Human medicines/Rare disease designation.