



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Questions and answers

Refusal of the marketing authorisation for Reasanz (serelaxin)

Outcome of re-examination

On 23 January 2014, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Reasanz, intended for the treatment of acute heart failure. The company that applied for authorisation is Novartis Europharm Ltd.

The applicant requested a re-examination of the opinion. After considering the grounds for this request, the CHMP re-examined the initial opinion, and confirmed the refusal of the marketing authorisation on 22 May 2014.

What is Reasanz?

Reasanz is a medicine that contains the active substance serelaxin. It was to be available as a concentrate to be diluted and given by infusion (drip) into a vein.

What was Reasanz expected to be used for?

Reasanz was expected to be used to treat the symptoms of acute heart failure (an episode of severe or worsening symptoms in patients in whom the heart cannot pump sufficient blood around the body). These symptoms include high blood pressure in the vessels leaving the lungs, leading to congestion (fluid build-up) and dyspnoea (shortness of breath). The medicine was to be used as an addition to other treatment.

How is Reasanz expected to work?

The active substance in Reasanz, serelaxin, is a recombinant form of relaxin-2, a hormone naturally found in the body. Recombinant means that it is produced by bacteria into which a gene (DNA) has been introduced that makes the bacteria able to produce the hormone. When serelaxin attaches to receptors for relaxin in the blood vessels, it causes these vessels to relax and widen. This lowers the



pressure in the blood vessels and makes it easier for the heart to pump blood around the body, which helps to relieve the symptoms of acute heart failure.

What did the company present to support its application?

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

The application was mainly based on the results of one main study involving 1,161 patients with an episode of acute heart failure. Reasanz infusion was compared with placebo (a dummy treatment) as an addition to their other treatment. The main measure of effectiveness was the extent to which dyspnoea was relieved, measured short-term (after 6, 12 and 24 hours) and over 5 days.

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

At the time of the initial evaluation, the CHMP noted that the study results did not demonstrate a benefit for short-term relief of dyspnoea over up to 24 hours, and although some benefit was shown over 5 days it was not clear how this was of clinical relevance. Furthermore, the Committee had concerns about the way the effectiveness of the medicine in the study had been analysed. The results included assigned values for a number of patients who had died or had required additional treatment for worsening symptoms and whose actual data were not used. In addition, the CHMP questioned whether the type of the background treatment given to patients in the two study groups might have influenced the results. Since only one main study was included in the application, the CHMP concluded that further studies would be needed to confirm the effectiveness of Reasanz in the treatment of acute heart failure.

During the re-examination, the CHMP reviewed again the data from the only main study submitted and confirmed its opinion that the effectiveness of Reasanz had not been sufficiently demonstrated. Therefore, although the safety of Reasanz seemed acceptable, the CHMP concluded that the benefits of Reasanz did not outweigh its risks and maintained its previous recommendation that the medicine 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 Reasanz.

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