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EPAR summary for the public

Krystexxa

pegloticase

This is a summary of the European public assessment report (EPAR) for Krystexxa. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Krystexxa.

What is Krystexxa?

Krystexxa is a medicine containing the active substance pegloticase. It is available as a concentrate that is made up into a solution for infusion (drip) into a vein.

What is Krystexxa used for?

Krystexxa is used to treat adult patients with severe chronic (long-term) tophaceous gout. This is where high levels of the substance uric acid develop in the blood and then crystallise in joints and tissues, forming tophi (stones) that cause pain and joint damage. Krystexxa is only used in patients who cannot control their uric acid levels even at maximum doses of conventional medicines called xanthine oxidase inhibitors, or who are unable to use such medicines.

The medicine can only be obtained with a prescription.

How is Krystexxa used?

Treatment with Krystexxa should be given under the supervision of a doctor who has experience in the treatment of severe chronic gout, in a setting where facilities for resuscitation are available.

Krystexxa is given as an infusion into a vein every two weeks, at a recommended dose of 8 mg. The infusion is given slowly over at least 2 hours. All patients are monitored for any reactions during the infusion and for at least one hour afterwards. To reduce the risk of these reactions, patients are given other medicines before treatment with Krystexxa.

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Reactions are more common in patients who develop antibodies (proteins produced by the immune system, the body's natural defences) that reduce the effect of the treatment. Levels of uric acid are therefore measured before each infusion and the doctor should only continue Krystexxa treatment as long as the patient continues to benefit with uric acid levels in the blood lowered below a threshold of 6 mg/dl. Patients should not take other medicines that lower uric acid levels during Krystexxa treatment, so that the effect of Krystexxa can be clearly judged.

For further information on the use of Krystexxa see the package leaflet.

How does Krystexxa work?

The active substance in Krystexxa, pegloticase, contains an enzyme called uricase. Uricase breaks down uric acid into another substance, allantoin, which can be passed out of the body in the urine. This lowers the levels of uric acid in the blood. Once levels of uric acid are below 6 mg/dl, this allows crystals in the joints to dissolve, slowly shrinking the tophi.

The uricase in Krystexxa is produced by a method known as 'recombinant DNA technology': it is made by a bacterium that has received a gene (DNA), which makes it able to produce uricase. In Krystexxa, uricase has been attached to a chemical, polyethylene glycol (PEG), which decreases the rate at which uricase is removed from the body, allowing its action to last longer.

How has Krystexxa been studied?

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

Krystexxa was studied in two main studies involving 225 patients with severe tophaceous gout in whom allopurinol, a xanthine oxidase inhibitor, had previously failed to control their uric acid levels or could not be used due to side effects. Krystexxa, given at a dose of 8 mg every two or four weeks, was compared with placebo (a dummy treatment), over a period of six months. The main measure of effectiveness was the number of patients who showed a persistent response to the treatment, defined as uric acid level in the blood below 6 mg/dl for at least 80% of the time during both the third and sixth months of the study.

What benefit has Krystexxa shown during the studies?

Krystexxa was shown to be more effective than placebo in reducing uric acid levels. Although uric acid levels were quickly lowered by Krystexxa, its effect was reduced within a few weeks in more than half the patients. Overall, 42% of patients (36 out of 85) given the medicine every two weeks showed a persistent response; the figure for those given Krystexxa every four weeks was 35% (29 out of 84). Placebo was not effective in any of the patients. Krystexxa given every two weeks resulted in fewer reactions to the infusion than when it was given every four weeks.

What is the risk associated with Krystexxa?

The most common serious side effects with Krystexxa are anaphylaxis (a severe allergic reaction), seen in about 7 patients in 100, infusion reactions (including flushing, skin rashes, itching, sweating, chest pain, difficulty in breathing, chills, and raised blood pressure), seen in about 26 patients in 100, and gout flares (worsening of gout symptoms) which were more common in the first 3 months of treatment.

For the full list of side effects reported with Krystexxa, see the package leaflet.

Krystexxa must not be used in people who are hypersensitive (allergic) to pegloticase or any of the other ingredients, and in people with a rare blood disorder called glucose 6-phosphate dehydrogenase (G6PD) deficiency (favism) or similar disorders.

Why has Krystexxa been approved?

The CHMP concluded that Krystexxa was highly effective in reducing uric acid levels. Although there may be serious side effects (such as infusion reactions and gout flares) these were considered manageable. For severely affected patients who cannot be treated effectively with conventional methods, the Committee considered that Krystexxa addressed an unmet need, since no alternative treatments are available. The CHMP therefore decided that Krystexxa's benefits are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe use of Krystexxa?

The company that makes Krystexxa will carry out a study of the long-term safety of the medicine, including its safety and effectiveness in patients who stop treatment and later restart it.

Other information about Krystexxa

The European Commission granted a marketing authorisation valid throughout the European Union for Krystexxa on 8 January 2013.

The full EPAR for Krystexxa can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Krystexxa, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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