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Withdrawal of application for the marketing authorisation of Xyndari (glutamine)

Emmaus Medical Europe Ltd withdrew its application for a marketing authorisation of Xyndari for the treatment of sickle cell disease.

The company withdrew the application on 18 September 2019.

What is Xyndari and what was it intended to be used for?

Xyndari was developed as a medicine for sickle cell disease, a genetic disease in which the red blood cells become rigid and crescent-shaped. The abnormal cells block the flow of blood around the body and release haemoglobin (the protein that carries oxygen) into the blood. This leads to pain, organ damage, repeated infections and anaemia (low levels of haemoglobin).

Xyndari contains the active substance glutamine and was to be available as a powder to be dissolved in liquid and taken by mouth. Glutamine is an active substance in several medicines used for parenteral nutrition (nutrients given by drip into a vein).

Xyndari was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 4 July 2012 for sickle cell disease. Further information on the orphan designation can be found on the Agency's website: ema.europa.eu/medicines/human/orphan-designations/eu3121011.

How does Xyndari work?

The way the active substance in Xyndari, glutamine, works in sickle cell disease is not well understood. Studies indicate that when taken up by the abnormal red blood cells in sickle cell disease, glutamine has an antioxidant effect (removes molecules called free radicals that damage cells) and reduces the stickiness of the blood cells to the walls of blood vessels. This was expected to improve blood flow to the organs, thereby reducing periods of pain (called sickle cell crises) experienced with sickle cell disease.

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What did the company present to support its application?

The company presented the results of a main study in 230 patients with sickle cell disease. Patients received either Xyndari or placebo (a dummy treatment) for a year. The main measure of effectiveness was the number of sickle cell crises the patients experienced. The study also looked at how often patients had to go to hospital with pain from sickle cell disease. The company also submitted results of a supportive study using similar measures of effectiveness in 70 patients who received either Xyndari or placebo.

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

The evaluation had finished and the European Medicines Agency had recommended refusing marketing authorisation, which was under re-examination at the company's request at the time of withdrawal. The company withdrew the application before the re-examination had completed and the European Commission had issued a decision on the Agency's recommendation.

What did the Agency recommend at that time?

Based on the review of the data, at the time of the withdrawal, the Agency was of the opinion that the marketing authorisation for Xyndari for the treatment sickle cell disease should be refused.

The Agency considered that the main study did not show that Xyndari was effective at reducing the number of sickle cell crises or hospital visits. A large number of patients, of which more were taking Xyndari than taking placebo, dropped out of the study before it was finished, and information on how the medicine worked for those patients was not available. The Agency considered that the way data from these patients were dealt with was not appropriate.

The Agency also had concerns about the supportive study, which involved a small number of patients, many of whom also dropped out of the study early. In addition, in this study more of the patients taking Xyndari than patients taking placebo had received a medicine for sickle cell disease called hydroxyurea. This could have influenced the results.

Therefore, at the time of the withdrawal, the Agency's opinion was that the company had not fully addressed its concerns and the benefits of Xyndari could not be established.

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

In its letter notifying the Agency of the withdrawal of the application, the company stated that the withdrawal is based on a change in the company's marketing strategy.

Does this withdrawal affect patients in clinical trials or compassionate use programmes?

The company informed the Agency that there are no ongoing clinical trials with Xyndari in Europe. The company will continue with its ongoing compassionate use programmes pending discussions with national authorities that have granted approval for compassionate use.

If you are in a compassionate use programme and need more information about your treatment, speak with your doctor.