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Update of 27 June 2019:

The applicant for Xyndari has requested a re-examination of the CHMP's May 2019 opinion. Upon receipt of the grounds of the request, the CHMP will re-examine its opinion and issue a final recommendation.

29 May 2019

Refusal of the marketing authorisation for Xyndari (glutamine)

On 29 May 2019, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Xyndari, intended for the treatment of sickle cell disease.

The company that applied for authorisation is Emmaus Medical Europe Limited. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Xyndari?

Xyndari is a medicine that contains the active substance glutamine. It was to be available as a powder to be dissolved in liquid and taken by mouth.

What was Xyndari expected to be used for?

Xyndari was expected to be used to treat 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 they use to carry oxygen) into the blood. This leads to pain, organ damage, repeated infections and anaemia (low levels of haemoglobin).

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 here.

Glutamine is an active substance in several nationally authorised medicines used for parenteral nutrition (nutrients given by drip into a vein).

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How does Xyndari work?

The way that 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 should reduce the stickiness of these 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.

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.

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

The CHMP 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, more who 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 CHMP considered that the way data from these patients were dealt with was not appropriate.

The CHMP 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 had received a medicine for sickle cell disease called hydroxyurea than patients taking placebo. This could have influenced the results.

Therefore, the CHMP was of the opinion that the benefits of Xyndari could not be established 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 ongoing clinical trials with Xyndari in Europe and that the consequences for patients in compassionate use programmes are not known. If you are in a compassionate use programme and need more information about your treatment, contact the doctor who is giving it to you.