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Withdrawal of application for the marketing authorisation of Livmarli (maralixibat chloride)

FGK Representative Service GmbH withdrew its application for a marketing authorisation of Livmarli for the treatment of progressive familial intrahepatic cholestasis type 2 (PFIC2) in patients 1 year of age and older.

The company withdrew the application on 23 August 2021.

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

Livmarli was developed as a medicine to treat progressive PFIC2 in patients 1 year of age and older. PFIC2 is an inherited liver disorder where bile acids build up in the blood and liver and cause itching and liver damage. These bile acids are components of bile, a fluid produced by the liver and released into the intestines to help digestion.

Livmarli contains the active substance maralixibat chloride and was to be available as a solution to be taken by mouth.

This medicine was designated an 'orphan medicine' (a medicine used in rare diseases) on 16 January 2014 for the treatment of progressive familial intrahepatic cholestasis. Further information on the orphan designation can be found on the Agency's website: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3131216.

How does Livmarli work?

The medicine is expected to reduce the amount of bile acids in the blood and liver. The active substance in Livmarli, maralixibat chloride, is thought to block the action of a protein known as ASBT that helps to transport bile acids from the intestines back to the blood and liver. When ASBT proteins are blocked, the bile acids are instead excreted from the body. This is expected to reduce the build-up of bile acids in the blood and liver, and so reduce the itching and liver damage seen in patients with PFIC2.

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What did the company present to support its application?

The company presented the results of a single study involving 25 patients with PFIC2 who were 1 to 13 years of age and were treated with Livmarli for up to 5 years or longer. The main measure of effectiveness was a decrease in the level of bile acids in the blood after 13 weeks of treatment. Livmarli was not compared with other medicines or placebo (a dummy treatment).

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the initial information from the company and had prepared questions for the company. The company had not responded to the questions at the time of the withdrawal.

What did the Agency recommend at that time?

Based on the review of the data, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Livmarli could not have been authorised for the treatment of PFIC2.

The Agency's concerns were about the effectiveness of the medicine in the treatment of PFIC2, based on important uncertainties about the available data. In terms of effectiveness, the study did not show a significant treatment effect in patients with PFIC2 after 13 weeks of treatment. It was therefore not possible to draw conclusions on the long-term effectiveness of Livmarli in the target patient population. The Agency also had concerns about some aspects of the manufacturing process and compliance with good manufacturing practices.

Therefore, at the time of the withdrawal, the Agency's opinion was that the benefits of Livmarli did not outweigh its risks.

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 decision to withdraw the application was based on a change in the company's business and regulatory strategies following discussion with CHMP and in anticipation of upcoming additional data.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials using Livmarli.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.