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Livmarli (*maralixibat chloride*)

An overview of Livmarli and why it is authorised in the EU

What is Livmarli and what is it used for?

Livmarli is a medicine used for treating patients aged 2 months and older with cholestatic pruritus (intense itching due to a build-up of bile) caused by Alagille syndrome. It is also used for treating patients aged 3 months and older with progressive familial intrahepatic cholestasis.

Alagille syndrome and progressive familial intrahepatic cholestasis are inherited diseases in which bile (a fluid produced in the liver that helps to break down fats) cannot drain properly from the liver, resulting in a build-up of bile acid in the liver and blood. One of the symptoms of this build-up is cholestatic pruritus. Intrahepatic cholestasis is associated with progressive liver damage and can lead to cirrhosis and end-stage liver impairment.

These diseases are rare, and Livmarli was designated an 'orphan medicine' (a medicine used in rare diseases). Further information on the orphan designations can be found on the EMA website (Alagille syndrome; progressive familial intrahepatic cholestasis).

Livmarli contains the active substance maralixibat chloride.

How is Livmarli used?

Treatment with Livmarli must be started and supervised by a doctor experienced in treating liver diseases such as Alagille syndrome and progressive familial intrahepatic cholestasis. The medicine can only be obtained with a prescription.

Livmarli is available as a solution to be taken by mouth. The dose depends on the disease that is being treated. In case the patient develops certain side effects the dose may have to be reduced or treatment interrupted. For patients who do not show an improvement after 3 months the doctor should consider an alternative treatment.

For more information about using Livmarli, see the package leaflet or contact your doctor or pharmacist.

How does Livmarli work?

The active substance in Livmarli, maralixibat chloride, blocks the action of a protein called apical sodium-dependent bile acid transporter (ASBT), also known as ileal bile acid transporter (IBAT), that

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helps to transport bile acid from the gut back to the blood and liver. By blocking ASBT, the medicine reduces the amount of bile acid that is transported from the gut into the liver. This leads to excess bile acid being removed from the body, thereby reducing the build-up of bile acid and relieving the symptoms of cholestatic pruritus.

What benefits of Livmarli have been shown in studies?

Alagille syndrome

The benefits of Livmarli were evaluated in two main studies. In the first study, 31 children aged from 1 to 18 years with Alagille syndrome were treated with Livmarli for 18 weeks, after which their response to treatment was evaluated.

The 29 patients who had a decrease in the levels of bile acid in their blood of at least 50% following the initial 18-week treatment with the medicine were subsequently assigned to receive either placebo (dummy treatment) or Livmarli for 4 weeks. Results showed that patients who continued treatment with Livmarli for 4 weeks still had a reduction in the level of bile acid while those who switched treatment to placebo had significant increases. After this 4-week period, all patients received Livmarli again. When the patients who took placebo resumed treatment with Livmarli, their blood levels reduced to levels previously observed with Livmarli. The study also showed that treatment with Livmarli improved symptoms of itching associated with the disease.

In the second study, involving 8 children aged from 2 months to less than 1 year, Livmarli was not compared with any other treatment or placebo. Results of the study showed that after 13 weeks of treatment, patients had, on average, an improvement in symptoms of itching associated with the disease and a reduction in the level of bile acids in their blood.

Progressive familial intrahepatic cholestasis

The benefits of Livmarli were evaluated in a main study involving 93 children aged from 1 to 15 years with progressive familial intrahepatic cholestasis. Patients received Livmarli or placebo for 26 weeks, after which their response to treatment was evaluated. Results showed that patients on Livmarli had a reduction in the level of bile acid in their blood, whereas bile acid levels did not change in patients given placebo. The severity of itching experienced by patients also decreased more in those given Livmarli compared with placebo.

What are the risks associated with Livmarli?

For the full list of side effects and restrictions with Livmarli, see the package leaflet.

In patients with Alagille syndrome, the most common side effects with Livmarli (which may affect more than 1 in 5 people) include diarrhoea and abdominal pain (belly ache). In patients with progressive familial intrahepatic cholestasis, diarrhoea may affect more than 1 in 5 people and abdominal pain may occur in up to 1 in 10 people.

Why is Livmarli authorised in the EU?

Alagille syndrome and progressive familial intrahepatic cholestasis are life-threatening diseases with limited options for treatment. As both diseases are very rare, the studies were small and subject to limitations, but Livmarli was shown to be effective at reducing the amount of bile acid in the blood of patients with progressive familial intrahepatic cholestasis and improving symptoms, such as intense itching, in patients with either disease. Although the data on the safety of Livmarli are limited and

further information needs to be gathered, the side effects seen to date are considered acceptable. The European Medicines Agency therefore decided that Livmarli's benefits are greater than its risks and it can be authorised for use in the EU.

Livmarli has been authorised under 'exceptional circumstances'. This is because it has not been possible to obtain complete information about Livmarli due to the rarity of the diseases. Every year, the European Medicines Agency will review any new information that becomes available, and this overview will be updated as necessary.

What information is still awaited for Livmarli?

Since Livmarli has been authorised under exceptional circumstances, the company that markets Livmarli will provide yearly updates on any new information concerning the safety and effectiveness of Livmarli. In addition, the company will conduct and submit the results of a study to further characterise the long-term safety and efficacy of the medicine for the treatment of cholestatic pruritus in patients with Alagille syndrome and progressive familial intrahepatic cholestasis.

What measures are being taken to ensure the safe and effective use of Livmarli?

The company that markets Livmarli will provide doctors with materials to help them explain to patients with progressive familial intrahepatic cholestasis when and how to take this medicine and how much they need to take.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Livmarli have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Livmarli are continuously monitored. Suspected side effects reported with Livmarli are carefully evaluated and any necessary action taken to protect patients.

Other information about Livmarli

Livmarli received a marketing authorisation under exceptional circumstances valid throughout the EU on 9 December 2022.

Further information on Livmarli can be found on the Agency's website: ema.europa.eu/en/medicines/human/EPAR/livmarli.

This overview was last updated in 07-2024.