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EPAR summary for the public

Orphacol

cholic acid

This is a summary of the European public assessment report (EPAR) for Orphacol. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Orphacol.

For practical information about using Orphacol, patients should read the package leaflet or contact their doctor or pharmacist.

What is Orphacol and what is it used for?

Orphacol is a medicine containing cholic acid, a substance found in the bile which is used to digest fats.

It is used to treat adults and children from one month of age who have a genetic abnormality that makes them unable to produce bile. Orphacol is used in patients who do not have enough of two specific liver enzymes (3β-Hydroxy-Δ^5-C_{27}-steroid oxidoreductase or Δ^4-3-Oxosteroid-5β-reductase). This makes their liver unable to produce enough of the main components of bile, called primary bile acids, such as cholic acid. When these primary bile acids are lacking, the body produces abnormal bile acids instead which can damage the liver, potentially leading to life-threatening liver failure.

Because the number of patients with inborn errors in primary bile acid synthesis is low, the condition is considered ‘rare’, and Orphacol was designated an ‘orphan medicine’ (a medicine used in rare diseases) on 18 December 2002.

How is Orphacol used?

The medicine can only be obtained with a prescription and treatment with Orphacol should be started and supervised by a doctor specialised in liver disease.

Orphacol is available as capsules and should be taken every day at approximately the same time, with a meal. The daily dose is between 5 and 15 mg per kg body weight, adjusted for each patient according to the state of their bile acid, with a minimum daily dose of 50 mg and a maximum of

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500 mg. For small children who cannot swallow capsules, the contents can be mixed in with infant formula or juice. Treatment should be stopped if liver function does not improve within three months.

How does Orphacol work?

Cholic acid is the main primary bile acid produced by the liver. The cholic acid contained in Orphacol replaces the patient's missing cholic acid. This helps to decrease the production of abnormal bile acids and contributes to the normal activity of bile in the digestive system, thereby relieving the symptoms of the condition.

What benefits of Orphacol have been shown in studies?

Because cholic acid is a well-known substance, and its use in these enzyme deficiencies is well established, the applicant presented data from the scientific literature. The applicant presented data on 49 patients with inborn errors in primary bile acid synthesis, taken from the scientific literature (38 patients with 3β-Hydroxy-Δ^5-C_{27}-steroid oxidoreductase deficiency and 11 patients with Δ^4-3-Oxosteroid-5β-reductase deficiency). It compared the outcomes of 28 patients who received cholic acid with others who were given different bile acids or did not receive bile acid treatment.

In the scientific literature, cholic acid treatment was shown to reduce the amount of abnormal bile acids in patients, to restore the normal functions of the liver and to help delay or prevent the need for a liver transplant.

What are the risks associated with Orphacol?

The side effects seen with Orphacol were diarrhoea, pruritus (itching), increases in transaminases (liver enzymes) and possibly gallstones, although their frequency could not be reliably estimated from the available limited data.

Orphacol should not be used in people who may be hypersensitive (allergic) to cholic acid or any of the other ingredients. It must not be taken by patients already taking phenobarbital, a medicine used to treat epilepsy.

Why is Orphacol approved?

The Committee for Medicinal Products for Human Use (CHMP) noted that the use of cholic acid to treat inborn errors in primary bile acid synthesis was well established in medical practice and documented in the scientific literature, although the number of documented cases was low due to the rarity of the condition. It decided that based on the evidence from the scientific literature Orphacol's benefits are greater than its risks and recommended that it be given marketing authorisation.

Orphacol has been authorised under 'exceptional circumstances'. This means that because the disease is rare, it has not been possible to obtain complete information about Orphacol. Every year, the European Medicines Agency will review any new information that may become available and this summary will be updated as necessary.

What information is still awaited for Orphacol?

Since Orphacol has been approved under exceptional circumstances, the company that markets Orphacol will establish a database of patients treated with Orphacol to monitor the safety and effectiveness of the treatment, and will submit the results to the CHMP at regular, specified intervals.

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

A risk management plan has been developed to ensure that Orphacol is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Orphacol, including the appropriate precautions to be followed by healthcare professionals and patients.

The company that makes Orphacol will also provide doctors in all Member States who will use Orphacol with a pack containing product literature and information regarding the correct diagnosis of these disease conditions, the risks of side effects and how to use the medicine properly.

Other information about Orphacol

The European Commission granted a marketing authorisation valid throughout the European Union for Orphacol on 12 September 2013.

The full EPAR for Orphacol 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 Orphacol, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Orphacol can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 09-2013.