EMA/851451/2018
EMEA/H/C/003822

Ravicti *(glycerol phenylbutyrate)*

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

What is Ravicti and what is it used for?

Ravicti is a medicine used to manage urea cycle disorders in adults and children, when the diseases cannot be managed by changes in diet alone. Patients with urea cycle disorders are not able to get rid of waste nitrogen from the body because they lack some liver enzymes. In the body, waste nitrogen is turned into ammonia, which is harmful when it accumulates. Ravicti is used in patients who lack one or more of the following enzymes: carbamoyl phosphate synthase-I, ornithine carbamoyltransferase, argininosuccinate synthetase, argininosuccinate lyase, arginase I and ornithine translocase.

Ravicti contains the active substance glycerol phenylbutyrate.

Urea cycle disorders are rare, and Ravicti was designated an 'orphan medicine' (a medicine used in rare diseases) for several forms of the disease on 10 June 2010. Further information on the orphan designations can be found on the European Medicines Agency's website ema.europa.eu/en/medicines/ /ema_group_types/ema_orphan.

How is Ravicti used?

Ravicti is available as a liquid (1.1 g/ml) to be taken by mouth, or given through a tube that goes from the nose to the stomach or through the belly into the stomach. It can only be obtained with a prescription and should be prescribed by a doctor who has experience in treating patients with urea cycle disorders.

Since proteins are a source of nitrogen, Ravicti must be used together with a special low-protein diet, and sometimes with dietary supplements (depending on the daily protein intake needed for growth and development).

The dose of Ravicti depends on the patient's diet, height and weight. Regular blood tests are needed to adjust the dose. The total daily dose of Ravicti should be divided into equal amounts and given with each meal. Ravicti may be a life-long treatment unless the patient has a successful liver transplant.

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

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How does Ravicti work?

The active substance in Ravicti, glycerol phenylbutyrate, is converted to phenylacetate in the body. Phenylacetate attaches to the amino acid glutamine found in proteins to form a substance that the kidneys can remove from the body. This removal of proteins decreases the levels of nitrogen in the body, reducing the amount of ammonia produced.

What benefits of Ravicti have been shown in studies?

Ravicti has been compared with sodium phenylbutyrate (another medicine used to treat urea cycle disorders) in a study involving 88 adults with urea cycle disorders. The main measure of effectiveness was the change in the blood level of ammonia after 4 weeks of treatment. The study showed that Ravicti was at least as effective as the comparator in controlling the blood level of ammonia: the estimated average ammonia level was about 870 micromoles per litre in patients treated with Ravicti, compared with about 980 micromoles per litre in patients treated with sodium phenylbutyrate. Data from additional studies showed a similar effect in children treated with Ravicti from birth.

What are the risks associated with Ravicti?

The most common side effects with Ravicti (which may affect more than 1 in 20 people) are diarrhoea, flatulence (passing gas), headache, decreased appetite, vomiting, tiredness, feeling sick and abnormal skin smell.

Ravicti must not be used to treat acute hyperammonaemia (sudden rise of blood ammonia levels). For the full list of side effects and restrictions with Ravicti, see the package leaflet.

Why is Ravicti authorised in the EU?

The European Medicines Agency decided that the benefits of Ravicti are greater than its risks and it can be authorised for use in the EU.

Ravicti is effective in reducing the blood level of ammonia in patients with urea cycle disorders. Ravicti is a sustained-release medicine, meaning the active substance is released throughout the day. Therefore, this results in a better control of blood ammonia levels over the whole day. For this same reason Ravicti must not be used to treat acute hyperammonaemia as more rapidly acting treatments are needed in these cases.

Additionally, the Agency considered that since Ravicti is available as a liquid this could make the medicine more palatable especially for children, compared with other medicines available as granules to be added to food; the liquid formulation also facilitates giving it through a tube to patients unable to swallow.

The side effects of Ravicti affect mainly the gut and are considered manageable. However, further data on the long-term safety of Ravicti are awaited.

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

The company that markets Ravicti will set up a registry of patients to obtain further information on the long-term benefits and safety of the medicine.

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

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

Other information about Ravicti

Ravicti received a marketing authorisation valid throughout the EU on 27 November 2015

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

This summary was last updated in 01-2019.