European Medicines Agency

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Ammonaps
sodium phenylbutyrate

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis of the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Ammonaps?
Ammonaps is a medicine that contains the active substance sodium phenylbutyrate. It is available as white oval tablets (500 mg) and as granules (940 mg/g).

What is Ammonaps used for?
Ammonaps is used to treat patients who have urea cycle disorders. These patients are not able to get rid of waste nitrogen from the body because they lack some enzymes that are usually found in the liver. In the body, waste nitrogen is in the form of ammonia, which is toxic, especially for the brain. Ammonaps is used in patients who lack one or more of the following enzymes: carbamylphosphate synthetase, ornithine transcarbamylase, or argininosuccinate synthetase. It can be used in patients with the following forms of the disease:
- 'early-onset' disease in babies who show a complete lack of one or more of these enzymes within the first month of life;
- 'late-onset' disease in patients who show a partial lack of an enzyme after the age of one month and have had brain damage caused by high blood ammonia levels.

The medicine can only be obtained with a prescription.

How is Ammonaps used?
Ammonaps treatment should be supervised by a doctor who has experience in treating patients with urea cycle disorders.
Ammonaps is used as an add-on to other treatments and with a special low-protein diet to reduce the intake of nitrogen. The daily dose of Ammonaps is adjusted for each patient individually and depends on the patient's diet, height and weight. Regular blood tests are needed to find the correct daily dose. The dose of Ammonaps should be divided into equal amounts and given with each meal.
The tablets are for adults and children, and the granules are used in babies and in patients who cannot swallow tablets. The granules are either mixed into food or drink immediately before being taken, or dissolved in water before being given through a tube leading through the tummy or nose to the stomach.
Ammonaps is a long-term treatment and needs to be taken until the patient has a successful liver transplant.

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How does Ammonaps work?
Eating protein brings nitrogen into the body, which is then transformed into ammonia. Patients with urea cycle disorders cannot get rid of ammonia from the body, so it can reach high levels, leading to serious problems including disability, brain damage and death. The active substance in Ammonaps, sodium phenylbutyrate, is converted into a substance called phenylacetate in the body. Phenylacetate combines with the amino acid glutamine, which contains nitrogen, to form a substance that can be removed from the body by the kidneys. This allows the levels of nitrogen in the body to decrease, reducing the amount of ammonia produced.

How has Ammonaps been studied?
Ammonaps has been studied in 82 patients with urea cycle disorders who were treated with Ammonaps and had not received other treatments for their disease before. Ammonaps was not compared with any other treatments. The main measure of effectiveness was survival, but the study also looked at the number of hyperammonaemic episodes (periods of very high blood ammonia levels), cognitive development (development of the ability to think, learn and remember), growth, and blood ammonia and glutamine levels.

What benefit has Ammonaps shown during the studies?
The overall survival rate was about 80% in newborn babies who received Ammonaps. In contrast, untreated newborns usually die within the first year of life. The survival rate was higher in patients who had developed the disease later in life. Early diagnosis and immediate treatment are important to reduce the risk of disability.

What is the risk associated with Ammonaps?
The most common side effects with Ammonaps (seen in more than 1 patient in 10) are amenorrhoea (absence of periods) and irregular menstruation (irregular periods), but these only occur in fertile female patients. Other common side effects include abnormal kidney function and blood cell counts (red cells, white cells and platelets). For the full list of all side effects reported with Ammonaps, see the Package Leaflet.
Ammonaps should not be used in people who may be hypersensitive (allergic) to sodium phenylbutyrate or any of the other ingredients. It must not be used in patients who are pregnant or breast-feeding.

Why has Ammonaps been approved?
The Committee for Medicinal Products for Human Use (CHMP) noted that urea cycle disorders are a serious disease with few treatments available, and that Ammonaps has been shown to prevent ammonia levels becoming too high. Therefore, despite the limited information available, the CHMP decided that Ammonaps's benefits are greater than its risks as adjunctive therapy in the chronic management of urea cycle disorders. The Committee recommended that Ammonaps be given marketing authorisation.
Ammonaps was authorised under 'Exceptional Circumstances', because, as the disease is rare, limited information was available at the time of approval. As the company had supplied the additional information requested, the 'Exceptional Circumstances' ended on 6 July 2004.

Other information about Ammonaps:
The European Commission granted a marketing authorisation valid throughout the European Union for Ammonaps on 8 December 1999. The marketing authorisation was renewed on 8 December 2004 and on 8 December 2009. The marketing authorisation holder is Swedish Orphan International AB.

The full EPAR for Ammonaps is available here.

This summary was last updated in 12-2009.