EMA/348518/2011
EMEA/H/C/000461

EPAR summary for the public

Carbaglu

carglumic acid

This is a summary of the European public assessment report (EPAR) for Carbaglu. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Carbaglu.

What is Carbaglu?

Carbaglu is a medicine that contains the active substance carglumic acid. It is available as dispersible tablets. 'Dispersible' means that the tablets can be dispersed (mixed) in water.

What is Carbaglu used for?

Carbaglu is used for the treatment of hyperammonaemia (high blood levels of ammonia) in patients with the following metabolic diseases:

- N-acetylglutamate synthase (NAGS) deficiency. Patients with this lifelong disease lack a liver enzyme called NAGS, which normally helps to break down ammonia. If the enzyme is not present, ammonia cannot be broken down and it builds up in the blood;
- some organic acidaemias (isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia) where patients lack certain enzymes involved in protein metabolism.

Because the number of patients with these diseases is low, they are considered 'rare' and Carbaglu was designated an 'orphan medicine' (a medicine used in rare diseases) on various dates (see below).

The medicine can only be obtained with a prescription.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

How is Carbaglu used?

Carbaglu treatment should be started by a doctor who has experience in treating patients with metabolic diseases.

In patients with NAGS deficiency, treatment may be started as early as the first day of life and the medicine is used for the patient's whole life. In patients with organic acidaemias, treatment is started when the patient has a hyperammonaemia crisis and continued until the crisis is finished.

The initial daily dose of Carbaglu should be 100 mg per kilogram body weight, but up to 250 mg/kg can be used if necessary. The dose should then be adjusted to maintain normal blood ammonia levels. The tablets should be dispersed (mixed) in a small amount of water before being given to the patient. They can easily be broken into two equal halves.

How does Carbaglu work?

When ammonia builds up in the blood, it is toxic to the body, especially the brain. Carbaglu is very similar in structure to N-acetylglutamate, which activates an enzyme that breaks down ammonia. Carbaglu therefore helps break down ammonia, reducing ammonia blood levels and its toxic effects.

How has Carbaglu been studied?

Carbaglu has been studied in 20 patients, 12 of whom had NAGS deficiency and were treated for an average of about three years. The other eight patients were treated for hyperammonaemia of another cause. The company also presented information from the published literature on a further four patients treated with the active substance in Carbaglu.

Carbaglu has also been studied in 57 patients (about two-thirds were newborn babies) with isovaleric acidaemia, methylmalonic acidaemia or propionic acidaemia who were treated with Carbaglu during hyperammonaemia crises.

In all of the studies, the main measure of effectiveness was the change in ammonia levels in the blood.

What benefit has Carbaglu shown during the studies?

In patients with NAGS deficiency, ammonia levels were brought back to normal after Carbaglu treatment. Patients on Carbaglu could be kept stable without a need for restrictions to the diet or the use of other medicines.

In patients with isovaleric acidaemia, methylmalonic acidaemia or propionic acidaemia, Carbaglu also induced a decrease in ammonia levels in the blood, following an average of 5.5 days of treatment.

What is the risk associated with Carbaglu?

The most common side effect with Carbaglu (seen in between 1 and 10 patients in 100) is increased sweating. For the full list of side effects reported with Carbaglu, see the package leaflet.

Carbaglu should not be used in people who may be hypersensitive (allergic) to carglumic acid or any of the other ingredients. Carbaglu must not be used in women who are breastfeeding.

Why has Carbaglu been approved?

The CHMP concluded that Carbaglu was effective in reducing blood ammonia to normal levels and decided that Carbaglu's benefits are greater than its risks. The Committee recommended that Carbaglu be given marketing authorisation.

Other information about Carbaglu

The European Commission granted a marketing authorisation valid throughout the European Union for Carbaglu to Orphan Europe on 24 January 2003. The marketing authorisation is valid for an unlimited period.

The summaries of opinion of the Committee for Orphan Medicinal Products for Carbaglu can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designations (NAGS deficiency: 18 October 2000; isovaleric acidaemia: 7 November 2008; methylmalonic acidaemia: 7 November 2008; propionic acidaemia: 7 November 2008).

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

This summary was last updated in 05-2011.