EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Recommendation for maintenance of orphan designation at the time of addition of new indications to the marketing authorisation

Carbaglu (carglumic acid) for the treatment of isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia

During its meeting of 4-5 May 2011, the Committee for Orphan Medicinal Products (COMP) reviewed the designations for Carbaglu (carglumic acid) as an orphan medicinal product for the treatment of isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia.[1] The COMP assessed whether, at the time of addition of these new indications to the marketing authorisation, the medicinal product still met the criteria for orphan designation. The Committee looked at the seriousness and prevalence of the conditions, and the existence of other satisfactory methods of treatment. As other satisfactory methods of treatment for patients with these conditions are authorised in the European Union (EU), the COMP also looked at the significant benefit of the product over existing treatments. The COMP recommended that the orphan designations of the medicine be maintained.[2]

Life-threatening or long-term debilitating nature of the conditions

In April 2011, The Committee for Medicinal Products for Human Use (CHMP) recommended extending the approved therapeutic indication for Carbaglu to include the following indications:

- treatment of hyperammonaemia due to isovaleric acidaemia;
- treatment of hyperammonaemia due to methymalonic acidaemia;
- treatment of hyperammonaemia due to propionic acidaemia.

This falls within the scope of the product's designated orphan conditions, which are: 'treatment of isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia'.

The COMP concluded that there had been no change in the seriousness of the conditions since the orphan designations in 2008. Isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia

[1] EU/3/08/575, EU/3/08/576 and EU/3/08/577
[2] The maintenance of the orphan designation at time of marketing authorisation would, except in specific situations, give an orphan medicinal product 10 years of market exclusivity in the EU. This means that in the 10 years after its authorisation similar products with a comparable therapeutic indication cannot be placed on the market.

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remain conditions that are debilitating in the long term and life threatening, particularly due to neurological complications caused by hyperammonaemia.

Prevalence of the conditions

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia remain below the ceiling for orphan designation, which is 5 people in 10,000. At the time of the review of the orphan designation, the prevalence of these conditions were still estimated to be approximately 0.01, 0.02 and 0.02 in 10,000 people, respectively. This is equivalent to a total of around 3,000 people in the EU affected by these conditions.

Existence of other satisfactory methods of treatment

At the time of the review of the orphan designations, other methods were authorised in the EU for the treatment of isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia. Treatments aimed to remove the ammonia that builds up in the blood, and included sodium benzoate (an ammonia scavenger). Patients were also advised to avoid further build-up of ammonia in the blood by reducing their intake of nitrogen by eating a low-protein diet.

Significant benefit over existing treatments

The COMP concluded that the claim of a significant benefit of Carbaglu in the treatment of isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia is justified on the basis of its new mechanism of action for reducing ammonia, which involves restoring the physiological pathway of ureagenesis. This is supported by data from an observational study including patients with isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia. The study showed that treatment with Carbaglu on its own or in combination with sodium benzoate induced a rapid decrease in ammonia levels in all age groups, reducing the risk of neurological complications.

Therefore, although other satisfactory methods for the treatment of these conditions have been authorised in the EU, the COMP concluded that Carbaglu is of significant benefit for patients affected by these conditions.

Conclusions

Based on the data submitted and the scientific discussion within the COMP, the COMP considered that Carbaglu still meets the criteria for designation as an orphan medicinal product and that it should remain in the Community Register of Orphan Medicinal Products.

Further information on the current regulatory status of Carbaglu can be found in the European public assessment report (EPAR) on the Agency's website ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.