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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Carglumic acid for the treatment of methylmalonic acidaemia

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Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 7 November 2008, orphan designation (EU/3/08/576) was granted by the European Commission to Orphan Europe SARL, France, for carglumic acid for the treatment of methylmalonic acidaemia.

What is methylmalonic acidaemia?

Methylmalonic acidaemia is an inherited disease that usually appears in early infancy. It is caused by an abnormal gene. For a patient to develop this disease, he or she needs to have inherited one copy of the abnormal gene from each parent. This is called 'autosomal recessive' transmission. Patients with methylmalonic acidaemia produce defective versions of an enzyme called methylmalonyl-coenzyme A mutase, which is involved in breaking down proteins and fats in the body. When this breakdown process does not happen normally, it results in a build-up of methylmalonic acid and the toxic substance ammonia in the blood. This causes symptoms such as poor feeding, vomiting, hypotonia (weak muscle tone causing floppiness), lethargy (lack of energy) and encephalopathy (problems with the brain).

The effects of methylmalonic acidaemia can be life-threatening.

What is the estimated number of patients affected by the condition?

At the time of designation, methylmalonic acidaemia affected approximately 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of around 1,000 people*, and is below the

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 502,800,000 (Eurostat 2008).

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ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

Current treatments for methylmalonic acidaemia aim to remove the ammonia that builds up in the blood. They include sodium benzoate, which is an ammonium scavenger (a substance that mops us ammonia in the blood). Patients can also avoid further build-up of ammonia in the blood by reducing their intake of nitrogen intake by eating a low-protein diet.

Carglumic acid could be of significant benefit for the treatment of methylmalonic acidaemia, because it acts differently from other medicinal products. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Carglumic acid is very similar in structure to N-acetylglutamate, which activates an enzyme that breaks down ammonia. Carglumic acid therefore helps break down ammonia, reducing ammonia blood levels and its toxic effects. This is expected to relieve the symptoms of methylmalonic acidaemia that are caused by high blood ammonia levels.

What is the stage of development of this medicine?

The effects of carglumic acid have not been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with methylmalonic acidaemia had been initiated.

At the time of submission carglumic acid was not authorised anywhere in the world for methylmalonic acidaemia or designated as orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 September 2008 recommending the granting of this designation.

Update: carglumic acid (Carbaglu) has been authorised in the EU since 27 May 2011 for treatment of hyperammonaemia due to methylmalonic acidaemia.

More information on 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

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Carglumic acid	Treatment of methylmalonic acidaemia
Bulgarian	Карглуминова киселина	Лечение на метилмалонова ацидемия
Czech	Acidum carglumicum	Léčba methylmalonové acidémie
Danish	Cargluminsyre	Behandling af methylmalonsyreæmi
Dutch	Carglumaatzuur	Behandeling van methylmalonische acidemie
Estonian	Kargluumhape	Metüülmaloon-atsideemia ravi
Finnish	Kargluumihappo	Metyylimalonihappoverisyyden hoito
French	Acide carglumique	Traitement de l'acidémie méthylmalonique
German	Carglumsäure	Behandlung der Methylmalonazidämie
Greek	Καργλουμινικό οξύ	Θεραπεία μεθυλμαλονικής οξυαιμίας
Hungarian	Kargluminsav	Metilmalonsav-acidaemia kezelése
Italian	Acido carglumico	Trattamento dell'acidemia metilmalonica
Latvian	Karglumīnskābe	Metilmalonacidēmijas ārstēšana
Lithuanian	Karglumo rūgštis	Metilmalono acidemijos gydymas
Maltese	Carglumic acid	Kura ta' l-aċidemija metilmalonika
Polish	Kwas kargluminowy	Leczenie acydemii metylomalonowej
Portuguese	Ácido carglúmico	Tratamento da acidémia metilmalónica
Romanian	Acid carglumic	Tratamentul acidemiei metilmalonice
Slovak	Kyselina karglumová	Liečba metylmalónovej acidémie
Slovenian	Kargluminska kislina	Zdravljenje acidemije zaradi metilmalonske kisline
Spanish	Ácido carglúmico	Tratamiento de la acidemia metilmalónica
Swedish	Cargluminsyra	Behandling av metylmalonisk acidemi
Norwegian	Kargluminsyre	Behandling av metylmalonisk acidemi
Icelandic	Carglúmín sýra	Meðferð við metýlmalón blóðsýringu

[1] At the time of designation