20 June 2016
EMA/COMP/306356/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Polyethylene glycol-modified human recombinant truncated cystathionine beta-synthase for treatment of homocystinuria

On 30 May 2016, orphan designation (EU/3/16/1664) was granted by the European Commission to Alan Boyd Consultants Ltd, United Kingdom, for polyethylene glycol-modified human recombinant truncated cystathionine beta-synthase for the treatment of homocystinuria.

What is homocystinuria?

Homocystinuria is an inherited disorder which causes a substance called homocysteine to accumulate in the blood and urine. Patients with homocystinuria usually lack a functioning cystathionine B-synthase, an enzyme that is responsible for breaking down homocysteine. When this enzyme does not work properly, excess homocysteine accumulates in the body which can be toxic at high levels. Symptoms of the disease usually appear in the first few days of life and long-term consequences include learning disabilities, brittle bones, problems with vision and blood disorders.

Homocystinuria is a long-term debilitating and life-threatening disease that leads to blood clots and problems with the heart and blood vessels, and is associated with poor overall survival.

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

At the time of designation, homocystinuria affected less than 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 10,000 people*, and is below the 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?

At the time of designation, betaine was authorised in the EU for the treatment of homocystinuria.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with homocystinuria because studies in experimental models suggested that 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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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medicine used together with the authorised treatment betaine could lower further homocysteine levels. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The medicine is an enzyme replacement therapy that is expected to work by replacing the malfunctioning enzyme in homocystinuria, helping to break down homocysteine and stopping it from building up in the body.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with homocystinuria had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for homocystinuria. Orphan designation of the medicine had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 April 2016 recommending the granting of this designation.

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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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Polyethylene glycol-modified human recombinant truncated cystathionine beta-synthase	Treatment of homocystinuria
Bulgarian	Полиетилен гликол-модифицирана човешка рекомбинантна скъсена цистатионин бета-синтаза	Лечение на хомоцистинурия
Croatian	Ljudska rekombinantna okrnjena cistationin beta sintaza modificirana polietilen glikolom	Liječenje homocistinurije
Czech	Polyetylen glykolem modifikovaná rekombinantní zkrácená cystathion beta syntetáza	Léčba homocystinurie
Danish	Polyethylenglycol-modificeret humant recombinant trunkeret cystathionin beta-synthase	Behandling af homocysteinuri
Dutch	Polyethyleen glycol-gemodifiëerd humaan recombinant getrunceerd cystathionine beta-synthase	Behandeling van homocystinurie
Estonian	Polüetüleenglükooliga modifitseeritud inimese rekombinantne lühendatud tsüstationiini beeta-süntaas	Homotsüstinuuria ravi
Finnish	Polyetyleeni glykoli-modifioitu ihmisen rekombinantti, typistetty kystationiini-beeta-syntaasi	Homokystinurian hoito
French	Cystathionine béta-synthase tronquée recombinante humaine polyéthylène-glycol modifiée	Traitement de l'homocystinurie
German	Mit Polyethylenglycol modifizierte, rekombinante und verkürzte Cystathionin Beta Synthase	Behandlung der Homocysteinurie
Greek	Ανθρώπινη ανασυνδυασμένη κολοβωμένη β-συνθάση κυσταθειονίνης, τροποποιημένη με πολυαιθυλενογλυκόλη.	Θεραπεία της ομοκυστινουρίας
Hungarian	Polietilén-glikollal módositott human rekombináns csonkitott cisztationin béta-szintáz	Homocisztinuria kezelése
Italian	Cystathionine beta-sintasi troncata ricombinante umana modificata con un polietiene-glicolico	Trattamento dell'omocistinuria
Latvian	Ar polietilēna glikolu modificēta saīsināta rekombinanta cilvēka cistationīna beta-sintāze	Homocistinūrijas ārstēšana
Lithuanian	Polietileno glikoliu modifikuota žmogaus rekombinantinė sutrumpinta cistationino beta sintazė	Homocistinurijos gydymas
Maltese	Cystathionine beta-synthase uman rikombinati maqtugħ modifikat b'polyethylene glycol	Kura tal-omoċistinurja
Polish	Ludzka rekombinowana skrócona beta-syntaza cystationinowa modyfikowana poli tlenkiem etylenu	Leczenie homocystynurii
Portuguese	Cistationina beta-sintase humana recombinante truncada e modificada por polietileno glicol	Tratamento da homocistinúria
Romanian	Cistationin beta-sintetaza umană trunchiată recombinantă modificată cu polietilenglicol	Tratamentul homocistinuriei

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Polyetylénglykolom modifikovaná ľudská rekombinantná skrátená cystationín beta-syntáza	Liečba homocystinúrie
Slovenian	S polietilenglikolom modificirana, skrajšana rekombinantna humana cistationin sintaza beta	Zdravljenje homocistinurije
Spanish	Sintasa de Cistacionina beta truncada y modificada con glycol polietilena	Tratamiento de la homocistinuria
Swedish	Humant rekombinant polyethylenglykolmodifierat trunkerat cystathionin betasyntas	Behandling för homocystinuri
Norwegian	Polyetylen glykol-modifisert humant rekombinant trunkert cystathionin beta-syntase	Behandling av homocysteinuri
Icelandic	Pólýethýlen glýkól-breytt manna raðbrigða stýfðurcýstathíónín beta sýnthasi	Meðferð hómócýstínmigu