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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with arginase 1 [cobalt cofactor] (synthetic human) (1:10), trimer for the treatment of hyperargininaemia

On 14 July 2016, orphan designation (EU/3/16/1701) was granted by the European Commission to ERA Consulting GmbH, Germany, for poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with arginase 1 [cobalt cofactor] (synthetic human) (1:10), trimer (also known as AEB1102) for the treatment of hyperargininaemia.

What is hyperargininaemia?

Hyperargininaemia is one of the inherited disorders known as 'urea-cycle disorders', which cause ammonia and other potentially toxic substances to accumulate in the blood. Patients with hyperargininaemia lack arginase type I, one of the liver enzymes needed to get rid of excess nitrogen. In the absence of this liver enzyme, excess nitrogen accumulates in the body in the form of potentially toxic substances including ammonia, which can be harmful at high levels, especially to the brain. Symptoms of the disease usually appear in the first few years of life and include developmental delay, stiffness especially in the legs, vomiting and seizures (fits).

Hyperargininaemia is a long-term debilitating and life-threatening disease that leads to learning disabilities and is associated with poor overall survival.

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

At the time of designation, hyperargininaemia affected approximately 0.06 in 10,000 people in the European Union (EU). This was equivalent to a total of around 3,000 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).

[*]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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What treatments are available?

At the time of designation, glycerol phenylbutyrate (Ravicti) was authorised in the EU for the treatment of urea cycle disorders including hyperargininaemia. Patients were generally advised to control their dietary intake of proteins, which are rich in nitrogen, to reduce the amount of ammonia formed in the body.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with hyperargininaemia because early laboratory studies showed that it may reduce levels of arginine, which contains nitrogen. 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?

This medicine is expected to replace arginase, the enzyme that is lacking in patients with hyperargininaemia. It is thus expected to assist the body to get rid of excess nitrogen, so reducing the amount of potentially toxic substances including ammonia that are produced and therefore the damage to the brain and other organs.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with hyperargininaemia had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for hyperargininaemia. Orphan designation of the medicine had been granted in the USA for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 June 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	Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-,amide with arginase 1 [cobalt cofactor] (synthetic human) (1:10), trimer	Treatment of hyperargininaemia
Bulgarian	Поли(окси-1,2-етанедил), alpha-(карбоксиметил)-омега-метокси-, амид с аргиназа 1 [кобалтов кофактор] (синтетична, човешка) (1:10), тример	Лечение на хипераргининемия
Croatian	Poli(oksi-1,2-etanediil), alpha-(karboksimetil)-omega-metoksi-, amid s arginazom 1 [kobaltni kofaktor] (sintetička humana) (1:10), trimer	Liječenje hiperargininemije
Czech	Poly(oxy-1,2-ethandiyl), alpha-(karboxymethyl)-omega-methoxy-amid s arginázou 1 [kobaltový kofaktor] (syntetická, lidská) (1:10), trimer	Léčba hyperargininémie
Danish	Poly(oxy-1,2-ethanediyl), alfa-(carboxymethyl)-omega-methoxy-, amid med arginase 1 [kofaktor: kobolt] (syntetisk human) (1:10), trimer	Behandling af hyperargininæmi
Dutch	Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide met arginase-1 [kobalt cofactor] (synthetisch humaan) (1:10), trimeer	Behandeling van hyperargininemia
Estonian	Polü(oksü-1,2-etaandiüül), alfa-(karboksümetüül)-omega-metoksü-, amiid arginaas I-ga [koobalti kofaktor] (sünteetiline inimpäritolu) (1:10), trimeer	Hüperargininеemia ravi
Finnish	Poly(oksi-1,2-etaanidiyyli), alpha-(karboksimetyyli)-omega-metoksi-, amidi yhdessä arginaasi 1:n kanssa [kobolttikofaktori] (ihmisen synteettinen) (1:10), trimeeri	Hyperargininemian hoito
French	Poly(oxy-1,2-éthanediyl), alpha-(carboxyméthyl)-omega-méthoxy-, amide avec arginase 1 [cofacteur : cobalt] (humaine de synthèse) (1:10), trimère	Traitement des hyperargininémies
German	Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amid mit Arginase 1 [Cobalt-Cofaktor] (synthetisch, human) (1:10), Trimer	Behandlung einer Hyperargininämie
Greek	Πολυ (οξυ-1,2-αιθανοδιϋλιο), αλφα- (καρβοξυμεθυλ) - ω-μεθοξυ-,αμίδιο με αργινάση 1 [συμπαράγοντα κοβαλτίου] (συνθετικό ανθρώπινο) (1:10), τριμερές	Θεραπεία της υπεραργινιναιμίας
Hungarian	Poli(oxi-1,2-etándiil), alpha-(karboxi-metil)-omega-metoxi-, amid argináz 1-gyel [kobalt kofaktor] (szintetikus humán) (1:10), trimer	Hyperargininaemia kezelésére
Italian	Poli(ossi-1,2-etanediil), alpha-(carbossimetil)-omega-metossi-, amide con arginasi 1 [cofattore cobalto] (umana sintetica) (1:10), trimero	Trattamento dell'iperargininemia

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Poli (oksi-1,2-etānediil), alfa-(karboksimetil)-omega-metoksi-, amīds ar arginānzi 1 [kobalta kofaktors] (sintētiska, cilvēka) (1:10), trimērs	Hiperarginīnēmijas ārstēšana
Lithuanian	Poli-(oksi-1,2-etanediil), alfa-(karboksimetil)-omega-metoksi-, amidas su arginaze 1 [kobalto kofaktorius] (sintetinis žmogaus) (1:10), trimeras	Hiperargininemijos gydymas
Maltese	Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-,amide b'arginase 1 [kofattur tal-cobalt] (sintetiku uman) (1:10), tirmer	Kura ta' l-iperarġininemija
Polish	Poli(oksy-1,2-etanediylo), alpha-(karboksymetylo)-omega-metoksy-, amid z arginazą 1 [kofaktor kobaltowy] (syntetyczną ludzką) (1:10), trimer	Leczenie hyperargininemii
Portuguese	Poli(oxi-1,2-etanodiil), alfa-(carboximetil)-omega-metoxi-, amida com arginase 1 [cofactor de cobalto] (humana sintética) (1:10), trímero	Tratamento da hiperargininémia
Romanian	Poli(oxi-1,2-etandiil), alfa-(carboximetil)-omega-metoxi-, amidă cu arginază 1 [cofactor cobalt] (umană sintetică) (1:10), trimer	Tratamentul hiperargininemiei
Slovak	Poly(oxy-1,2-etándiyl), alpha-(karboxymetyl)-omega-metoxy, amid s arginázou 1 [kofaktor kobalt] (syntetickou ľudskou) (1:10), trimér	Liečba hyperargininémie
Slovenian	Poli(oksi-1,2-etanedil), alpha-(karboksimetil)-omega-metoksi-, amid z arginazo 1 [kofaktor kobalt] (sintetična humana) (1:10), trimer	Zdravljenje hiperargininemije
Spanish	Poli(oxi-1,2-etanediil), alpha-(carboximetil)-omega-metoxi-, amida con arginasa 1 [cofactor cobalto] (humana sintética) (1:10), trímero	Tratamiento de la hiperargininemia
Swedish	Poly(oxi-1,2-etanediyl), alpha-(karboximetyl)-omega-metoxi-, amid med arginas 1 [kobolt kofaktor] (syntetisk human) (1:10), trimer	Behandling av hyperargininemi
Norwegian	Poly(oksy-1,2-etandiyl), alfa-(karboksymetyl)-omega-metoksy-, amid med arginase 1 [kobolt kofaktor] (syntetisk humant) (1:10), trimer	Behandling av hyperargininemi
Icelandic	Pólý(oxý-1,2-etandíýl), alpha-(karboxýmetýl)- ómega-metoxý-, amíð ásamt argínasa 1 [kóbalt hjálparþáttur] (tilbúið úr mönnum) (1:10), þríþætt	Meðferð á hýperargíníndreyra