15 August 2013
EMA/COMP/413220/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Heterologous human adult liver-derived progenitor cells for the treatment of citrullinaemia type 2

On 17 July 2013, orphan designation (EU/3/13/1166) was granted by the European Commission to Promethera Biosciences, Belgium, for heterologous human adult liver-derived progenitor cells for the treatment of citrullinaemia type 2.

What is citrullinaemia type 2?

Citrullinaemia type 2 is one of the inherited disorders known as 'urea cycle disorders', which cause ammonia to accumulate in the blood. Patients with this disorder lack 'glutamate aspartate transporter', one of the liver enzymes that are needed to get rid of excess nitrogen. In the absence of this liver enzyme, excess nitrogen accumulates in the body in the form of ammonia, which can be toxic at high levels, especially to the brain. Symptoms of the disease may appear during adulthood and include lethargy (lack of energy), vomiting, loss of appetite, seizures (fits) and coma.

Citrullinaemia type 2 is a long-term debilitating and life-threatening disease that leads to mental retardation and is associated with poor overall survival.

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

At the time of designation, citrullinaemia type 2 affected between 0.01 and 0.09 in 10,000 people in the European Union (EU). This was equivalent to a total of between 500 and 4,500 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, no satisfactory methods were authorised in the EU for the treatment of citrullinaemia type 2. Patients were advised to control their dietary intake of proteins, which are rich in nitrogen, to reduce the amount of ammonia formed in the body.

*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. This represents a population of 509,000,000 (Eurostat 2013).

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How is this medicine expected to work?

This medicine is an advanced therapy medicine that belongs to the group called 'somatic cell therapy products'. These are medicines that contain cells or tissues that have been manipulated to change their biological characteristics so that they can be used to cure, diagnose or prevent a disease. The medicine is made up of progenitor (immature) cells derived from the liver of an adult donor ('heterologous'). When implanted into the liver of a patient, it is believed that these heterologous liver-derived progenitor cells will develop into mature, healthy liver cells that can produce the glutamate aspartate transporter enzyme. The new cells are thereby expected to reduce the accumulation of ammonia and to relieve the symptoms of the disease.

What is the stage of development of this medicine?

The effects of heterologous human adult liver-derived progenitor cells have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with urea cycle disorders were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for citrullinaemia type 2. Orphan designation of the medicine had been granted in the United States for urea cycle disorders.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 June 2013 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:

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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	Heterologous human adult liver-derived progenitor cells	Treatment of citrullinaemia type 2
Bulgarian	Хетероложни човешки прогенитorни клетки, получени от черен дроб на възрастен	Лечение на цитрилинемия тип 2
Czech	Heterologní progenitorové buňky získané z jater dospělého člověka	Léčba citrulinémie typu 2
Croatian	Heterologne progenitorske stanice izolirane iz jetre odraslog čovjeka	Liječenje citrulinemije tipa 2
Danish	Heterologe humane leverderiverede progenitorceller fra voksne	Behandling af citrullinæmi type 2
Dutch	Uit de adulte lever afgeleide heterologe humane progenitorcellen	Behandeling van citrullinemia type2
Estonian	Heteroloogilised täiskasvanud inimese maksast pärinevad eellasrakud	2.tüüpi tsitrullineemia ravi
Finnish	Heterologiset aikuisen ihmisen maksaperäiset progenitorisolut	2-Tyypin sitrullinemian hoito
French	Cellules progénitrices hétérologues dérivées du foie adulte humain	Traitement de la citrullinémie de type 2
German	Aus der adulten Leber abgeleitete heterologe Vorläuferzellen	Behandlung einer Citrullinämie Typ 2
Greek	Ανθρώπινα ετερόλογα προγονικά κύτταρα προερχόμενα από ήπαρ ενηλίκου	Θεραπεία της κιτρουλιναιμίας τύπου 2.
Hungarian	Heterológ humán felnőttek májából származó progenitor sejtek	2-es típusú citrullinaemia kezelésére
Italian	Cellule progenitrici eterologhe di fegato umano adulto	Trattamento della citrullinemia di tipo 2
Latvian	Heterologas pieauguša cilvēka aknu priekšgājēju šūnas	2. tipa citrulinēmijas ārstēšana
Lithuanian	Heterologinės pirminės ląstelės, išskirtos iš suaugusio žmogaus kepenų	Citrulinemijos 2 tipo gydymas
Maltese	Ċelloli proġenituri eteroloġi mnisslin minn fwied adult uman	Kura taċ-ċitrullinemija tat-tip 2
Polish	Ludzkie heterologiczne komórki progenitorowe izolowane z wątroby osoby dorosłej	Leczenie cytrulinemii typu 2
Portuguese	Células progenitoras heterólogas derivadas do fígado de adultos humanos	Tratamento da citrulimémia Tipo 2
Romanian	Celule progenitoare heterologe umane derivate din celule hepatice adulte	Tratamentul citrulinemiei de tip 2

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Heterológne progenitorové bunky derivované z pečene dospelého človeka	Liečba citrulinémie 2. typu
Slovenian	Heterologne progenitorne celice pridobljene iz jeter odraslega človeka	Zdravljenje citrulinemije tipa 2
Spanish	Células progenitoras heterólogas extraídas de hígado humano adulto	Tratamitento de la citrulinemia de tipo 2
Swedish	Humana heterologa leverderiverade progenitorceller från vuxna	Behandling av citrullinemi typ 2
Norwegian	Heterologe leverderiverte progenitorceller fra voksne	Behandling av citrullinemi type 2
Icelandic	Ósamgena lifrarforstigsfrumur úr fullorðnum	Meðferð á cítrúllíndreyra gerð 2