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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Heterologous human adult liver-derived progenitor cells for the treatment of argininosuccinic aciduria

On 17 July 2013, orphan designation (EU/3/13/1163) was granted by the European Commission to Promethera Biosciences, Belgium, for heterologous human adult liver-derived progenitor cells for the treatment of argininosuccinic aciduria.

What is argininosuccinic aciduria?

Argininosuccinic aciduria is one of the inherited disorders known as 'urea cycle disorders', which cause ammonia to accumulate in the blood. Patients with this disorder lack 'argininosuccinate lyase', 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 usually appear in the first few days of life and include lethargy (lack of energy), vomiting, loss of appetite, seizures (fits) and coma.

Argininosuccinic aciduria is a long-term debilitating and life-threatening disease that leads to mental retardation and is associated with a high mortality rate.

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

At the time of designation, argininosuccinic aciduria affected approximately 0.19 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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, no satisfactory methods were authorised in the EU for the treatment of argininosuccinic aciduria. 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 argininosuccinate lyase 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 argininosuccinic aciduria. 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 argininosuccinic aciduria
Bulgarian	Хетероложни човешки прогениторни клетки, получени от черен дроб на възрастен	Лечение на аргининосукцининова ацидурия
Czech	Heterologní progenitorové buňky získané z jater dospělého člověka	Léčba argininosukcinátové acidurie
Croatian	Heterologne progenitorske stanice izolirane iz jetre odraslog čovjeka	Liječenje argininosukcinske acidurije
Danish	Heterologe humane leverderiverede progenitorceller fra voksne	Behandling af argininravsyreuri
Dutch	Uit de adulte lever afgeleide heterologe humane progenitorcellen	Behandeling van argininosuccinic aciduria
Estonian	Heteroloogilised täiskasvanud inimese maksast pärinevad eellasrakud	Argininosuktsiin-atsiduuria ravi
Finnish	Heterologiset aikuisen ihmisen maksaperäiset progenitorisolut	Argininosukkinaattiasidurian hoito
French	Cellules progénitrices hétérologues dérivées du foie adulte humain	Traitement de l'acidurie argininosuccinique
German	Aus der adulten Leber abgeleitete heterologe Vorläuferzellen	Behandlung einer Argininosukzinoazidurie
Greek	Ανθρώπινα ετερόλογα προγονικά κύτταρα προερχόμενα από ήπαρ ενηλίκου	Θεραπεία της αργινοηλεκτρικής οξυουρίας.
Hungarian	Heterológ humán felnőttek májából származó progenitor sejtek	Argininoszukcinin anuria kezelésére
Italian	Cellule progenitrici eterologhe di fegato umano adulto	Trattamento dell'aciduria argininosuccinica
Latvian	Heterologas pieauguša cilvēka aknu priekšgājēju šūnas	Arginīna sukcināta acidūrijas ārstēšana
Lithuanian	Heterologinės pirminės ląstelės, išskirtos iš suaugusio žmogaus kepenų	Arginino sukcininės acidurijos gydymas
Maltese	Ċelloli proġenituri eteroloġi mnisslin minn fwied adult uman	Kura tal-aċidurja arġininosuċċinika
Polish	Ludzkie heterologiczne komórki progenitorowe izolowane z wątroby osoby dorosłej	Leczenie acydurii argininobursztynianowej
Portuguese	Células progenitoras heterólogas derivadas do fígado de adultos humanos	Tratamento da acidúria argininosuccínica
Romanian	Celule progenitoare heterologe umane derivate din celule hepatice adulte	Tratamentul aciduriei argininosuccinice

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Heterológne progenitorové bunky derivované z pečene dospelého človeka	Liečba arginínosukcinátovej acidúrie
Slovenian	Heterologne progenitorne celice, pridobljene iz jeter odraslega človeka	Zdravljenje argininsukcinilne acidurije
Spanish	Células progenitoras heterólogas extraídas de hígado humano adulto	Tratamiento de la aciduria argininsuccínica
Swedish	Humana heterologa leverderiverade progenitorceller från vuxna	Behandling av argininbärnstensaciduri
Norwegian	Heterologe leverderiverte progenitorceller fra voksne	Behandling av argininsuccinaturiravsyreuril
Icelandic	Ósamgena lifrarforstigsfrumur úr fullorðnum	Meðferð á arginínósúksíniksýrumigu