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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

heterologous human adult liver derived stem cells for the treatment of ornithine-transcarbamylase deficiency

On 4 February 2008, orphan designation (EU/3/08/530) was granted by the European Commission to Prof Etienne Sokal, Belgium, for heterologous human adult liver derived stem cells for the treatment of ornithine-transcarbamylase deficiency.

The sponsorship was transferred to Promethera Biosciences, Belgium, in June 2010.

What is ornithine-transcarbamylase deficiency?

Ornithine-transcarbamylase deficiency is a congenital error of metabolism, which causes hyperammonemia (abnormally high levels of ammonia in the blood) because a genetic mutation renders one of the liver enzymes responsible for ammonium elimination non-functional. As ammonia cannot be eliminated easily, it accumulates in the body. Ammonia is toxic for the brain, and leads to neurological damage depending on the duration and degree of hyperammonaemia. The disease is usually milder in females than in males, because it is caused by a damaged gene on the X chromosome; as females have two X chromosomes, the normal gene on the other chromosome usually compensates the damage at least partially. Males however have only one X chromosome, so if the gene is damaged there is no compensation. The condition is chronically debilitating and life-threatening.

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

At the time of designation, ornithine-transcarbamylase deficiency affected less than 0.6 in 10,000 people in the European Union (EU)*. This is equivalent to a total of fewer than 30,000 people, and is below the threshold 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 based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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What treatments are available?

The long-term management of the disease is based on low-protein diet to avoid excess ammonia production and pharmacological treatment to detoxify ammonium. Liver transplantation is a complex operation, with important surgical risks, and it can be associated with postoperative mortality. At the time of submission of the application for orphan drug designation, other methods of treatment of hyperammonemia were authorised in the Community. However, liver transplantation is currently the only curative treatment. Liver transplantation is a procedure in which the failed liver is removed from the patient's body, and liver tissue from a healthy donor is transplanted into the same location.

Heterologous human adult liver derived stem cells might be of potential significant benefit for the treatment of ornithine-transcarbamylase deficiency because they may improve the long-term outcome of the patients. The 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?

Liver cells are able to perform certain specific functions. Heterologous human adult liver derived stem cells are stem cells isolated from the adult liver itself. Stem cells have the capacity to differentiate (to change their characteristics and capacities and acquire new specific functions) into more mature liver cells. The cells will come from a donor, not from the patient (heterologous). The mechanism of action is not fully understood but it is believed that the heterologous human adult liver derived stem cells will become mature and functional liver cells, therefore they will be able to provide the enzymes lacking in the condition.

What is the stage of development of this medicine?

The evaluation of the effects of heterologous human adult liver derived stem cells in experimental models is ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with ornithine-transcarbamylase deficiency were initiated.

Heterologous human adult liver derived stem cells was not authorised anywhere worldwide for ornithine-transcarbamylase deficiency or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

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

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 European Union) 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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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 stem cells	Treatment of ornithine-transcarbamylase deficiency
Bulgarian	Човешки хетероложни стволови клетки, получени от черен дроб на възрастен	Лечение на дефицит на орнитин транскарбамилаза
Czech	Heterologní buňky získané z jater dospělého člověka	Léčba nedostatku transkarbamylázy ornithinu
Danish	Heterologe humane leverderiverede stamceller fra voksne	Behandling af ornithin transcarbamylase defekt
Dutch	Uit adulte lever afgeleide heterologe humane stamcellen	Behandeling van ornithine transcarbamylase deficiëntie
Estonian	Heteroloogilised täiskasvanu inimese maksast pärinevad tüvirakud	Ornitiintranskarbamülaasi puudulikkuse ravi
Finnish	heterologisia aikuisen ihmisen maksaperäisiä kantasoluja	Ornitiinitranskarbamylaasin puutoksen hoito
French	Cellules souches heterologues extraites de foie adulte humain	Traitement du déficit en ornithine transcarbamylase
German	Aus Lebergewebe isolierte heterologe adulte humane Stammzellen	Behandlung des Ornithintranscarbamylase-Mangels
Greek	Ανθρώπινα ετερόλογα βλαστικά κύτταρα από ήπαρ ενήλικος	Αγωγή για την έλλειψη της τρανσκαρβαμυλάσης της ορνιθίνης
Hungarian	Heterológ human felnőtt máj eredetű őssejt	Ornitin transzkarbamiláz hiány kezelése
Italian	cellule staminali eterologhe di fegato umano adulto	Trattamento del deficit di ornitina-transcarbamilasi
Latvian	Heteroloģisku pieaugušā cilvēka aknu cilmes šūnas	Ornitīna transkarbamilāzes nepietiekamības ārstēšana
Lithuanian	Heterologinės suaugusiojo žmogaus kepenų kamieninės ląstelės	Ornitintranskarbamilazės stokos gydymas
Maltese	Ċelloli staminali eteroloġi mnisslin minn fwied adult uman	Kura ta' defiċjenza ta’ l-Ornithine Transcarbamylase
Polish	Ludzkie heterologiczne komórki pnia izolowane z wątroby	Leczenie pacjentów z niedoborem transkarbamylazy ornitynowej
Portuguese	Células estaminais humanas de tecido hepático heterologo adulto	Tratamento da deficiência de ornitina-transcarbamilase
Romanian	celule stem heterologe extrase din tesut hepatic uman adult	Tratamentul deficitului de ornitin-transcarbamilază

[1] At the time of designation

Language	Active Ingredient	Indication
Slovak	Heterológne kmeňové bunky získané z pečene dospelého človeka	Liečba nedostatku transkarbamylázy ornitínu
Slovenian	heterologne jetrne zarodne celice pridobljene iz odraslega človeka	Zdravljenje pomanjkanja ornitin-transkarbamilaze
Spanish	Células madre humanas extraídas de tejido hepático heterólogo adulto	Tratamiento de la deficiencia de ornitina transcarbamilasa
Swedish	Heterologa vuxna mänskliga leverderiverade stamceller	Behandling av brist på ornitintranskarbamylas
Norwegian	Heterologe humane leverstamceller fra voksen	Behandling av ornitintranskarbamylase-mangel
Icelandic	Manna-lifrarstofnfrumur úr fullorðnum	Meðferð við skorti á ornitín transkarbamýlasa