13 October 2011
EMA/COMP/661152/2011
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 27 September 2011, orphan designation (EU/3/11/904) was granted by the European Commission to Fresenius Medical Care Deutschland GmbH, Germany, for heterologous human adult liver-derived stem cells for the treatment of ornithine transcarbamylase deficiency.

What is ornithine transcarbamylase deficiency?

Ornithine transcarbamylase deficiency is one of the inherited disorders known as 'urea cycle disorders', which cause ammonia to accumulate in the blood. Patients with ornithine transcarbamylase deficiency lack 'ornithine transcarbamylase', one of the liver enzymes that are needed to get rid of excess nitrogen. In the absence of this enzyme, 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.

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 their other X chromosome usually compensates for the damage. Men have an X and a Y chromosome.

Ornithine transcarbamylase deficiency is a long-term debilitating and life-threatening disease due to the irreversible damage it can cause to the nervous system.

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

At the time of designation, ornithine transcarbamylase deficiency affected less than 0.1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of fewer than 5,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 506,300,000 (Eurostat 2011).

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What treatments are available?

At the time of designation, sodium phenylbutyrate was authorised in the EU for the treatment of some urea cycle disorders, including ornithine transcarbamylase deficiency. In addition, 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. Liver transplantation had also been used in some patients.

The sponsor has provided sufficient information to show that heterologous human adult liver-derived stem cells might be of significant benefit for patients with ornithine transcarbamylase deficiency because it works in a different way to existing treatments and early studies in experimental models show that it might improve the treatment of patients with this condition by re-establishing a normally functioning urea cycle. 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 made up of stem cells derived from the liver of an adult donor ('heterologous'). Stem cells are cells that can develop into different types of cell. When implanted in a patient, it is believed that these heterologous liver-derived stem cells will develop into mature, healthy liver cells that can produce the ornithine transcarbamylase enzyme. The new cells are therefore expected to restore the normal urea cycle and thereby relieve the symptoms of the disease.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, no clinical trials with the medicinal product in patients with ornithine transcarbamylase deficiency had been started.

At the time of submission, the medicinal product was not authorised anywhere in the EU for ornithine transcarbamylase deficiency or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 July 2011 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 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 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
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

[1] At the time of designation

Language	Active ingredient	Indication
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