5 June 2012
EMA/COMP/222564/2012
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Heterologous human adult liver-derived stem cells for the treatment of acute liver failure

On 26 April 2012, orphan designation (EU/3/12/983) 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 acute liver failure.

What is acute liver failure?

Acute liver failure is the sudden loss of normal liver functions in a patient with a previously normal liver and without evidence of chronic (long-term) liver disease. The most common first sign of liver failure is jaundice (yellowing of the skin). Acute liver failure brings serious complications such as bruising and bleeding due to impaired blood clotting, cerebral oedema (swelling around the brain), convulsions (fits) and coma. The most common causes of acute liver failure in Europe are toxic damage (for example due to consumption of large amounts of alcohol or overdose of medicines such as paracetamol) or viral hepatitis (an infectious disease that affects the liver).

Acute liver failure is a long-term debilitating and life-threatening disease because of its damaging effects on the brain and other organs.

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

At the time of designation, acute liver failure affected approximately 0.6 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 30,000 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, the main treatment option for acute liver failure was liver transplantation. Patients with acute liver failure caused by paracetamol overdose were treated with N-acetylcysteine.

[*]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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The sponsor has provided sufficient information to show that heterologous human adult liver-derived stem cells might be of significant benefit for patients with acute liver failure, because early studies show that this medicine may improve the liver's ability to function and delay the need for liver transplantation. In addition the greater availability of liver stem cells used to make the medicine compared with new livers for transplantation may contribute to improving the outcome of patients. These assumptions 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. The new cells are expected to improve the liver's ability to function and thereby relieve the symptoms of the disease.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of heterologous liver-derived stem cells in experimental models was ongoing.

At the time of submission, no clinical trials with heterologous liver-derived stem cells in patients with acute liver failure had been started.

At the time of submission, heterologous liver-derived stem cells was not authorised anywhere in the EU for acute liver failure 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 March 2012 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 stem cells	Treatment of acute liver failure
Bulgarian	Хетероложни човешки стволови клетки, получени от черен дроб на възрастен	Лечение на остра чернодробна недостатъчност
Czech	Heterologní buňky získané z jater dospělého člověka	Léčba Akutní jaterní insuficience
Danish	Heterologe humane leverderiverede stemceller fra voksne	Behandling af akut leversvigt
Dutch	Heterologe humaan adulte lever-afgeleide stamcellen	Behandeling van acuut leverfalen
Estonian	Heteroloogilised täiskasvanud inimese maksast pärinevad tüvirakud	Akuutse maksapuudulikkuse ravi
Finnish	Heterologisia, aikuisen ihmisen maksaperäisiä kantasoluja	Akuutin maksan vajaatoiminnan hoito
French	Cellules souches hétérologues extraites de foie adulte humain	Traitement de l'insuffisance hépatique aiguë
German	Aus Lebergewebe isolierte heterologe adulte humane Stammzellen	Behandlung des akuten Leberversagens
Greek	Ανθρώπινα ετερόλογα βλαστικά κύτταρα προερχόμενα από ήπαρ ενηλίκου	Θεραπεία της οξείας ηπατικής ανεπάρκειας
Hungarian	Heterológ humán felnőtt máj eredetű őssejt	Akut májelégtelenség kezelése
Italian	Cellule staminali eterologhe di fegato umano adulto	Trattamento della insufficienza epatica acuta
Latvian	Heteroloģisku pieaugušā cilvēka aknu cilmes šūnas	Akūtas aknu mazspējas ārstēšana
Lithuanian	Heterologinės kamieninės ląstelės, išskirtos iš suaugusiojo žmogaus kepenų	Ūmaus kepenų nepakankamumo gydymas
Maltese	Ċelloli staminali eteroloġi mnisslin minn fwied adult uman	Kura ta' insuffiċjenza akuta tal-fwied
Polish	Ludzkie heterologiczne komórki macierzyste izolowane z wątroby	Leczenie ostrej niewydolności wątroby
Portuguese	Células estaminais Heterólogas Derivadas do Fígado de Humanos Adultos	Tratamento da insuficiência hepática aguda
Romanian	Celule stem heterologe extrase din ţesut hepatic uman adult	Tratamentul insuficienţei hepatice acute
Slovak	Heterológne kmeňové bunky z pečene dospelého človeka	Liečba akútneho zlyhania pečene
Slovenian	Heterologne matične celice, pridobljene iz jeter odraslega človeka	Zdravljenje akutne jetrne odpovedi
Spanish	Células madre heterólogas extraídas de	Tratamiento de la insuficiencia hepática

[1] At the time of designation

Language	Active ingredient	Indication
	tejido hepático humano adulto	aguda
Swedish	Humana heterologa vuxna leverderiverade stamceller	Behandling av akut leversvikt
Norwegian	Humane heterologe leverderiverte stamceller fra voksne	Behandling av akutt leversvikt
Icelandic	Manna ósamgena lifrarstofnfrumur úr fullorðnum	Meðferð bráðrar lifrarbilunar