



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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 Crigler-Najjar syndrome

On 29 November 2007, orphan designation (EU/3/07/506) was granted by the European Commission to Prof Etienne Sokal, Belgium, for heterologous human adult liver derived stem cells for the treatment of Crigler-Najjar syndrome.

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

What is Crigler-Najjar syndrome?

Crigler-Najjar syndrome is an inherited disorder that results in failure of proper bilirubin elimination from the liver via the bile. Bilirubin is a product that results from the breakdown of hemoglobin from old or damaged red blood cells. When bilirubin cannot be released from the liver, it accumulates in the body and becomes toxic for the brain. It is associated with jaundice (yellowish colour of the skin and the eyes). The condition is chronically debilitating and life-threatening.

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

At the time of designation, Crigler-Najjar syndrome affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 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).

What treatments are available?

Phototherapy, which breaks down bilirubin, is used in these patients. However, the only curative treatment is liver transplantation. Liver transplantation refers to a procedure in which a failed liver is removed from the patient's body and liver tissue from a healthy donor is transplanted into the same location. The procedure is the most common method used to transplant livers. However, liver transplantation is a complex operation, with important surgical risks, and is often associated with significant postoperative mortality. At the time of submission of the application for orphan drug

*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. At the time of designation, this represented a population of 500,300,000 (Eurostat 2007).



designation, other methods of treatment for Crigler-Najjar syndrome were authorised in the Community.

Heterologous human adult liver derived stem cells might be of potential significant benefit for the treatment of Crigler-Najjar syndrome because they might 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 specialised to perform certain specific functions. Heterologous human adult liver derived stem cells are stem cells isolated from an adult liver with 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 and not the patient (heterologous). It is planned to isolate and treat the cells in such a way that they might be given to patients suffering from Crigler-Najjar syndrome. 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, giving support to the liver function.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the effects of heterologous human adult liver derived stem cells had been evaluated in experimental models.

Heterologous human adult liver derived stem cells were not authorised anywhere in the world for the treatment of Crigler-Najjar syndrome, or designated as an 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 October 2007 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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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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Heterologous Human Adult Liver Derived Stem Cells	Treatment of Crigler-Najjar syndrome
Bulgarian	Човешки хетероложни стволони клетки, получени от черен дроб на възрастен	Лечение на синдром на Crigler-Najjar
Czech	Heterologní buňky získané z jater dospělého člověka	Léčba Crigler-Najjarova syndromu
Danish	Heterologe humane leverderiverede stamceller fra voksne	Behandling af Crigler-Najjar syndrom
Dutch	Uit adulte lever afgeleide heterologe humane stamcellen	Behandeling van Crigler-Najjar syndroom
Estonian	Heteroloogilised täiskasvanu inimese maksast pärinevad tüvirakud	Crigler-Najjar'i sündroomi ravi
Finnish	heterologisia aikuisen ihmisen maksaperäisiä kantasoluja	Crigler-Najjar syndrooman hoito
French	Cellules souches heterologues extraites de foie adulte humain	Traitement du syndrome de Crigler-Najjar
German	Aus Lebergewebe isolierte heterologe adulte humane Stammzellen	Behandlung des Crigler-Najjar Syndroms
Greek	Ανθρώπινα ετερόλογα βλαστικά κύτταρα από ήπαρ ενήλικος	Θεραπεία σύνδρομο Crigler-Najjar
Hungarian	Heterológ human felnőtt máj eredetű őssejt	Crigler-Najjar szindróma kezelése
Italian	cellule staminali eterologhe di fegato umano adulto	Trattamento della sindrome di Crigler-Najjar
Latvian	Heterológisku pieaugušā cilvēka aknu cilmes šūnas	Krīglera un Nadžāra sindroma ārstēšana
Lithuanian	Heterologinės suaugusiojo žmogaus kepenų kamieninės ląstelės	Crigler Nadjjar'o sindromo gydymas
Maltese	Ċelloli staminali eteroloġi mnislin minn fwied adult uman	Kura tas-sindrome ta' Crigler Najjar
Polish	Ludzkie heterologiczne komórki pnia izolowane z wątroby	Leczenie zespołu Criglera-Najjara
Portuguese	Células estaminais humanas de tecido hepático heterologo adulto	Tratamento de síndrome de Crigler-Najjar
Romanian	celule stem heterologe extrase din tesut hepatic uman adult	Tratamentul sindromului Crigler Najjar
Slovak	Heterológne kmeňové bunky získané z pečene dospelého človeka	Liečba Crigler-Najjarovho syndrómu
Slovenian	heterologne jetrne zarodne celice pridobljene iz odraslega človeka	Zdravljenje sindroma Crigler-Najjar

¹ At the time of designation

Language	Active Ingredient	Indication
Spanish	Células madre humanas extraídas de tejido hepático heterólogo adulto	Tratamiento del síndrome de Crigler-Najjar
Swedish	heterologa vuxna mänskliga leverderiverade stamceller	Behandling av Crigler-Najjar syndrom
Norwegian	Heterologe humane leverstamceller fra voksne	Behandling av Crigler Najjar syndrom
Icelandic	Manna-lifrarstofnfrumur úr fullorðnum	Meðfrð við Crigler-Najjar heilkenni