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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Immortalised human C3A hepatoblastoma cells for the treatment of acute liver failure

On 19 June 2013, orphan designation (EU/3/13/1143) was granted by the European Commission to Vital Therapies Limited, United Kingdom, for immortalised human C3A hepatoblastoma 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 life-threatening disease because of its damaging effects on the liver, brain and other organs.

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

At the time of designation, acute liver failure affected less than 1 person in 10,000 per year in the European Union (EU). This was equivalent to a total of fewer than 50,000 people per year[*], and is below the ceiling for orphan designation. 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 509,000,000 (Eurostat 2013).

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The sponsor has provided sufficient information to show that immortalised human C3A hepatoblastoma cells might be of significant benefit for patients with acute liver failure, because early studies show that they may temporarily relieve some of the symptoms of the condition and delay the need for liver transplantation. 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 product consists of a cartridge containing many fine tubes lined with membranes, on the other side of which are cells derived from a type of liver tumour (hepatoblastoma). The cells are able to function like normal liver cells, but they can survive and grow inside the device (hence they are called 'immortalised'). The device is expected to act as a temporary 'artificial liver' outside the patient's body. The patient's blood is continuously drawn from a vein, and the plasma (the liquid part of the blood) is separated and passes through the tubes in the cartridge. Toxins that affect the brain in patients with liver failure can pass through the membrane to the hepatoblastoma cells, which break them down. In turn, the cells produce substances needed for blood clotting and other functions, which can pass back into the plasma. The plasma is then recombined with the other parts of the blood and the blood is returned to the patient. In this way, the product is expected to carry out the liver's essential functions, thereby relieving the symptoms of acute liver failure.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with immortalised human C3A hepatoblastoma cells in patients with acute liver failure were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for acute liver failure. Orphan designation had been granted in the United States of America for the treatment of acute liver failure.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 15 May 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	Immortalised human C3A hepatoblastoma cells	Treatment of acute liver failure
Bulgarian	Безсмъртни човешки C3A хепатобластомни клетки	Лечение на остра чернодробна недостатъчност
Czech	Imortalizované lidské buňky C3A hepatoblastoma	Léčba Akutní jaterní insuficience
Danish	Immortaliseret humane C3A hepatoblastom celler	Behandling af akut leversvigt
Dutch	Geïmmortaliseerde humane C3A hepatoblastoma cellen	Behandeling van acuut leverfalen
Estonian	Pidevalt paljunevad (*immortalised*) inimese C3A hepatoblastoomi rakud	Akuutse maksapuudulikkuse ravi
Finnish	Immortalisoidut ihmisen C3A-hepatoblastoomasolut	Akuutin maksan vajaatoiminnan hoito
French	Hepatoplastome C3A humains immortalisées	Traitement de l'insuffisance hépatique aiguë
German	Immortalisierte humane C3A Hepatoblastom Zellen	Behandlung des akuten Leberversagens
Greek	Αθανατοποιημένα ανθρώπινα κύτταρα ηπατοβλαστώματος C3A	Θεραπεία της οξείας ηπατικής ανεπάρκειας
Hungarian	Immortalizált humán C3A hepatoblastoma sejtek	Akut májelégtelenség kezelése
Italian	Cellule immortalizzate umane di epatoblastoma C3A	Trattamento della insufficienza epatica acuta
Latvian	Dzīvotspējīgas cilvēka C3A hepatoblastomas šūnas	Akūtas aknu mazspējas ārstēšana
Lithuanian	Imortalizuotos žmogaus C3A hepatoblastomos ląstelės	Ūminio kepenų nepakankamumo gydymas
Maltese	Ċelloli epatoblastoma C3A umani magħmula immortali	Kura ta' insuffiċjenza akuta tal-fwied
Polish	Ludzkie komórki *pomitotyczne odwracalne* C3A hepatoblastomy	Leczenie ostrej niewydolności wątroby
Portuguese	Células imortalizadas C3A derivadas do hepatoblastoma humano	Tratamento da insuficiência hepática aguda
Romanian	Celule de hepatoblastom C3A umane imortalizate	Tratamentul insuficienţei hepatice acute
Slovak	Imortalizované bunky ľudského hepatoblastómu C3A	Liečba akútneho zlyhania pečene
Slovenian	Nesmrtne celice človeškega C3A hepatoblastoma	Zdravljenje akutne jetrne odpovedi

[1] At the time of designation

Language	Active ingredient	Indication
Spanish	Células humanas inmortalizadas de hepatoblastoma C3A	Tratamiento de la insuficiencia hepática aguda
Swedish	Immortaliserade humana C3A hepatoblastomceller	Behandling av akut leversvikt
Norwegian	Immortaliserte humane C3A hepatoblastomceller	Behandling av akutt leversvikt
Icelandic	C3A hepatóblastóma frumur sem hafa verið gerðar gerðar ódauðlegar	Meðferð bráðrar lifrarbilunar