



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public summary of opinion on orphan designation

Allogeneic hepatoblastoma cells encapsulated in alginate, ex vivo expanded for the treatment of acute liver failure

On 21 August 2020, orphan designation EU/3/20/2312 was granted by the European Commission to ESPL Regulatory Consulting Limited, Ireland, for allogeneic hepatoblastoma cells encapsulated in alginate, ex vivo expanded for the treatment of acute liver failure.

What is acute liver failure?

Acute liver failure is the sudden loss of normal liver function 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 excessive bleeding due to impaired blood clotting, swelling around the brain, convulsions (fits) and coma.

The most common causes of acute liver failure are viral hepatitis (an infectious disease that affects the liver), overdose of medicines such as paracetamol or consumption of toxic substances such as poisonous mushrooms.

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 acute liver failure?

At the time of designation, acute liver failure affected approximately 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).



What treatments are available?

At the time of designation, the main treatment option for acute liver failure was liver transplantation. In addition, medicines were used to treat complications of liver failure such as hepatic encephalopathy. Early treatment with acetylcysteine was used to prevent liver failure due to paracetamol overdose.

The sponsor has provided sufficient information to show that this product might be of significant benefit for patients with acute liver failure because laboratory data suggest it could improve liver function. 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?

The medicine is made of liver cells that have been modified and grown in a laboratory. The cells are embedded in a device to create a temporary artificial liver while the patient's liver heals. It is expected that when plasma from the patient's blood passes through this artificial liver, the liver cells in it will remove harmful substances, produce necessary new proteins and help to keep the correct balance of substances in the plasma. This can help to prevent some complications 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, no clinical trials with the medicine had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of acute liver failure or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 16 July 2020, 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

Contact details of the current sponsor for this orphan designation can be found on [EMA website](#).

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	Allogeneic hepatoblastoma cells encapsulated in alginate, ex vivo expanded	Treatment of acute liver failure
Bulgarian	Алогенни хепатобластомни клетки, енкапсулирани в алгинат, експандирани ex vivo	Лечение на остра чернодробна недостатъчност
Croatian	Alogene ex vivo ekspandirane stanice hepatoblastoma enkapsulirane unutar alginata	Liječenje akutnog zatajenja jetre
Czech	Alogenní buňky hepatoblastomu enkapsulované do alginátu, ex vivo expandované	Léčba akutní jaterní insuficience
Danish	Allogene hepatoblastomceller indkapslet i alginat, ex vivo-ekspanderede	Behandling af akut leversvigt
Dutch	Allogene hepatoblastoomcellen ingekapseld in alginat, ex vivo geëxpandeerd	Behandeling van acuut leverfalen
Estonian	Alginaati kapseldatud ex vivo paljundatud allogeensed hepatoblastoomi rakud	Akuutse maksapuudulikkuse ravi
Finnish	Alginaattiin kapseloidut allogeeniset hepatoblastoomasolut, ex vivo -laajennetut	Akuutin maksan vajaatoiminnan hoito
French	Cellules d'hépatoblastome allogéniques encapsulées dans de l'alginate, expansées ex vivo	Traitement de l'insuffisance hépatique aiguë
German	Allogene, mit Alginat verkapselte Hepatoblastomzellen, ex vivo expandiert.	Behandlung des akuten Leberversagens
Greek	Ex vivo πολλαπλασιασμένα, αλλογενή κύτταρα ηπατοβλαστώματος ενθυλακωμένα σε αλγινικό άλας	Θεραπεία της οξείας ηπατικής ανεπάρκειας
Hungarian	Alginát tokba zárt, ex vivo tenyésztett allogén hepatoblastoma sejtek	Akut májelégtelenség kezelése
Italian	Cellule di epatoblastoma allogeniche incapsulate in alginato, espanse ex-vivo	Trattamento della insufficienza epatica acuta
Latvian	Alginātā iekapsulētas, ex vivo pavairotas alogēniskas hepatoblastomas šūnas	Akūtas aknu mazspējas ārstēšana
Lithuanian	Alogeninės hepatoblastomos ląstelės, inkapsuliuotos alginate, pagausintos ex vivo	Ūminio kepenų nepakankamumo gydymas
Maltese	Ċelloli tal-epatoblastoma alloġeniċi inkapsulati f'alġinat, imwessa' ex vivo	Kura ta' insuffiċjenza akuta tal-fwied
Polish	Allogeniczne komórki wątrobiaka zarodkowego kapsułkowane w alginianie, namnożone ex vivo	Leczenie ostrej niewydolności wątroby

¹ At the time of designation

Language	Active ingredient	Indication
Portuguese	Células de hepatoblastoma alogénicas encapsuladas em alginato, expandidas ex vivo	Tratamento da insuficiência hepática aguda
Romanian	Celule alogene de hepatoblastom încapsulate în alginat, extinse ex vivo	Tratamentul insuficienței hepatice acute
Slovak	Alogénne bunky hepatoblastómu enkapsulované do alginátu, expandované ex vivo	Liečba akútneho zlyhania pečene
Slovenian	Alogene hepatoblastomske celice, inkapsulirane v alginatu, ex vivo razširjene	Zdravljenje akutne jetrne odpovedi
Spanish	Células de hepatoblastoma alogénicas encapsuladas en alginato, expandidas ex vivo	Tratamiento de la insuficiencia hepática aguda
Swedish	Allogena hepatoblastomceller inkapslade i alginat, expanderade ex vivo	Behandling av akut leversvikt
Norwegian	Allogene hepatoblastomceller innkapslet i alginat, ekspandert ex vivo	Behandling av akutt leversvikt
Icelandic	Ósamgena lífrarkímsæxlisfrumur hjúpaðar með algínati, fjölgað ex vivo	Meðferð bráðrar lífrarbilunar