8 March 2017
EMA/3424/2017
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Human hepatoma cell line HepaRG in bioartificial liver for the treatment of acute liver failure

On 12 January 2017, orphan designation (EU/3/16/1818) was granted by the European Commission to Hep-Art Medical Devices BV, the Netherlands, for human hepatoma cell line HepaRG in bioartificial liver (also known as HepaRG-AMC-BAL) 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 the condition?

At the time of designation, acute liver failure affected approximately 0.06 in 10,000 people in the European Union (EU). This was equivalent to a total of around 3,000 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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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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.

The sponsor has provided sufficient information to show that this product might be of significant benefit for patients with acute liver failure because early results suggest it could improve survival in patients waiting for a liver transplant. 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 product consists of a medical device that contains cultured liver cells. These cells are attached to multiple layers of a supporting structure. 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 passed between the supporting layers in the device. Toxins that affect the brain in patients with liver failure, such as ammonia, are converted to less toxic substances by the liver cells in the device in the same way as in a normal liver. 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 help support the patient's own liver by carrying out some of its essential functions, thereby relieving the symptoms of acute liver failure until a transplant can be obtained. This support may also permit some improvement in the function of the patient's damaged liver.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, no clinical trials with this product in patients with acute liver failure had been started.

At the time of submission, the product 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 December 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Human hepatoma cell line HepaRG in bioartificial liver	Treatment of acute liver failure
Bulgarian	Човешка хепатомна клетъчна линия HepaRG в биосинтетичен черен дроб	Лечение на остра чернодробна недостатъчност
Croatian	Stanične linije hepatoma čovjeka HepaRG u bioumjetnoj jetri	Liječenje akutnog zatajenja jetre
Czech	Buněčné linie HepaRG humánního hepatomu v biologických umělých játrech	Léčba akutní jaterní insuficience
Danish	Human hepatomacellelinie HepaRG i biosyntetisk lever	Behandling af akut leversvigt
Dutch	Humane hepatoma cellijn HepaRG in bioartificiële lever	Behandeling van acuut leverfalen
Estonian	Inimese hepatoomi rakuliin HepaRG biotehislikus maksas	Akuutse maksapuudulikkuse ravi
Finnish	Ihmisen hepatoomasolulinja HepaRG keinomaksassa	Akuutin maksan vajaatoiminnan hoito
French	Lignée cellulaire d'hépatome humain HepaRG dans un foie bioartificiel	Traitement de l'insuffisance hépatique aiguë
German	Menschliche Hepatom-Zelllinie HepaRG in bioartifizieller Leber	Behandlung des akuten Leberversagens
Greek	Ανθρώπινη κυτταρική σειρά ηπατώματος HepaRG σε βιοτεχνητό ήπαρ	Θεραπεία της οξείας ηπατικής ανεπάρκειας
Hungarian	Humán hepatoma HepaRG sejtvonal mesterséges biológiai májban	Akut májelégtelenség kezelése
Italian	Linea cellulare di epatoma umano HepaRG in fegato bioartificiale	Trattamento della insufficienza epatica acuta
Latvian	Cilvēka hepatomas HepaRG šūnu līnija bioloģiskās-mākslīgās aknās	Akūtas aknu mazspējas ārstēšana
Lithuanian	Žmogaus hepatomos ląstelių linija HepaRG dirbtinėse kepenyse	Ūminio kepenų nepakankamumo gydymas
Maltese	Linja ta' ċelloli epatoma umana HepaRG fil-fwied bijoartifiċjali	Kura ta' insuffiċjenza akuta tal-fwied
Polish	Ludzka linia komórek wątrobiaka HepaRG w biosztucznej wątrobie	Leczenie ostrej niewydolności wątroby
Portuguese	Linha de células de hepatoma humano HepaRG no fígado bioartificial	Tratamento da insuficiência hepática aguda
Romanian	Linie celulară de hepatom uman HepaRG în ficat bioartificial	Tratamentul insuficienţei hepatice acute
Slovak	Ľudské bunkové línie hepatómov HepaRG v bioumelej pečeni	Liečba akútneho zlyhania pečene

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Hepatom celična linija Human HepaRG v bio-umetnega jetrih	Zdravljenje akutne jetrne odpovedi
Spanish	Linea de células de hepatoma humano HepaRG en un hígado bioartificial	Tratamiento de la insuficiencia hepática aguda
Swedish	bioartificiell lever med human hepatomcellinje HepaRG	Behandling av akut leversvikt
Norwegian	Human hepatomcellelinje HepaRG i biosyntetisklever	Behandling av akutt leversvikt
Icelandic	Human lifrarkrabbameins frumulína HepaRG í bioartificial lifur	Meðferð bráðrar lifrarbilunar