



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of recombinant human hepatocarcinoma-intestine-pancreas / pancreatic associated protein for the treatment of acute liver failure

On 11 February 2009, orphan designation (EU/3/08/611) was granted by the European Commission to Alfact Innovation SAS, France, for recombinant human hepatocarcinoma-intestine-pancreas / pancreatic associated protein for the treatment of acute liver failure.

What is acute liver failure?

Acute liver failure is characterised by the sudden loss of the normal liver functions in a patient with a previously normal liver and without evidence of chronic liver disease. The most common first sign of liver failure is yellowing of the skin (jaundice). Acute liver failure has serious complications such as confusion, drowsiness, bruising and haemorrhages secondary to impaired blood clotting. The most common causes of acute liver failure are viral hepatitis (infectious disease that affects the liver) or toxic damage (e.g. alcohol and paracetamol). Acute liver failure is chronically debilitating and life-threatening.

What is the estimated number of patients affected by acute liver failure?

At the time of designation acute liver failure affected less than 3.5 in 10,000 people in the European Union (EU) *. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation, which is 5 in 10,000. This is equivalent to a total of around 161,000 people.

What treatments are available?

Treatment of acute liver failure depends mainly on the stage of the liver damage. In cases of advanced liver damage, liver transplantation (getting a liver from a donor) is performed.

The sponsor has provided sufficient information to show that recombinant human hepatocarcinoma-intestine-pancreas/pancreatic associated protein might be of significant benefit, as through its mechanism of action it may result on a reduction of the liver damage that this organ suffers in a situation of acute liver failure, and therefore could contribute to a better clinical outcome of patients affected by acute liver failure. 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?

Recombinant human hepatocarcinoma-intestine-pancreas / pancreatic associated protein is a protein produced in microorganisms (recombinant) derived from the human protein HIP/PAP (Hepatocarcinoma-Intestine-Pancreas /Pancreatitis Associated Protein). HIP/PAP is a protein that has shown in experiments to be able to help cells generating new cells (cell proliferation) and to protect

* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).

cells from dying after being damaged (anti apoptotic effect). These functions are hoped to limit the liver damage and to improve the healing of the liver in acute liver failure.

What is the stage of development of this medicine?

The effects of recombinant human hepatocarcinoma-intestine-pancreas / pancreatic associated protein have been evaluated in experimental models.

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

At the time of submission, Recombinant human hepatocarcinoma-intestine-pancreas/pancreatic associated protein for the treatment of acute liver failure 'was not authorised anywhere in the world for acute liver failure or designated as 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 10 December 2008 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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

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**Translations of the active ingredient and indication in all official EU languages,
Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Recombinant human hepatocarcinoma-intestine-pancreas / pancreatic-associated protein	Treatment of acute liver failure
Bulgarian	Рекомбинантен човешки хепатокарцином-черва-панкреас / свързан с панкреатит протеин	Лечение на остра чернодробна недостатъчност
Czech	Rekombinantní lidský hepatokarcinomový-střevní- pankreatický s pankreatem asociovaný protein	Léčba Akutní jaterní insuficience
Danish	Rekombinant humant leverkarcinom-tarm-pankreas / pankreas bindende protein (HIP/PAP)	Behandling af akut leversvigt
Dutch	Recombinant humaan hepatocarcinoma-darm-pancreas-geassocieerd eiwit	Behandeling van acuut leverfalen
Estonian	Rekombinantne inimese hepatokartsinoom-sool-pankreas/pankreasega seotud valk	Akuutse maksapuudulikkuse ravi
Finnish	Rekombinantti ihmisen maksasyöpä suoli – haima / haimaan liittyvä proteiini	Akuutin maksan vajaatoiminnan hoito
French	Protéine humaine recombinante associée aux hépatocarcinomes, à l'intestin et au pancréas	Traitement de l'insuffisance hépatique aiguë
German	Rekombinantes menschliches Hepatokarzinom-Darm-Bauchspeicheldrüsen- / Bauchspeicheldrüsen-assoziiertes Protein	Behandlung des akuten Leberversagens
Greek	Ανασυνδυασμένη ανθρώπινη πρωτεΐνη σχετιζόμενη με ηπατοκαρκινώματα στο έντερο και παγκρέας και παγκρεατίτιδα.	Θεραπεία της οξείας ηπατικής ανεπάρκειας
Hungarian	Rekombináns humán hepatocarcinoma-bél-pancreas / pancreatitis-asszociált protein	Akut májelégtelenség kezelése
Italian	Proteina ricombinante umana specifica degli epatocarcinomi, dell'intestino e del pancreas, associata alle pancreatiti	Trattamento della insufficienza epatica acuta
Latvian	Rekombinantais cilvēka hepatokarcinomas -zarnu - aizkuņģa dziedzera/ar aizkuņģa dziedzeri saistītais proteīns	Akūtās aknu mazspējas ārstēšana
Lithuanian	Rekombinantinis žmogaus hepatokarcinomos-žarnyno-kasos/asocijuotas su kasa baltymas	Ūmaus kepenų nepakankamumo gydymas
Maltese	Proteina rikombinanti umana speċifika għall-epatokarcinoma-imsaren-frixa, assoċjata mal-frixa	Kura ta' insuffiċjenza akuta tal-fwied
Polish	Rekombinowane ludzkie białko trzustkowe wywodzące się z komórek raka wątrobowokomórkowego-jelita-trzustki	Leczenie ostrej niewydolności wątroby
Portuguese	Proteína humana recombinante associada ao pâncreas, de expressão tecidual específica do hepatocarcinoma e carcinomas do intestino e pâncreas	Tratamento da insuficiência hepática aguda

Romanian	Proteină umană recombinantă pancreatică asociată cu carcinomul hepatic-intestinal-pancreatic	Tratamentul insuficienței hepatice acute
Slovak	(Rekombinantný ľudský proteín špecifický pre karcinóm pečene - čreva a pankreasu/proteín súvisiaci s pankreasom)	Liečba akútneho zlyhania pečene
Slovenian	Rekombinantna človeška beljakovina hepatoma-črevesja-pankreas/povezana s pankreasom	Zdravljenje akutne jetrne odpovedi
Spanish	Proteína recombinante humana hepatocarcinoma-intestino-pancreas / proteína asociada al páncreas	Tratamiento de la insuficiencia hepática aguda
Swedish	Rekombinant mänskligt HIP/PAP (Levercarcinom-Tarm-Pankreas / Pankreas-associerat protein)	Behandling av akut leversvikt
Norwegian	Rekombinant humant leverkarsinom-tarm-pankreas / pankreas-assosiert protein	Behandling av akutt leversvikt
Icelandic	Raðbrigða manna lifrarkrabbameins-þarma-bris / bristengt prótein	Meðferð bráðrar lifrabilunar