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 L-asparaginase encapsulated in erythrocytes for the treatment of pancreatic cancer

On 15 May 2009, orphan designation (EU/3/09/633) was granted by the European Commission to Erytech Pharma SA, France, for L-asparaginase encapsulated in erythrocytes for the treatment of pancreatic cancer.

What is pancreatic cancer?
Pancreatic cancer is a cancer of the pancreas, a small organ that lies behind the stomach. The pancreas has two functions: producing a juice that helps with the digestion of food, and producing hormones such as insulin. About 95% of pancreatic cancers affect the cells that make the pancreatic juice. These are called adenocarcinomas.
Pancreatic cancer is a very severe and life-threatening disease that leads to poor long-term survival.

What is the estimated number of patients affected by the condition?
At the time of designation, pancreatic cancer affected approximately 1.3 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 66,000 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 knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?
At the time of submission of the application for orphan drug designation, several medicines were authorised for pancreatic cancer in the EU. The choice of treatment for pancreatic cancer depends on several factors, including the stage of the disease. Treatments may include surgery, radiotherapy (treatment with radiation) and chemotherapy (medicines to treat cancer).
The sponsor has provided sufficient information to show that L-asparaginase encapsulated in erythrocytes might be of significant benefit for patients with pancreatic cancer because it works in a different way to the other medicines for pancreatic cancer, and may be used in combination with existing treatments to improve effectiveness. 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?
L-asparaginase is an enzyme that breaks down the substance L-asparagine, which is required for cell growth. Certain cancer cells, such as the cancerous cells in pancreatic cancer, cannot make L-asparagine, so they need to take it up from the blood in order to grow. By reducing the levels of L-asparagine in the blood, this medicine is expected to deprive the cancerous pancreatic cells of their

[*]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 504,800,000 (Eurostat 2009).

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supply of L-asparagine, causing them to die. L-asparaginase has already been used for the treatment of acute lymphoblastic leukaemia (a cancer of the white blood cells) since the 1970s.
This medicine is made up of erythrocytes (red blood cells) that have been loaded with L-asparaginase so that the L-asparaginase is 'encapsulated' (contained) within the erythrocytes. The erythrocytes reduce the exposure of L-asparaginase to the immune system (the body's natural defences). This results in the immune system producing fewer antibodies against L-asparaginase, which could otherwise cause side effects such as allergic reactions.
The erythrocytes also form tiny compartments where the breakdown of L-asparagine can take place. Together, these properties are expected to increase how long L-asparaginase remains active in the body and to allow a lower dose of the enzyme to be used for the same anticancer effect as the free enzyme.

What is the stage of development of this medicine?
The effects of L-asparaginase encapsulated in erythrocytes have been evaluated in experimental models.
At the time of submission of the application for orphan designation, no clinical trials in patients with pancreatic cancer had been started.
At the time of submission, L-asparaginase encapsulated in erythrocytes was not authorised anywhere in the EU for pancreatic cancer 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 2 April 2009 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 Community) 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.

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

Language	Active ingredient	Indication
English	L-asparaginase encapsulated in erythrocytes	Treatment of pancreatic cancer
Bulgarian	L-аспарагиназа капсулирана в еритроцити	Лечение на рак на панкреаса
Czech	L-asparagináza uzavřená v erytrocytech	Léčba karcinomu pankreatu
Danish	L-asparaginase indkapslet i erytrocytter	Behandling af pancreascancer
Dutch	L-asparaginase, ingekapseld in erythrocyten	Behandeling van pancreaskanker
Estonian	Punaverelibledesse kapseldatud L-asparaginaas	Pankreasevähi ravi
Finnish	Punasoluihin kapseloitu L-asparaginaasi	Haimasyövän hoito
French	L-Asparaginase encapsulée dans des érythrocytes	Traitement du cancer pancréatique
German	In Erythrozyten verkapselte L-Asparaginase	Behandlung des Pankreaskarzinoms
Greek	L-ασπαραγινάση ενθυλακωμένη σε ερυθρά αιμοσφαίρια	Θεραπεία καρκίνου του παγκρέατος
Hungarian	Erythrocytába kapszulázott L-aszparagináz	Hasnyálmirigyrák kezelése
Italian	L-asparaginasi incapsulata in eritrociti	Trattamento del cancro pancreatico
Latvian	Eritrocītos iekapsulēta L-asparagināze	Aizkuņģa dziedzera vēža ārstēšana
Lithuanian	L-Asparaginazė, absorbuota eritrocituose	Kasos vėžio gydymas
Maltese	L-Asparaginase inkapsulat f' ċelluli tad-demm ħomor	Kura tal-kanċer tal-frixa
Polish	L-asparaginaza zawarta w erytrocytach	Leczenie raka trzustki
Portuguese	L-asparaginase encapsulada em eritrócitos	Tratamento do cancro do pâncreas
Romanian	L-asparaginază încapsulată în eritrocite	Tratamentul cancerului pancreatic
Slovak	L-asparagináza uzavretá v erytrocytoch	Liečba rakoviny pankreasu
Slovenian	L-asparaginaza inkapsulirana v eritrocitih	Zdravljenje raka trebušne slinavke
Spanish	L-asparraginasa encapsulada en eritrocitos	Tratamiento del cáncer de páncreas
Swedish	L-asparaginas inkapslad i erytrocyter	Behandling av pankreascancer
Norwegian	L-asparaginase innkapslet i røde blodlegemer	Behandling av pankreascancer
Icelandic	L-asparagínasi hjúpaður inn í rauðum blóðkornum	Meðferð briskrabbameins