



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

pegylated arginine deiminase for the treatment of hepatocellular carcinoma

On 20 June 2005, orphan designation (EU/3/05/289) was granted by the European Commission to F. Izzo, Italy, for pegylated arginine deiminase for the treatment of hepatocellular carcinoma.

What is hepatocellular carcinoma?

Tumours that begin in the liver are known as liver tumours. Liver tumours that have the potential to infiltrate healthy tissues and spread to other parts of the body are called hepatocellular carcinomas. The most common factors known to be associated with this disease are the viral infections causing liver inflammations (the so-called hepatitis B and hepatitis C) and an alcohol-induced liver disease (the so-called liver cirrhosis). Hepatocellular carcinoma is a life-threatening condition.

What are the methods of treatment available?

The choice of the treatment of hepatocellular cancer depends on several factors, mainly the stage of the disease. Treatments may include surgery, radiation therapy (using high-energy rays to kill cancer cells), chemotherapy (using drugs to kill cancer cells) or immunotherapy (treatment by stimulation of the body's own defence system against the cancer cells). At the time of submission of the application for orphan drug designation, several products were authorised for the condition in some countries of the Community.

Pegylated arginine deiminase could be of potential significant benefit for the treatment of hepatocellular carcinoma because it might improve the long-term outcome of the patients. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

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

According to the information provided by the sponsor, hepatocellular carcinoma was considered to affect about 46,000 persons in the European Union.

How is this medicinal product expected to act?

Arginine is a substance usually produced by the normal cells in the human body, which is important for the cell survival. Certain cancer cells, such as liver cancer cells, are unable to produce arginine and therefore take it from the blood since they need it for their rapid growth. Arginine deiminase is an enzyme (a protein that speeds up the conversion of certain substances into other substances) which is isolated from certain bacteria. When administering arginine deiminase to patients with hepatocellular carcinoma, it destroys the arginine present in the blood, and the cancer cells are thus deprived of their supply. The consequence is that they cannot grow and eventually die.

What is the stage of development of this medicinal product?

The effects of pegylated arginine deiminase were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with hepatocellular carcinoma were ongoing.

Pegylated arginine deiminase was not authorised anywhere worldwide for hepatocellular carcinoma, at the time of submission. Orphan designation of pegylated arginine deiminase was granted in the United States for treatment of hepatocellular carcinoma.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 12 May 2005 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products, which were considered for 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 will be necessary before this product can be granted a marketing authorisation.

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

Language	Active Ingredient	Indication
English	pegylated arginine deiminase	Treatment of the hepatocellular carcinoma
Czech	pegylovaná arginin deimináza	Léčba hepatocelulárního karcinomu
Danish	pegyleret arginin deiminase	Behandling af hepatocellulært carcinom
Dutch	gepegyleerd arginine deiminase	Behandeling van hepatocellulair carcinoom
Estonian	PEGüülitud arginiindeiminasaas	Hepatotsellulaarse kartsinoomi ravi
Finnish	pegyloitu arginiininen deiminaasi	Hepatosellulaarisen karsinooman hoito
French	déiminase d'arginine pégylée	Traitement du carcinome hépatocellulaire
German	pegylierte arginin deiminase	Behandlung des Leberzellkarzinoms
Greek	Πολυαιθυλενογλυκολιωμένη απαμινάση της αργινίνης	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Pegilált arginin-deimináz	Hepatocelluláris carcinoma kezelése
Italian	Arginina deaminasi pegilata	Trattamento del carcinoma epatocellulare
Latvian	pegilēta arginīndeimināze	Hepatocellulāras karcinomas ārstēšana
Lithuanian	pegiliuota arginino deziminazė	Hepatoceliulinės karcinomos gydymas
Polish	pegylowana argininy deiminaza	Leczenie raka wątrobowokomórkowego
Portuguese	Deiminase da arginina peguilada	Tratamento do carcinoma hepatocelular
Slovak	Pegylovaná arginín deimináza	Liečba hepatocelulárneho karcinómu
Slovenian	pegilirana arginin dezaminaza	Zdravljenje hepatocelularnega karcinoma
Spanish	Arginina deaminasa pegilada	Tratamiento de carcinoma hepatocelular
Swedish	pegylerat arginindeiminase	Behandling av hepatocellulärt carcinom
Norwegian	peg arginin deiminase	Behandling av hepatocellulært karsinom
Icelandic	PEG arginín deíminasi	Meðferð við lifrarfrumukrabbameini