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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF 4-imino-1, 3-diazobicyclo-[3.1.0]-hexan-2-one for the treatment of pancreatic cancer

On 27 July 2005, orphan designation (EU/3/05/299) was granted by the European Commission to ICON Clinical Research (U.K.) Limited, United Kingdom, for 4-imino-1, 3-diazobicyclo-[3.1.0]-hexan-2-one for the treatment of pancreatic cancer.

What is pancreatic cancer?

Cancer that begins in the pancreas is called pancreatic cancer. The pancreas is a small organ that lies behind the stomach and in front of the spine. The pancreas has two main functions in the body; it makes a juice that helps to digest (break down) food and it produces hormones, such as insulin, that help to control blood sugar levels. About 95% of pancreatic cancers come from the cells that make the juice to digest. These cancers of the pancreas are called adenocarcinomas. Pancreatic cancer is life-threatening.

What are the methods of treatment available?

The choice of the treatment of pancreatic cancer depends on several factors, including the stage of the disease. Treatments may include surgery, radiation therapy (using high-dose x-rays or other high-energy rays to kill cancer cells), and chemotherapy (using drugs to kill cancer cells). There are anti-cancer drugs that have been authorised for treatment of pancreatic cancer. 4-imino-1, 3-diazobicyclo-[3.1.0]-hexan-2-one might be of potential significant benefit for the treatment of pancreatic cancer, particularly in combination with currently authorised medicinal products, because it might improve the long-term outcome of the patients. This 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, pancreatic cancer was considered to affect about 55,000 persons in the European Union.

How is this medicinal product expected to act?

Cells contain several substances needed for their normal functioning (e.g. glutathione, cysteine, thiols). They also contain small structures (so-called mitochondria), responsible for the production of the energy necessary for the cell functioning, through a process named "cellular respiration". 4-imino-1, 3-diazobicyclo-[3.1.0]-hexan-2-one might induce a certain reaction in the cancer cells leading to a shortage of the cell fundamental substances and the destruction of the surface of the mitochondria. This would then induce the destruction of the cell itself, through a process called "programmed cell death" (apoptosis).

What is the stage of development of this medicinal product?

The effects of 4-imino-1, 3-diazobicyclo-[3.1.0]-hexan-2-one were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with pancreatic cancer were ongoing.

4-imino-1, 3-diazobicyclo-[3.1.0]-hexan-2-one was not authorised anywhere worldwide for pancreatic cancer, at the time of submission. Orphan designation of 4-imino-1, 3-diazobicyclo-[3.1.0]-hexan-2-one was granted in the United States for the treatment of pancreatic adenocarcinoma, for treatment of multiple myeloma and for treatment of metastatic malignant melanoma.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 15 June 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.

For more information:

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*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 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients' associations contact points:

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

Language	Active Ingredient	Indication
English	4-imino-1, 3-diazobicyclo- [3.1.0]-hexan-2-one	Treatment of pancreatic cancer
Czech	4-imino-1, 3-diazobicyklo- [3.1.0]-hexan-2-on	Léčba karcinomu pankreatu
Danish	4-imino-1, 3-diazobicyclo- [3.1.0]-hexan-2-one	Behandling af pancreascancer
Dutch	4-imino-1, 3-diazobicyclo- [3.1.0]-hexan-2-one	Behandeling van pancreaskanker
Estonian	4-imino-1, 3-diasobitsüklo- [3.1.0]-heksaan-2-oon	Pankreasevähki ravi
Finnish	4-imino-1, 3-diaatsobisyklo- [3.1.0]-heksaani-2-oni	Haimasyövän hoito
French	4-imino-1, 3-diazobicyclo- [3.1.0]-hexan-2-un	Traitement du cancer pancréatique
German	4-Imino-1, 3-Diazobicyclo- [3,1,0]-hexan-2-on	Behandlung von Pankreaskarzinom
Greek	4-ιμινο-1, 3-διαζωδικυκλο- [3.1.0]-εξαν-2-όνη	Θεραπεία καρκίνου του παγκρέατος
Hungarian	4-imino-1, 3-diazo-biciklo- [3.1.0]-hexán-2-on	Hasnyálmirigyrák kezelése
Italian	4-imino-1, 3-diazobiciclo- [3.1.0]-esan-2-one	Trattamento del cancro pancreatico
Latvian	4-imino-1, 3-diazobiciklo- [3,1,0]-heksan-2-ons	Aizkuņģa dziedzera vēža ārstēšanai
Lithuanian	4-imino-1, 3-diazobiciklo- [3.1.0]-heksano-2-onas	Kasos vėžio gydymas
Polish	4-imino-1, 3-diazobicyklo- [3.1.0]-heksan-2-on	Leczenie raka trzustki
Portuguese	4-imino-1, 3-diazobiciclo- [3.1.0]-hexan-2-ona	Tratamento do cancro do pâncreas
Slovak	4-imino-1, 3-diazobicyklo- [3.1.0]-hexan-2-ón	Liečba rakoviny pankreasu
Slovenian	4-imino-1, 3-diazobiciklo- [3.1.0]-heksan-2-on	Zdravljenje raka trebušne slinavke
Spanish	4-imino-1, 3-diazobiciclo- [3.1.0]-hexano-2-uno	Tratamiento del cáncer de páncreas
Swedish	4-imino-1, 3-diazobicyklo- [3.1.0]-hexan-2-en	Behandling av pancreascancer
Norwegian	4-imino-1, 3-diazobicyklo- [3.1.0]-hexan-2-on	Behandling av pancreascancer
Icelandic	4-ímínó-1, 3-díazóbícykló- [3.1.0]-hexan-2-on	Meðferð krabbameins í brisi