14 August 2013
EMA/COMP/402338/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl)diamidophosphate for the treatment of pancreatic cancer

On 17 July 2013, orphan designation (EU/3/13/1152) was granted by the European Commission to Merck KGaA, Germany, for (1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl)diamidophosphate (also known as TH-302) for the treatment of pancreatic cancer.

What is pancreatic cancer?

Pancreatic cancer is cancer of the pancreas, a small organ that lies behind the stomach. The pancreas has two functions: to produce a juice that helps with the digestion of food, and to produce hormones such as insulin. Due to the absence of symptoms in the early stages of pancreatic cancer, the majority of patients are diagnosed when the cancer has spread locally or to other parts of the body.

Pancreatic cancer is a very severe and life-threatening disease that is associated with shortened life expectancy.

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

At the time of designation, pancreatic cancer affected approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 102,000 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).

What treatments are available?

At the time of designation, several medicines were authorised in the EU for treating pancreatic cancer. The choice of treatment depended on several factors, including how far the disease had advanced. Treatments included surgery, radiotherapy (treatment with radiation) and chemotherapy (medicines to treat cancer).

*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 509,000,000 (Eurostat 2013).

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The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with pancreatic cancer because early studies have shown that it may improve the outcome of patients with this condition when used alone or in combination with gemcitabine. 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?

Pancreatic cancer, like most solid tumours, has areas with poor blood supply and therefore low levels of oxygen. The low level of oxygen in these areas is known to make tumour cells more resistant to standard chemotherapy. This medicine is expected to be converted into an active, toxic form called bromo-isophosphoramide mustard under conditions of low oxygen, allowing it to attack the tumour cells in low oxygen areas. This medicine is intended to be given with standard chemotherapy medicines and this is expected to help kill the tumour cells in low oxygen areas as well as other areas of the tumours.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, clinical trials with the medicinal product in patients with pancreatic cancer were ongoing.

At the time of submission, the medicine 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 13 June 2013 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:

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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	(1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl)diamidophosphate	Treatment of pancreatic cancer
Bulgarian	(1-метил-2-нитро-1H-имидазол-5-ил)метил N,N'-бис(2-бромоетил)диамидофосфат	Лечение на рак на панкреаса
Czech	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil)diamidofosfát	Léčba karcinomu pankreatu
Croatian	(1-metil-2-nitro-1H-imidazol-5-il)metil-N,N'-bis(2-bromoetil)diamidofosfat	Liječenja raka gušterače
Danish	(1-methyl-2-nitro-1H-imidazol-5-yl)methyl N,N'-bis(2-bromoethyl)diamidphosphat	Behandling af pancreascancer
Dutch	(1-methyl-2-nitro-1H-imidazool-5-yl)methyl N,N'-bis(2-bromoethyl)diamidofosfaat	Behandeling van pancreaskanker
Estonian	(1-metüül-2-nitro-1H-imidasool-5-üül)metüül N,N'-bis(2-bromoetüül)diamidofosfaat	Pankreasevähi ravi
Finnish	(1-metyyli-2-nitro-1H-imidatsoli-5-yl)metyyli N,N'-bis(2-bromietyyli)diamidifosfaatti	Haimasyövän hoito
French	(1-méthyl-2-nitro-1H-imidazole-5-yl)méthyl N,N'-bis(2-bromoéthyl) diamidophosphate	Traitement du cancer pancréatique
German	(1-Methyl-2-Nitro-1H-Imidazol-5-yl)Methyl N,N'-bis(2-Bromoethyl)Diamidophosphat	Behandlung des Pankreaskarzinoms
Greek	φωσφορικό (1-μεθυλο-2-νιτρο-1Η-ιμιδαζολ-5-υλο)μεθυλο Ν,Ν'-δις(2-βρωμοαιθυλο) διαμίδιο	Θεραπεία καρκίνου του παγκρέατος
Hungarian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bisz(2-bromoetil) diamid foszfát	Hasnyálmirigyrák kezelése
Italian	(1-metil-2-nitro-1H-imidazolo-5-il)metil N,N'-bis(2-bromoetil) diamido fosfato	Trattamento del cancro pancreatico
Latvian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-brometil)-diamidofosfāts	Aizkuņģa dziedzera vēža ārstēšana
Lithuanian	(1-metil-2-nitro-1H-imidazolo-5-il)metil N,N'-bis(2-bromoetil)diamidofosfatas	Kasos vėžio gydymas
Maltese	(1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl)diamidophosphate	Kura tal-kanċer tal-frixa
Polish	(1-metylo-2-nitro-1H-imidazol-5-ylo)metylu N,N'-bis(2-bromoetylo)diamidofosforan	Leczenie raka trzustki
Portuguese	(1-metil-2-nitro-1H-imidazole-5-il)metilN,N'-bis(2-brometil) fosfato de diamido	Tratamento do carcinoma do pâncreas
Romanian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil)diamidofosfat	Tratamentul cancerului pancreatic
Slovak	(1-metyl-2-nitro-1H-imidazol-5-yl)metyl N,N'-bis(2-brómetyl)diamidofosfát	Liečba rakoviny pankreasu

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil)diamidofosfat	Zdravljenje raka trebušne slinavke
Spanish	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil)diamidofosfato	Tratamiento del cáncer de páncreas
Swedish	(1-metyl-2-nitro-1H-imidazol-5-yl)metyl N,N'-bis(2-bromoetyl)diamidofosfat	Behandling av pankreascancer
Norwegian	(1-metyl-2-nitro-1H-imidazol-5-yl)metyl N,N'-bis(2-bromoetyl)diamidofosfat	Behandling av pankreascancer
Icelandic	(1-metýl-2-nítro-1H-ímídasól-5-ýl)metýl N,N'-bis(2-brómetýl)díamíðófosfat	Meðferð briskrabbameins