



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

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in July 2009 on request of the Sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of 5,10-methylene-tetrahydrofolic acid for the treatment of pancreatic cancer in combination with 5-fluorouracil

On 2 September 2004, orphan designation (EU/3/04/221) was granted by the European Commission to Interface International Consultancy Ltd, United Kingdom, for 5,10-methylene-tetrahydrofolic acid for the treatment of pancreatic cancer in combination with 5-fluorouracil.

What is pancreatic cancer?

Cancer that begins in the pancreas is called pancreatic cancer. The pancreas is an 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. It makes 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 is the estimated number of patients affected by the condition*?

At the time of designation, pancreatic cancer affected not more than 1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of not more than 46,000 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?

The choice of the treatment of pancreatic cancer depends on several factors, including the stage of the disease. Treatments may include surgery, radiation therapy, and chemotherapy (using drugs to kill cancer cells). There are anti-cancer agents that have been authorised for treatment of pancreatic cancer. 5,10-methylene-tetrahydrofolate might be of potential significant benefit for the treatment of pancreatic cancer, since it might increase the efficacy of another anti-cancer agent, 5-fluorouracil. It has been shown that fluorouracil is more effective when given together with a substance called calcium folinate. However, in order for calcium folinate to be active, the body must first chemically convert it to a compound called 5,10-methylene-tetrahydrofolate. By giving 5,10-methylene-tetrahydrofolate directly, it is possible that this will make fluorouracil even more effective. This assumption remains to be proven. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

*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 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

5,10-methylene-tetrahydrofolate belongs to a group of substances that are called folates. Folates, are necessary for the human body. They are obtained from the diet or from bacteria that live normally in the gut. They help in the building of new body substances. Cancer cells need to build new genetic material in order to grow. Several proteins work in the cells in order to build the new genetic material. One of these proteins is called thymidylate synthase. It builds new genetic material using 5,10-methylene-tetrahydrofolate, which is transformed in the process. If fluorouracil is present, however, the transformation stops, and the protein is blocked. This damages the cells that are growing, because the building of new genetic material becomes impossible. Fluorouracil works best only if folates are present. As the folates from the diet may not be sufficient, it is expected that by giving additional 5,10-methylene-tetrahydrofolate, this will help fluorouracil to block the thymidylate synthase. Thus, giving 5,10-methylene-tetrahydrofolate together with fluorouracil could help to stop the growth of pancreatic cancer cells.

What is the stage of development of this medicine?

The effects of 5,10-methylene-tetrahydrofolic acid 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.

The medicinal product was not marketed anywhere worldwide for treatment of pancreatic carcinoma in combination with 5-fluorouracil or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 22 July 2004 a positive opinion recommending the grant of the above-mentioned 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.

For more information:

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Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	5,10-methylene-tetrahydrofolic acid	Treatment of pancreatic cancer in combination with 5-fluorouracil
Czech	Kyselina 5,10-methylen-tetrahydrofolová	Léčba karcinomu pankreatu v kombinaci s 5-fluorouracilem
Danish	5,10-methylen-tetrahydrofolinsyre	Behandling af pancreas cancer i kombination med 5-fluorouracil
Dutch	5,10 methyleen-tetrahydrofolaatzuur	Behandeling van alvleesklier carcinoom in combinatie met 5-fluorouracil
Estonian	5,10-metüleen-tetra-hüdrofoolhape	Pankreasevähi ravi kombinatsioonis koos 5-fluorouratsiiliga
Finnish	5,10-metyleenitetrahydrofoolihappo	Haimasyövän hoito yhdistettynä 5-fluorourasiiliin
French	acide 5-10- méthylène tétrahydrofolique	Traitement du cancer du pancréas en association avec le 5-fluorouracil
German	5,10-Methylen-Tetrahydrofolsäure	Behandlung von Pankreaskarzinom in Kombination mit 5-Fluoruracil
Greek	5,10-μεθυλενο-τετραϋδροφολικό Οξύ	Θεραπεία παγκρεατικού καρκίνου σε συνδυασμό με 5-φθοριοουρακίλη
Hungarian	5,10-metilén tetrahidrofolsav	Hasnyálmirigy rák kezelése 5-fluorouracillal kombinálva
Italian	Acido 5,10- metilen-tetraidrofolico	Trattamento del carcinoma pancreatico in combinazione con 5-fluorouracile
Latvian	5,10-metilēntetrahidrofolijskābe	Aizkuņģa dziedzera vēža ārstēšanai savienojumā ar 5-fluoruracilu
Lithuanian	5,10-metileno-tetrahidrofolio rūgštis	Kasos vėžio gydymas derinant su 5-fluoruracilu
Maltese	5,10-methylene-tetrahydrofolic acid	Treatment of pancreatic cancer in combination with 5-fluorouracil
Polish	Kwas 5,10-metyleno-tetrahydrofoliowy	Leczenie raka trzustki w skojarzeniu z 5-fluorouracylem
Portuguese	Ácido 5,10-metilenotetrahidrofólico	Tratamento de cancro pancreático em combinação com 5-fluorouracilo
Slovak	kyselina 5,10-metylén-tetrahydrofolová	Liečba rakoviny pankreasu v kombinácii s 5-fluorouracilom
Slovenian	5,10-metilentetrahidrofolna kislina	Zdravljenje raka trebušne slinavke v kombinaciji s 5-fluorouracilom
Spanish	Ácido 5,10 metilentetrahidrofólico	Tratamiento del cáncer de páncreas en combinación con 5-fluorouracilo
Swedish	5,10-metyl-tetrahydrofolsyra	Behandling av pankreascancer i kombination med 5-fluoruracil
Norwegian	5,10-metylen-tetrahydrofolsyre	Behandling av pankreascancer i kombinasjon med 5-fluorouracil
Icelandic	5,10 metýlen-tetrahýdrófólín sýra	Meðferð við krabbameini í brisi