



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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in July 2009 on request of the Sponsor.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-tetrahydrofolate for the treatment of pancreatic cancer in combination with 5-fluorouracil

On 11 June 2003, orphan designation (EU/3/03/143) was granted by the European Commission to Biofol AB, Sweden, for 5-10-methylene-tetrahydrofolate for the treatment of pancreatic cancer in combination with 5-fluorouracil.

The sponsorship was transferred to Interface International Consultancy Ltd, United Kingdom, in July 2005.

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. 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 approximately 1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 38,000 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. 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 leucovorin. However, in order for leucovorin to be active, the body must first convert it to 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.

*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

How is this medicine expected to work?

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 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. 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?

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, at the time of submission. Orphan designation of 5-10 methylene-tetrahydrofolate has not been granted in other countries.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 15 April 2003 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.

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