



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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in December 2008 on request of the sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of fluorouracil for the treatment of glioblastoma

On 18 October 2000, orphan designation (EU/3/00/004) was granted by the European Commission to Ethypharm S.A., France, for fluorouracil for the treatment of glioblastoma.

What is glioblastoma?

Tumours that begin in brain tissue are known as primary brain tumours. Primary brain tumours are classified by the type of tissue from which they originate, the most common being gliomas, which begin in the glial (supportive) tissue. Gliomas are classified according to the particular kind of cell they originate from and the severity of the tumour. Gliomas are graded according to their likely rate of growth, from grade 1 (slowest growing) to grade 4 (fastest growing). Grade 4 gliomas are usually the so called glioblastomas multiforme which are arising from astrocytic cells. Patients affected by glioblastoma can suffer from severe symptoms of the nervous system, depending on where in the brain the tumour develops. Glioblastoma is life-threatening.

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

At the time of designation glioblastoma affected approximately 0.12 to 0.18 in 10,000 people in the European Union (EU)*. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 4,500 to 6,800 people.

What treatments are available?

No medicinal product was authorized for the treatment of glioblastoma in the Community at the time of submission of the application for orphan drug designation. Treatment for glioblastoma depends on a number of factors and encompasses several methods such as surgery, radiotherapy (using high-dose x-rays or other high-energy rays to kill cancer cells) or chemotherapy (using drugs to kill cancer cells), as well as some symptomatic treatments, including certain steroid hormones (corticosteroids) to control the effects of raised pressure within the skull, and medication to help control seizures.

How is this medicine expected to work?

Fluorouracil interrupts the action of thymidilate synthase, an enzyme (a protein that can trigger chemical reactions in the body) essential for processes involved in reproduction of genetic material (DNA) and cell proliferation (or cell division; cells increase in number by dividing). Tumour cells divide and increase in numbers more rapidly than healthy cells. By blocking thymidilate synthase,

*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).

fluorouracil can eventually kill tumour cells. In this medicinal product, fluorouracil is contained in so-called microspheres, which will be implanted in the site of the cancer after surgical removal of the tumour. Once implanted there, the active substance is expected to destroy tumour cells remaining after surgery.

What is the stage of development of this medicine?

The effects of fluorouracil were evaluated in experimental models.

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

Fluorouracil was authorised in many countries worldwide for the treatment of several cancers, at the time of submission. Orphan designation of fluorouracil was granted in the United States for the treatment of glioblastoma multiforme.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 13 September 2000 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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the quality, safety and efficacy is necessary before a 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	Fluorouracil	treatment of glioblastoma
Danish	Fluorouracil	Behandling af glioblastoma
Dutch	Fluoro-uracil	Behandeling van glioblastoom
Finnish	Fluorourasiili	Glioblastooman hoito
French	Fluoro-uracile	Traitement du glioblastome
German	Fluorouracil	Behandlung von Glioblastom
Greek	Φθοριοπουλακίλη	Θεραπεία του γλοιοβλαστώματος
Italian	fluorouracile	Trattamento del glioblastoma
Potuguese	fluoruracilo	Tratamento do glioblastoma
Spanish	fluorouracilo	Tratamiento del glioblastoma
Swedish	Fluorouracil	Behandling av glioblastom