European Medicines Agency

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EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)

GLIOLAN

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis of the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Gliolan?

Gliolan is a powder to be made up into a solution to be taken by mouth. It contains the active substance 5-aminolevulinic acid hydrochloride (30 mg/ml).

What is Gliolan used for?

Gliolan is used in adult patients with malignant glioma (a type of brain tumour). Gliolan helps surgeons to see the tumour more clearly during an operation to remove it from the brain.
Because the number of patients with malignant glioma is low, the disease is considered 'rare', and Gliolan was designated an 'orphan medicine' (a medicine used in rare diseases) on 13 November 2002.
The medicine can only be obtained with a prescription.

How is Gliolan used?

Gliolan should only be used by experienced brain surgeons who are familiar with surgery of malignant glioma, who have an in-depth knowledge of the anatomy of the brain, and who have completed a training course in surgery guided by fluorescence.
The recommended dose of Gliolan is 20 mg per kilogram body weight, taken two to four hours before the patient is anaesthetised. Gliolan powder should be dissolved in 50 ml tap water by a nurse or pharmacist before the patient drinks the solution. Gliolan should be used with caution in patients who have problems with their liver or kidneys.

How does Gliolan work?

The active substance in Gliolan, 5-aminolevulinic acid, is a 'sensitiser used in photodynamic therapy'. It is absorbed by cells in the body, where it is converted by enzymes into fluorescent chemicals, particularly protoporphyrin IX (PPIX). Since glioma cells take up more of the active substance and convert it more rapidly into PPIX, higher levels of PPIX accumulate in the cancer cells than in normal tissue. When illuminated under blue light of a specific wavelength, the PPIX in the tumour glows an intense red, while the normal brain tissue appears blue. This enables the surgeon to see the tumour more clearly during brain surgery and to remove it more accurately, sparing healthy brain tissue.

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How has Gliolan been studied?
The effects of Gliolan were first tested in experimental models before being studied in humans. However, because 5-aminolevulinic acid is a naturally occurring substance which is already used in some other conditions, the company also presented data from the published literature.
Gliolan has been studied in one main study involving 415 patients with malignant glioma who were about to undergo brain surgery to remove the tumour. The outcome of the operation was compared between patients taking Gliolan (operated under blue light) and that of patients who did not take any medicines to improve the visibility of the tumour (operated under normal white light). The main measures of effectiveness were the proportion of patients who had no visible tumour on a brain scan taken 72 hours after the operation, and the proportion who survived six months without the brain tumour coming back or getting bigger ('progressing'). The brain scans were analysed by an expert who did not know whether the patients had received Gliolan or not.

What benefit has Gliolan shown during the studies?
Removal of the brain tumour during surgery was more complete when Gliolan was used. At 72 hours after the operation, 63.6% of the patients given Gliolan had no visible tumour on a brain scan, compared with 37.6% of those who did not receive Gliolan. After six months, 20.5% of the patients given Gliolan were still alive without progression, compared with 11.0% of those who did not receive the medicine.

What is the risk associated with Gliolan?
The most common side effects seen with Gliolan are due to a combination of the medicine itself, as well as anaesthesia and the removal of the tumour. The side effects seen most commonly (in more than 1 patient in 10) are anaemia (low red blood cell counts), thrombocytopenia (low blood platelet counts), leukocytosis (high levels of leukocytes, a type of white blood cell) and increased levels of liver enzymes in the blood (bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase and amylase). For the full list of all side effects reported with Gliolan, see the Package Leaflet.
Gliolan should not be used in people who may be hypersensitive (allergic) to 5-aminolevulinic acid hydrochloride or porphyrins. It should also not be used by patients who have porphyria (an inability to break down porphyrins) or during pregnancy.

Why has Gliolan been approved?
The Committee for Medicinal Products for Human Use (CHMP) noted that surgical treatment for malignant glioma should aim to remove as much of the tumour as possible while sparing healthy brain tissue. It concluded that Gliolan increases the ability of the tumour to be distinguished from healthy brain tissue during surgery, and that it increases the proportion of patients whose tumours are completely removed and extends the time that patients survive without progression.
The Committee decided that Gliolan's benefits are greater than its risks for the visualisation of malignant tissue during surgery for malignant glioma. It recommended that Gliolan be given marketing authorisation.

Which measures are being taken to ensure the safe use of Gliolan?
Before the medicine is launched, the company that makes Gliolan will set up training courses in all Member States for brain surgeons to inform them about how to use the medicine safely and effectively during surgery.

Other information about Gliolan:
The European Commission granted a marketing authorisation valid throughout the European Union for Gliolan to m e d a c Gesellschaft für klinische Spezialpräparate mbH on 7 September 2007.

The summary of opinion of the Committee for Orphan Medicinal Products for Gliolan is available here.
The full EPAR for Gliolan can be found here.

This summary was last updated in 07-2007.