8 March 2017
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

5-Aminolevulinic acid for the treatment of glioma

On 12 January 2017, orphan designation (EU/3/16/1811) was granted by the European Commission to Centre Hospitalier Universitaire de Lille, France, for 5-aminolevulinic acid for the treatment of glioma.

What is glioma?

Glioma is a type of brain tumour that affects the 'glial' cells (the cells that surround and support the nerve cells). Patients with glioma can have severe symptoms, but the types of symptoms depend on where the tumour develops in the brain.

Symptoms can include headaches, nausea (feeling sick), loss of appetite, vomiting, and changes in personality, mood, mental capacity and concentration. About one-fifth of patients with glioma have seizures (fits) for months or years before the disease is diagnosed.

Glioma is a long-term debilitating and life-threatening disease because of the severe damage to the brain, and is associated with poor long-term survival.

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

At the time of designation, glioma affected approximately 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 134,000 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 for the treatment of glioma in the EU. Treatments for glioma included surgery, radiotherapy (treatment with radiation), and chemotherapy (medicines to treat cancer) to improve survival. Patients also received treatments for the symptoms of glioma, including corticosteroids to reduce pressure within the skull and medicines to prevent seizures.

[*]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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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The sponsor has provided sufficient information to show that 5-aminolevulinic acid might be of significant benefit for patients with glioma because early studies show that it may improve patients' survival when used in combination with authorised treatments. 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?

When 5-aminolevulinic acid is absorbed by cells in the body, it is converted by enzymes into protoporphyrin IX (PPIX), a photosensitising agent (a substance that changes when exposed to light). Since glioma cells take up more of 5-aminolevulinic acid, higher levels of PPIX accumulate in the cancer cells than in normal tissue.

When red light of a specific wavelength is shone onto the brain tissue during surgery, the PPIX in the cancer cells is activated and reacts with oxygen in the cells to create a highly reactive and toxic type of oxygen called 'singlet oxygen' (a free radical). This is expected to kill the cancer cells by reacting with and destroying their internal components, such as their proteins and DNA.

What is the stage of development of this medicine?

The effects of 5-aminolevulinic acid have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with 5-aminolevulinic acid for the treatment of patients with glioma had been started.

At the time of submission, 5-aminolevulinic acid was authorised in EU for the treatment of skin cancer and diagnosis of glioma. It was not authorised anywhere in the EU for treatment of glioma 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 8 December 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	5-aminolevulinic acid	Treatment of glioma
Bulgarian	5-аминолевулинова киселина	Лечение на глиома
Croatian	5-aminolevulinske kiseline	Liječenje glioma
Czech	5-aminolevulová kyselina	Léčba gliomů
Danish	5-aminolevulinsyre	Behandling af gliom
Dutch	5-aminolevulinezuur	Behandeling van glioma
Estonian	5-aminolevuliinhappe	Glioomi ravi
Finnish	5-aminolevuliinihappo	Gliooman hoito
French	Acide 5 aminolévulinique	Traitement des gliomes
German	5-Aminolävulinsäure	Behandlung von Gliomen
Greek	5-αμινολεβουλινικό οξύ	Θεραπεία του γλοιώματος
Hungarian	5-aminolevulinsav	Glioma kezelése
Italian	Acido 5-aminolevulinico	Trattamento del glioma
Latvian	5-aminolevulīnskābe	Gliomas ārstēšana
Lithuanian	5-aminolevulino rūgštis	Gliomos gydymas
Maltese	5-aminolevulinić aċidu	Kura tal-glioma
Polish	Kwasu 5-aminolewulinowego	Leczenie glejaka
Portuguese	Ácido 5-aminolevulínico	Tratamento do glioma
Romanian	Acid 5-aminolevulinic	Tratamentul gliomului
Slovak	Kyseliny 5-aminolevulínová	Liečba gliómu
Slovenian	5-aminolevulinske kisline	Zdravljenje glioma
Spanish	Ácido 5-aminolevulínico	Tratamiento del glioma
Swedish	5-aminolevulinsyra	Behandling av gliom
Norwegian	5-aminolevulinsyre	Behandling av gliom
Icelandic	5-amínoóevúlínik sýra	Meðferð á glíóma

[1] At the time of designation