15 January 2019
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Public summary of opinion on orphan designation

Larotrectinib for the treatment of glioma

On 19 November 2018, orphan designation (EU/3/18/2097) was granted by the European Commission to Bayer AG, Germany, for larotrectinib 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 it 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 135,000 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 radiotherapy (treatment with radiation), chemotherapy (medicines to treat cancer) and surgery. 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 517,400,000 (Eurostat 2018).

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The sponsor has provided sufficient information to show that larotrectinib might be of significant benefit for patients with glioma because early data showed that the condition did not get worse in patients in whom authorised treatments were not effective. 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?

Some patients with glioma have genetic mutations (changes) called *NTRK* gene fusions which result in the production of altered TRK proteins that can cause cancer.

Larotrectinib blocks the activity of the altered TRK proteins, thus preventing or slowing down the growth of glioma.

What is the stage of development of this medicine?

The effects of larotrectinib have been evaluated in experimental models.

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

At the time of submission, larotrectinib was not authorised anywhere in the EU for glioma. Orphan designation of the medicine had been granted in the United States for soft tissue sarcoma, solid tumors with NTRK-fusion proteins and infantile fibrosarcoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 October 2018 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	Larotrectinib	Treatment of glioma
Bulgarian	Ларотректиниб	Лечение на глиома
Croatian	Larotrectinib	Liječenje glioma
Czech	Larotrectinib	Léčba gliomů
Danish	Larotrectinib	Behandling af gliom
Dutch	Larotrectinib	Behandeling van glioma
Estonian	Larotrektiniib	Glioomi ravi
Finnish	Larotrektinibi	Glioman hoito
French	Larotrectinib	Traitement des gliomes
German	Larotrectinib	Behandlung von Gliomen
Greek	Λαροτρεκτινίμπη	Θεραπεία του γλοιώματος
Hungarian	Larotrectinib	Glioma kezelése
Italian	Larotrectinib	Trattamento del glioma
Latvian	Larotrektinibs	Gliomas ārstēšana
Lithuanian	Larotrektinibas	Gliomos gydymas
Maltese	Larotrektinib	Kura tal-glioma
Polish	Larotrektynib	Leczenie glejaka
Portuguese	Larotrectinib	Tratamento do glioma
Romanian	Larotrectinib	Tratamentul gliomului
Slovak	Larotrektinib	Liečba gliómu
Slovenian	Larotrektinib	Zdravljenje glioma
Spanish	Larotrectinib	Tratamiento del glioma
Swedish	Larotrektinib	Behandling av gliom
Norwegian	Larotrektinib	Behandling av gliom
Icelandic	Larótrektíníb	Meðferð á glíóma

[1] At the time of designation