31 March 2016
EMA/COMP/72380/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-(4-Methoxyphenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidin-4-amine for treatment of glioma

On 16 February 2016, orphan designation (EU/3/16/1618) was granted by the European Commission to FLAG Therapeutics Ltd, UK, for N-(4-methoxyphenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidin-4-amine 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 experienced 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 included surgery, radiotherapy (treatment with radiation), and chemotherapy (medicines

*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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to treat cancer) to improve survival. Patients also received treatments for the symptoms of glioma, including corticosteroids to reduce pressure in the skull and medicines to prevent seizures.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with glioma because studies in experimental models showed that the medicine might lead to greater reductions in the size of the tumour compared with temozolomide (a chemotherapy medicine often used in patients with glioma). 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?

The medicine is thought to act in two different ways. Firstly, it attaches to a protein in cells called 'tubulin', which is important in the formation of the internal 'skeleton' that cells need to assemble when they divide. By attaching to tubulin in cancer cells, the medicine stops the formation of this skeleton, preventing the division and growth of the cancer cells.

Secondly, the medicine blocks the activity of several enzymes known as tyrosine kinases, such as those that are present in receptors called EGFR, PDGFR and VEGFR. These receptors are involved in the development of blood vessels and are found in high amounts in glioma cells. By blocking the tyrosine kinases in these receptors, the medicine is expected to prevent or slow the development of blood vessels that the cancer tissue needs to continue growing and spreading within the body.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with glioma had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for 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 21 January 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	N-(4-methoxyphenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidin-4-amine	Treatment of glioma
Bulgarian	N-(4-Метоксифенил)-N,2,6-триметилфуро[2,3-d]пиримидин-4-амин	Лечение на глиома
Croatian	N-(4-metoksifenil)-N,2,6-trimetilfuro[2,3-d]pirimidin-4-amin	Liječenje glioma
Czech	N-(4-methoxyfenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidin-4-amin	Léčba gliomů
Danish	N-(4-methoxyphenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidin-4-amine	Behandling af gliom
Dutch	N-(4-methoxyfenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidine-4-amine	Behandeling van glioma
Estonian	N-(4-metoksüfenüül)-N,2,6-trimetüülfuro[2,3-d]pürimidiin-4-amiin	Glioomi ravi
Finnish	N-(4-metoksifenyyli)-N,2,6-trimetyyli-furo[2,3-d]pyrimidiini-4-amiini	Glioman hoito
French	N-(4-méthoxyphényl)-N,2,6-triméthylfuro[2,3-d]pyrimidine-4-amine	Traitement des gliomes
German	N-(4-Methoxyphenyl)-N,2,6-trimethylfuro[2,3-d]-pyrimidin-4-amin	Behandlung von Gliomen
Greek	N-(4-μεθοξυφαινυλ)-N, 2,6-τριμεθυλοφωσφορο[2,3-d]πυριμιδιν-4-αμίνη	Θεραπεία του γλοιώματος
Hungarian	N-(4-metoxi-fenil)-N,2,6-trimetilfuro[2,3-d]pirimidin-4-amin	Glioma kezelése
Italian	N-(4-metossifenil)-N,2,6-trimetil-furo[2,3-d]pirimidin-4-ammina	Trattamento del glioma
Latvian	N-(4-metoksifenil)-N,2,6-trimetilfuro[2,3-d]pirimidīn-4-amīns	Gliomas ārstēšana
Lithuanian	N-(4-metoksifenil)-N,2,6-trimetilfuro[2,3-d]pirimidin-4-aminas	Gliomos gydymas
Maltese	N-(4-methoxyphenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidin-4-amine	Kura tal-glioma
Polish	N-(4-metoksyfenylo)-N,2,6-trimetylofuro[2,3-d]pirymidyno-4-amina	Leczenie glejaka
Portuguese	N-(4-metoxifenil)-N,2,6-trimetilfuro[2,3-d]pirimidin-4-amina	Tratamento do glioma
Romanian	N-(4-metoxifenil)-N,2,6-trimetilfuro[2,3-d]pirimidin-4-amină	Tratamentul gliomului
Slovak	N-(4-metoxyfenyl)-N,2,6-trimetylfuro[2,3-d]pyrimidín-4-amín	Liečba gliómu
Slovenian	N-(4-metoksifenil)-N,2,6-trimetilfuro[2,3-d]pirimidin-4-	Zdravljenje glioma

[1] At the time of designation

Language	Active ingredient	Indication
	amin	
Spanish	N-(4-metoxifenil)-N,2,6-trimetilfuro[2,3-d]pirimidin-4-amina	Tratamiento del glioma
Swedish	N-(4-metoxyfenyl)-N,2,6-trimetylfuro[2,3-d]pyrimidin-4-amin	Behandling av gliom
Norwegian	N-(4-metoksyfenyl)-N,2,6-trimetylfuro[2,3-d]pyrimidin-4-amin	Behandling av gliom
Icelandic	N-(4-metoxýfenýl)-N,2,6-trímetýlfúró[2,3-d]pýrimídín-4-amín	Meðferð á glíóma