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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinoline-6-carboxamide monohydrate for the treatment of glioma

On 26 April 2013, orphan designation (EU/3/13/1120) was granted by the European Commission to Eli Lilly Nederland B.V., the Netherlands, for 4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinoline-6-carboxamide monohydrate 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 a 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 2.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 112,000 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

*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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).

(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.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with glioma because early studies in patients whose disease got worse after treatment with existing methods show a reduction of tumour size in these patients. 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?

Transforming growth factor beta (TGF- β) is a protein secreted by cells in the human body that is thought to play a role in stimulating the growth of glioma cells through several mechanisms, such as stimulating development of new blood vessels that supply the growing tumour, promoting the spreading of cancerous cells and suppressing the immune system (the body's natural defences). This medicine blocks the action of TGF- β , and is therefore expected to reduce the growth of the glioma.

What is the stage of development of this medicine?

The effects of 4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinoline-6-carboxamide monohydrate 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, this medicine was not authorised anywhere in the EU for glioma. Orphan designation of the medicine had been granted in the United States of America for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 March 2013 recommending the granting of this 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;
- 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:

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinoline-6-carboxamide monohydrate	Treatment of glioma
Bulgarian	4-[2-(6-метилпиридин-2-ил)-5,6-дихидро-4H-пироло[1,2-b]пиразол-3-ил]-хинолин-6-карбоксами́д монохидрат	Лечение на глиома
Czech	4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-chinolin-6-karboxamid monohydrát	Léčba gliomů
Danish	4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinolin-6-carboxamid monohydrat	Behandling af gliom
Dutch	4-[2-(6-methylpyridine-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-chinoline-6-carboxamide monohydraat	Behandeling van glioma
Estonian	4-[2-(6-metüülpüridiin-2-üül)-5,6-dihüdro-4H-pürolo[1,2-b]pürasool-3-üül]-kinoliin-6-karboksamiid monohüdraat	Glioomi ravi
Finnish	4-[2-(6-metyyliipyridiini-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyratsoli-3-yl]-kinoliini-6-karboksamidi monohydraatti	Gliooman hoito
French	4-[2-(6-méthylpyridine-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinoline-6-carboxamide monohydrate	Traitement des gliomes
German	4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinolin-6-carboxamidmonohydrat	Behandlung von Gliomen
Greek	4-[2-(6-μεθυλπυριδιν-2-υλο)-5,6-δι-υδρο-4H-πυρόλο[1,2-b]πυραζολ-3- υλο]-κινολινο-6-μονουδρικο καρβοξαμίδιο	Θεραπεία του γλοιώματος
Hungarian	4-[2-(6-metilpiridin-2-yl)-5,6-dihidro-4H-pirrolo[1,2-b]pirazol-3-yl]-kinolin-6-karboxamid monohidrát	Glioma kezelése
Italian	4-[2-(6-metilpiridin-2-il)-5,6-deidro-4H-pirrolo[1,2-b]pirazol-3-il]-chinolin-6-carbossamide monoidrato	Trattamento del glioma
Latvian	4-[2-(6-metilpiridīn-2-il)-5,6-dihidro-4H-pirrolo[1,2-b]pirazol-3-il]-kvinolin-6-karboksamīda monohidrāts	Gliomas ārstēšana
Lithuanian	4-[2-(6-metilpiridin-2-il)-5,6-dihidro-4H-pirolol[1,2-b]pirazol-3-il]-kvinolin-6-karboksamido monohidratas	Gliomos gydymas
Maltese	4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinoline-6-carboxamide monohydrate	Kura tal-glioma
Polish	4-[2-(6-metylopirydyń-2-ylo)-5,6-dihydro-4H-pirolol[1,2-b]pirazol-3-ylo]-chinolino-6-karboksyamid jednowodny	Leczenie glejaka
Portuguese	4-[2-(6-metilpiridina-2-il)-5,6-dihidro-4H-pirrolo[1,2-b]pirazol-3-il]-quinolina-6- carboxamida mono-hidratada	Tratamento do glioma

¹ At the time of designation

Language	Active ingredient	Indication
Romanian	4-[2-(6-metilpiridin-2-il)-5,6-dihidro-4H-pirol[1,2-b]pirazol-3-il]-chinolin-6-carboxamid monohidrat	Tratamentul gliomului
Slovak	monohydrát 4-[2-(6-metylpyridín-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-chinolín-6-karboxamidu	Liečba gliómu
Slovenian	4-[2-(6-metilpiridin-2-il)-5,6-dihidro-4H-pirol[1,2-b]pirazol-3-il]-kinolin-6-karboksamid monohidrat	Zdravljenje glioma
Spanish	4-[2-(6-metilpiridina-2-il)-5,6-dihidro-4H-pirrol[1,2-b]pirazol-3-yl]-quinolina-6-carboxamida monohidrato	Tratamiento del glioma
Swedish	4-[2-(6-metylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-kinolin-6-karboxamidmonohydrat	Behandling av gliom
Norwegian	4-[2-(6-metylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-kinolin-6-karboksamidmonohydrat	Behandling av gliom
Icelandic	4-[2-(6-metýlpýridín-2-ýl)-5,6-tvíhýdró-4H-pýrróló[1,2-b]pýrazól-3-ýl]-kínólín-6-karboxamíð einhýdrat	Meðferð á glíóma