



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 October 2013
EMA/COMP/240065/2009 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4] diazepin-11-one for the treatment of glioma

First publication	5 June 2009
Rev.1: withdrawal from the Community Register	8 October 2013
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in July 2012 on request of the Sponsor.

On 15 May 2009, orphan designation (EU/3/09/639) was granted by the European Commission to Albany Regulatory Consulting Limited, United Kingdom, for 4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4] diazepin-11-one 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 debilitating and life-threatening disease because of the severe damage to the brain that leads to poor long-term survival.



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

At the time of designation, glioma affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 50,000 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 (using radiation to kill the cancer cells) and chemotherapy (medicines to treat cancer). 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 4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4] diazepin-11-one might be of significant benefit for the patients with glioma because it works in a different way to existing medicines and preliminary experiments indicate that it may represent an alternative treatment for 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?

The way that this medicine works is not fully understood, but it is thought to interfere with the way that some proteins work inside cells, which leads to the cancerous cells undergoing 'apoptosis' (controlled cell death). As a result, it is expected to stop the tumour from growing.

The medicine also attaches to some receptors called 'peripheral benzodiazepine receptors' (PBRs), which are found in high amount in glioma cells. It is not yet clear whether this contributes to the medicine's activity against glioma, but it may help the medicine accumulate within glioma cells.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial in patients with glioma was ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for glioma or designated as 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 2 April 2009 recommending the granting of this designation.

*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. At the time of designation, this represented a population of 504,800,000 (Eurostat 2009).

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:

Albany Regulatory Consulting Limited
Sumpter House
8 Station Road
Histon
Cambridge CB4 9LQ
United Kingdom
Telephone: +44 12 23 30 27 03
Telefax: +44 12 23 30 27 03
E-mail: information@albanyregulatory.co.uk

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	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Treatment of glioma
Bulgarian	4,6,8-трихидрокси-10-(3,7,11-триметилдодека-2,6,10-триенил)-5,10-дихидродибензо[b,e][1,4]диазепин-11-ен	Лечение на глиома
Czech	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Léčba gliomů
Danish	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-on	Behandling af gliom
Dutch	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Behandeling van glioma
Estonian	4,6,8-trihüdroksü-10-(3,7,11-trimetüüldodeka-2,6,10-trienüül)-5,10-dihüdrodibenzo[b,e][1,4]diazepin-11-üks	Glioomi ravi
Finnish	4,6,8-trihydroksi-10-(3,7,11-trimetyylidodeka-2,6,10-trienyyli)-5,10-dihydrodibentso[b,e][1,4]diatsepiini-11-yksi	Gliooman hoito
French	4,6,8-trihydroxy-10-(3,7,11-triméthyldodéca-2,6,10-triènyl)-5,10-dihydrodibenzo[b,e][1,4]diazépine-11-one	Traitement des gliomes
German	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Behandlung von Gliomen
Greek	4,6,8-τριυδροξυ-10-(3,7,11-τριμεθυλδωδεκα-2,6,10-τριενυλ)-5,10-διυδροδιβενζο[b,e][1,4]διαζεπιν-11-ονη	Θεραπεία του γλοιώματος
Hungarian	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Glioma kezelése
Italian	4,6,8-triidrossi-10-(3,7,11-trimetildodeca-2,6,10-trienil)-5,10-diidrodibenzo[b,e][1,4]diazepin-11-one	Trattamento del glioma
Latvian	4,6,8-trihidroksi-10-(3,7,11-trimetildodeka-2,6,10-trienil)-5,10-dihidrodibenzo[b,e][1,4]diazepīn-11-one	Gliomas ārstēšana
Lithuanian	4,6,8-trihidroksi-10-(3,7,11-trimetildodeka-2,6,10-trienil)-5,10-dihidrodibenzo[b,e][1,4]diazepin-11-onas	Gliomos gydymas

¹ At the time of designation

Language	Active ingredient	Indication
Maltese	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Kura tal-glioma
Polish	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Leczenie glejaka
Portuguese	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Tratamento do glioma
Romanian	4,6,8-trihidroxi-10-(3,7,11-trimetildodeca-2,6,10-trienil)-5,10-dihidrobenzo[b,e][1,4]diazepin-11-onă	Tratamentul gliomului
Slovak	4,6,8-trihydroxy-10-(3,7,11-trimetyldodeka-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-ón	Liečba gliómu
Slovenian	4,6,8-trihidroksi-10-(3,7,11-trimetildodeka-2,6,10-trienil)-5,10-dihidrobenzo[b,e][1,4]diazepin-11-one	Zdravljenje glioma
Spanish	4,6,8-trihidroxi-10-(3,7,11-trimetildodeca-2,6,10-trienil)-5,10-dihidrobenzo[b,e][1,4]diazepin-11-on	Tratamiento del glioma
Swedish	4,6,8-trihydroxy-10-(3,7,11-trimethyldodeca-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-one	Behandling av gliom
Norwegian	4,6,8-trihydroksy-10-(3,7,11-trimetyldodeka-2,6,10-trienyl)-5,10-dihydrodibenzo[b,e][1,4]diazepin-11-on	Behandling av gliom
Icelandic	4,6,8-tríhýdroxý-10-(3,7,11-trímethýldodeca-2,6,10-tríenýl)-5,10-díhýdrodibenzó[b,e][1,4]diazepín-11-one	Meðferð á glíóma