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Public summary of opinion on orphan designation

(3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-one fumarate for the treatment of glioma

On 24 August 2018, orphan designation (EU/3/18/2055) was granted by the European Commission to IQVIA RDS Ireland Limited, Ireland, for (3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-one fumarate (also known as ACT001 or dimethylaminomicheliolide) for the treatment of glioma.

What is glioma?

Glioma is a 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 2.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 140,000 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).

*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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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). Patients also received treatments for the symptoms of glioma, including corticosteroids to reduce pressure inside the skull and medicines to prevent seizures.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit to patients with glioma because early studies have shown improvement in patients whose glioblastoma (a fast-growing form of glioma) could not be treated or had come back after treatment. 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?

This medicine blocks the effects of a protein system called NF-kappaB. This protein system, which controls several cell activities including division and survival, becomes overactive in tumours such as glioma. Moreover, the medicine increases the levels of oxygen-containing molecules inside tumour cells which are harmful to the cell. Together these actions are expected to lead to the death of glioma cells and slow down the growth of the tumour.

What is the stage of development of this medicine?

The effects of the medicine 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, the medicine was not authorised anywhere in the EU for glioma. Orphan designation of the medicine had been granted in the United States for glioblastoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 July 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	(3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-one fumarate	Treatment of glioma
Bulgarian	(3R,3aS,9R,9aS,9bS)-3-((диметиламино)метил)-9-хидрокси-6,9-диметил-3,3a,4,5,7,8,9,9a-октахидроазулено[4,5-Ь]фуран-2(9ЬН)-он фумарат	Лечение на глиома
Croatian	(3R,3aS,9R,9aS,9bS)-3-((dimetilamino)metil)-9-hidroksi-6,9-dimetil-3,3a,4,5,7,8,9,9a-oktahidroazuleno[4,5-b]furan-2(9bH)-onfumarat	Liječenje glioma
Czech	(3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9dimethyl-3,3a,4,5,7,8,9,9a-oktahydroazuleno[4,5-b]furan-2(9bH)-on-fumarátu	Léčba gliomů
Danish	(3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-onfumarat	Behandling af gliom
Dutch	(3R,3aS,9R,9aS,9BS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-onfumaraat	Behandeling van glioma
Estonian	(3R,3aS,9R,9aS,9bS)-3-((dimetüülamino)metüül)-9-hüdroksü-6,9-dimetüül-3,3a,4,5,7,8,9,9a-oktahüdroasuleno[4,5-b]furaan-2(9bH)-oonfumaraat	Glioomi ravi
Finnish	(3R,3aS,9R,9aS,9bS)-3-((dimetyyliamino)metyyli)-9-hydroksi-6,9-dimetyyli-3,3a,4,5,7,8,9,9a-oktahydroatsuleeni[4,5-b]furaani-2(9bH)-oni-fumaraatti	Glioooman hoito
French	(3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-onefumarate	Traitement des gliomes
German	(3R,3aS,9R,9aS,9bS)-3-((Dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]Furan-2(9bH)-on-Fumarat	Behandlung von Gliomen
Greek	(3R,3aS,9R,9aS,9bS)-3-((διμεθυλαμινο)μεθυλ)-9-υδροξυ-6,9-διμεθυλ-3,3α,4,5,7,8,9,9α-οκταϋδροαζουλενο [4,5-b]φουραν-2(9bH)-όνη	Θεραπεία του γλοιώματος
Hungarian	(3R,3aS,9R,9aS,9bS)-3-((dimetil-amino)-metil)-9-hidroxi-6,9-dimetil-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furán-2(9bH)-on-fumarát	Glioma kezelése
Italian	(3R,3aS,9R,9AS,9BS)-3-((dimetilammino)metil)-9-idrossi-6,9-dimetil-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-unafumarato	Trattamento del glioma
Latvian	(3R,3aS,9R,9aS,9bS)-3-((dimetilamino)metil)-9-hidroksi-6,9-dimetil-3,3a,4,5,7,8,9,9a-oktahidroazuleno[4,5-b]furān-2(9bH)-ona fumarāts	Gliomas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	(3R,3aS,9R,9aS,9bS)-3-((dimetilamino)metil)-9-hidroksi-6,9-dimetil-3,3a,4,5,7,8,9,9a-oktahidroazuleno[4,5-b]furan-2(9bH)- ono fumaratas	Gliomos gydymas
Maltese	(3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-onefumarate	Kura tal-glioma
Polish	(3R,3aS,9R,9aS,9bS)-3-((dimetyloamino)metylo)-9-hydroksy-6,9-dimetylo-3,3a,4,5,7,8,9,9a-oktahydroazuleno[4,5-b]furan-2(9bH)-jedenfumaran	Leczenie glejaka
Portuguese	(3R,3aS,9R,9aS,9bS)-3-((dimetilamino)metil)-9-hidroxi-6,9-dimetil-3,3a,4,5,7,8,9,9a-octa-hidroazuleno[4,5-b]furan-2(9bH)-onefumarato	Tratamento do glioma
Romanian	Fumarat de (3R,3aS,9R,9aS,9bS)-3-((dimetilamino)metil)-9-hidroxi-6,9-dimetil-3,3a,4,5,7,8,9,9a-octahidroazuleno[4,5-b]furan-2(9bH)-onă	Tratamentul gliomului
Slovak	(3R,3aS,9R,9aS,9bS)-3-((dimetylamino)metyl)-9-hydroxy-6,9-dimetyl-3,3a,4,5,7,8,9,9a-oktahydroazuleno [4,5-b]furan-2(9bH)-ónfumarátu	Liečba gliómu
Slovenian	(3R,3aS,9R,9aS,9bS)-3-((dimetilamino)metil)-9-hidroksi-6,9-dimetil-3,3a,4,5,7,8,9,9a-oktahidroazuleno[4,5-b]furan-2(9bH)-onfumarat	Zdravljenje glioma
Spanish	(3R,3aS,9R,9aS,9bS)-3-((dimetilamino)metil)-9-hidroxi-6,9-dimetil-3,3a,4,5,7,8,9,9a-octahidroazuleno[4,5-b]furan-2(9bH)-onafumarato	Tratamiento del glioma
Swedish	(3R,3aS,9R,9aS,9bS)-3-((dimetylamino)metyl)-9-hydroxi-6,9-dimetyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-onfumarat	Behandling av gliom
Norwegian	(3R,3aS,9R,9aS,9BS)-3-((dimetylamino)metyl)-9-hydroksy-6,9-dimetyl-3,3a,4,5,7,8,9,9a-oktahydroazuleno[4,5-b]furan-2(9bH)-onfumarat	Behandling av gliom
Icelandic	(3R,3aS,9R,9aS,9bS)-3-((dímetýlamínó)metýl)-9-hýdroxý-6,9-dímetýl-3,3a,4,5,7,8,9,9a-oktahýdróasúlenó[4,5-b]fúran-2(9bH)-onfúmarat	Meðferð á glíóma