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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Doxorubicin (administered after synthetic double-stranded siRNA oligonucleotide directed against Claudin-5 complexed with polyethyleneimine) for the treatment of glioma

On 28 November 2012, orphan designation (EU/3/12/1006) was granted by the European Commission to Avena Therapeutics Ltd, Ireland, for doxorubicin (administered after synthetic double-stranded siRNA oligonucleotide directed against Claudin-5 complexed with polyethyleneimine) 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 that 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 less than 2.2 in 10,000 people in the European Union (EU)*. This is equivalent to a total of fewer than 111,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 506,300,000 (Eurostat 2011).

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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) 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 the medicine might be of significant benefit for patients with glioma on the basis of studies in experimental models showing that the medicine might prolong survival and reduce tumour size. 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?

Doxorubicin has been available as an anticancer medicine given into the vein since the 1960s. It is a cytotoxic (cell-killing) medicine that belongs to the group 'anthracyclines'. It works by interfering with the DNA within cells, preventing them from making more copies of DNA and making proteins. This means that cancer cells cannot divide and eventually die.

Doxorubicin can only work against the cancer cells in glioma if it is able to cross the blood brain barrier in sufficient amounts. For that to happen, a small strand of synthetic genetic material, called 'small interfering RNA' (siRNA), will first be injected into the patient followed by doxorubicin. The siRNA is designed to target the gene for the protein claudin-5 at the blood-brain barrier, thereby blocking its production. Claudin-5 is responsible for the tight junctions between the cells in the barrier. By blocking claudin-5, the siRNA is expected to increase the permeability of the blood brain barrier, allowing doxorubicin to reach the glioma cells in the brain.

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 medicinal product in experimental models was ongoing.

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

At the time of submission, the medicinal product 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 11 May 2012 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:

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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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Doxorubicin (administered after synthetic double-stranded siRNA oligonucleotide directed against claudin-5 complexed with polyethyleneimine)	Treatment of glioma
Bulgarian	Доксорубицин (приложен след синтетичен двойноверижен siРНК олигонуклеотид насочен срещу клаудин 5 свързан с полиетиленеимин)	Лечение на глиом
Czech	Doxorubicin (po podání syntetického dvojřetězcového oligunukleotidu siRNA cíleného proti komplexu polyethyleniminu s claudine-5)	Léčba gliomů
Danish	Doxorubicin (administreret efter syntetisk dobbeltstrenget siRNA oligonukleotid rettet mod claudin-5 kompleksbundet med polyetylenimin)	Behandling af gliom
Dutch	Doxorubicine (toegediend na synthetisch dubbelstrengig siRNA oligonucleotide gericht tegen claudine-5 gecomplexeerd aan polyethylenëimine)	Behandeling van glioma
Estonian	Doxorubicin (manustatud peale sünteetilise double-stranded siRNA oligonucleotide directed against claudin-5 complexed with polyethyleneimine)	Glioomi ravi
Finnish	Doksorubisiini, jota ennen annetaan synteettistä, kaksiketjuista siRNA:ta, joka on kohdennettu klaudiini-5:een, joka on yhdistetty polyetyleeniminiin	Glioman hoito
French	Doxorubicine (administrée après l'oligonucléotide synthétique siARN double brin dirigé contre la claudine 5 couplée au polyethyleneimine)	Traitement des gliomes
German	Doxorubicin (nach Verabreichung eines synthetischen doppelstrang-siRNA Oligonukleotids gegen claudin-5, komplexiert mit Polyethyleneimin)	Behandlung von Gliomen
Greek	Δοξορουμπικίνη (χορηγούμενη μετά από συνθετικό δίκλωνο si-RNA ολιγονουκλεοτίδιο έναντι της κλωντίνης-5 συμπλεγμένο με πουλυαιθυλενεϊμίνη)	Θεραπεία του γλοιώματος
Hungarian	Doxorubicin (polyethyleneimin-claudin-5 komplex-ellenes szintetikus kettős szálú siRNA oligonukleotid után adagolva)	Glioma kezelése
Italian	Doxorubicina (somministrata dopo un oligonucleotide sintetico siRNA a doppia elica diretto alla claudina-5 complessata con polyethileneimina	Trattamento del glioma
Latvian	Doksorubicīns (ievadīts pēc sintētiskā dubutspirāļu siRNS oligonukleotīda, kurš vērsts prêt klaudīna-5 kompleksa ar polietilēnimīnu)	Gliomas ārstēšana
Lithuanian	Doksorubicinas (paskirtas po sintetinio dvigrandžio siRNR oligonukleotido nukreipto prieš klaudiną-5 komplekse su polietileneiminu)	Gliomos gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Doxorubicin (amministrat wara oligonukleotide sintetiku tas-siRNA b'katina doppja dirett kontra claudin-5 magħqud ma' polyethyleneimine)	Kura tal-glioma
Polish	Doksorubicyna (podana po syntetycznym dwułańcuchowym oligonukleotydzie siRNA skierowanym przeciw klaudynie-5 połączonym z polietylenoiminą)	Leczenie glejaka
Portuguese	Doxorubicin (administered after synthetic double-stranded siRNA oligonucleotide directed against claudin-5 complexed with polyethyleneimine)	Tratamento do glioma
Romanian	Doxorubicină (administrată post oligonucleotid sintetic dublu catenar siARN direcţionat împotriva complexului claudină-5 polietilenimină)	Tratamentul gliomului
Slovak	Doxorubicín (podávaný po syntetickom jednovláknovom siRNA oligonukleotide cielenom proti klaudínu-5 v spojení s polyetylénimínom)	Liečba gliómu
Slovenian	Doksorubicin (po aplikaciji sintetičnega dvojnovijačnega RNK oligonukleotida usmerjenega proti klaudinu-5 vezanega na polietilenimin	Zdravljenje glioma
Spanish	Doxorubicina (administrada tras un oligonucleótido de ARN corto de interferencia sintético de doble cadena dirigido contra claudina-5 que forma un complejo con polietileneimina)	Tratamiento del glioma
Swedish	Doxorubicin (administrerat efter ett komplex av polyetylenimin och syntetiskt dubbelsträngat siRNA riktat mot claudin-5)	Behandling av gliom
Norwegian	Doksorubicin (administrert etter syntetisk dobbelt-trådet siRNA oligonukleotid rettet mot claudin-5 polyetylenimin kompleks)	Behandling av gliom
Icelandic	Doxórúbicín (gefið á eftir nýgerðu tvíþátta siRNA ólígónúkleótíði sem beinist gegn claudín-5 fléttað með pólýetýlenímíni)	Meðferð á glíóma