21 March 2014
EMA/COMP/78/2002 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

TGF-ß2-specific phosphorothioate antisense oligodeoxynucleotide for the treatment of high-grade glioma

First publication	6 January 2003
Rev.1: administrative update	8 January 2003
Rev.2: sponsor's name and address change	21 March 2014

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.

On 22 March 2002, orphan designation (EU/3/02/091) was granted by the European Commission to Antisense Pharma GmbH, Germany, for transforming growth factor TGF-β2-specific phosphorothioate antisense oligodeoxynucleotide for the treatment of high-grade glioma.

In February 2014, Antisense Pharma GmbH changed name to Isarna Therapeutics GmbH.

What is high-grade glioma?

Tumours that begin in the brain are known as primary brain tumours. Primary brain tumours are classified by the type of tissue from which they originate. The most common brain tumours are gliomas, which begin in the glial (supportive) tissue. There are several types of gliomas and these are grouped by grade, which refer to some cell characteristics that can be identified with a microscope. Cells from higher grade tumours are more abnormal looking and generally grow faster than cells from lower grade tumours. High-grade gliomas are more malignant than low grade tumours and are life-threatening.

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

At the time of designation, high-grade glioma affected approximately 0.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 27,000 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?

Treatment for high-grade gliomas depends on a number of factors and may include surgery, radiotherapy or chemotherapy as well as symptomatic treatments, such as corticosteroids to control the effects of raised intracranial pressure, and anticonvulsants to help control seizures, as required. Methods of treatment of the condition had been authorised at the time of submission of the application for orphan designation. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that TGF- ß2 antisense oligonucleotide might be of potential significant benefit for the treatment of high-grade gliomas, particularly in terms of its novel mechanism of action.

How is this medicine expected to work?

The proposed TGF-ß2 antisense oligonucleotide is a synthetic 18-mer phosphorothioate oligodeoxynucleotide that was designed as complementary sequence to an appropriate area of the mRNA of the TGF-β2 gene. It is expected to inhibit the formation of TGF-β2, which is involved in the progression of high-grade gliomas. The product is administered directly into the brain tumour.

What is the stage of development of this medicine?

The effects of TGF-ß2 antisense oligonucleotide have been evaluated in experimental models.

At the time of submission of the application, a clinical trial in patients with high-grade glioma was ongoing.

TGF-ß2 antisense oligonucleotide had not been marketed anywhere worldwide for high-grade glioma or designated as an orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 23 January 2002 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.

*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.
At the time of designation, this represented a population of 380,600,000 (Eurostat 2002).

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	TGF-β2 specific phosphorothioate antisense oligodeoxynucleotide	Treatment of high-grade glioma
Danish	TGF-β2 specifik phosphorothioat antisense oligodeoxynucleotid	Behandling af høj grads gliomer
Dutch	TGF-β2 specifiek phosphorothioate antisense oligodeoxynucleotide	Behandeling van hooggradig glioma
Finnish	TGF-β2 spesifinen fosforotioaatti antisense oligodeoksinukleotidi	Korkea-asteisen glioman hoito
French	Oligodéoxynucléotide antisens (phosphorothioate) spécifique anti-TGF-β2	Traitement du gliome de haut grade
German	TGF-β2 spezifisches Phosphorothioat-Antisense-Oligodeoxynukleotid	Behandlung von malignem Gliom
Greek	Ειδικό για το TGF-β2 αντιπληροφοριακό φωσφοροθειονικό ολιγοδεοξυνουκλεοτίδιο	Θεραπεία του υψηλού βαθμού γλοιώματος
Italian	oligodeoxinucleotide antisenso (fosforothioato) specifico contro TGF-β2	Trattamento dei gliomi ad alto grado
Portuguese	Oligodeoxinucleotido fosforotioato antisentido específico de encontro TGF-β2	Tratamento do glioma de alto grado
Spanish	Oligodeoxinucleótido antisentido (fosforotioato) específico contra TGF-β2	Tratamiento de glioma de alto grado
Swedish	TGF-β2 specifik phosphorothioat-antisens-oligodeoxynucleotid	Behandling av höggradigt gliom

[1] At the time of designation