21 March 2014
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adenovirus-mediated *Herpes simplex* virus – thymidine kinase (HSV-tk) gene for the treatment of high-grade glioma with subsequent use of ganciclovir sodium

First publication, rev.1 & 2	6 January 2003
Rev.3: sponsor's change of address	12 March 2013
Rev.4: 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 6 February 2002, orphan designation (EU/3/01/083) was granted by the European Commission to Ark Therapeutics Limited, United Kingdom, for adenovirus-mediated *Herpes simplex* virus thymidine kinase gene for the treatment of high-grade glioma with subsequent use of ganciclovir sodium.

In February 2014, Ark Therapeutics Limited changed name to Finvector Vision Therapies Limited.

What is high-grade glioma?

Tumours that begin in brain tissue 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 refers 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 tumours are more malignant than low grade tumours and are life-threatening.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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 were authorised at the time of submission of the application for orphan designation. The potential for adenovirus-mediated *Herpes simplex* virus thymidine kinase gene to be of potential significant benefit for the treatment of glioma was based on the novel mechanism of action in particular with regards to improved efficacy.

How is this medicine expected to work?

At the end of the surgical operation to remove the tumour, the thymidine kinase gene is injected into the underlying brain tissue, where it is taken up into the cells. This is followed by systemic administration of the drug ganciclovir, which is a prodrug (a drug which needs to be activated before it can act). The transferred gene expressed in the cells is able to metabolise ganciclovir transforming it into a drug that is toxic for tumour cells that divide. The toxic form of the drug can also spread to neighbouring cells 'by-stander effect'.

What is the stage of development of this medicine?

Clinical studies of the medicinal product in association with ganciclovir are ongoing in adults with high grade glioma.

The product had not been marketed in any country at the time of submission of the application for orphan designation.

In the US orphan drug status was granted for use with ganciclovir in the treatment of malignant glioma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 November 2001 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.
At the time of designation, this represented a population of 380,600,000 (Eurostat 2002).

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:

Finvector Vision Therapies Limited
Sanderum House
Oakley Road Chinnor
Oxfordshire OX39 4TW
United Kingdom
Tel. +44 1844 3556244
Fax +44 1844 353553

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	Adenovirus-mediated *Herpes Simplex* Virus-thymidine kinase gene	Treatment of high-grade glioma with subsequent use of ganciclovir sodium
Danish	Adenovirus-medieret *herpes simplex* virus-thymidin kinase gen	Behandling af høj grad gliom med efterfølgende brug af ganciclovir natrium
Dutch	Adenovirus-gemedieerd *herpes-simplex*-virus thymidinekinase gen	Behandeling van maligne glioom gevolgd door ganciclovir
Finnish	Adenovirusvälitteinen *herpes simplex* -viruksen tymidiinikinaasi-geeni	Korkea-asteisen gliooman hoito, jota seuraa hoito gansikloviiri natriumilla
French	Vecteur adénoviral porteur du gène de la thymidine-kinase du virus *Herpes simplex*	Traitement du gliome de haut grade préalablement à administration de ganciclovir sodique
German	Adenovirus-vermitteltes *Herpes-simplex*-Virus-Thymidinkinase-Gen	Behandlung des malignen Glioms mit nachfolgender Applikation von Ganciclovir
Greek	Γονίδιο θυμιδίνης κινάσης του ιού του απλού έρπητα με τη μεσολάβηση αδενοϊού	Θεραπεια του κακοήθους γλοιωματος σε συνδυασμο με γανκικλοβίρη
Italian	Gene della timidina chinasi del virus *herpes simplex* mediato attraverso l'adenovirus	In associazione con ganciclovir sodio nel trattamento del glioma maligno
Portuguese	Gene da timidina quinase do vírus *Herpes simplex* mediado por adenovirus	Tratamento do Glioma maligno de alto grau com uso subsequente de ganciclovir sódico
Spanish	Gen de la quinasa de timidina del virus herpes simple mediado por el adenovirus	Tratamiento de glioma de alto grado con posterior administración de ganciclovir sódico
Swedish	Adenovirusmedierad *herpes simplex* virus tymidinkinas gen	Behandling av höggradiga gliom med efterföljande användning av ganciclovir natrium

[1] At the time of designation