



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of autologous tumour-derived gp96 heat shock protein-peptide complex for the treatment of glioma

On 29 April 2009, orphan designation (EU/3/09/624) was granted by the European Commission to Antigenics Therapeutics Limited, Ireland, for autologous tumour-derived gp96 heat shock protein-peptide complex 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 is equivalent to a total of around 50,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and 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 used to kill cancer cells). Patients also received treatments for the symptoms of glioma, including corticosteroids to reduce pressure within the skull and medicines to prevent fits. The sponsor has provided sufficient information to show that autologous tumour-derived gp96 heat shock protein-peptide complex might be of significant benefit for the patients because it works in a different way to existing medicines. 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?

Autologous tumour-derived gp96 heat shock protein-peptide complex is expected to work as a tumour vaccine. It is made up of substances extracted from the patient's tumour, a protein called 'gp96 heat shock protein' and peptides (protein fragments), which form a fingerprint for that tumour.

*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 504,800,000 (Eurostat 2009).

When the patient is given the vaccine, the heat shock protein and the peptides are now recognised as 'foreign' by the immune system (the body's natural defences), stimulating an immune response. This is expected to lead to the immune system being able to attack and kill the tumour cells and not cells elsewhere in the body.

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, clinical trials in patients with glioma and other types of cancer were 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 4 March 2009 recommending the granting of this designation.

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 Community) 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.

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**Translations of the active ingredient and indication in all official EU languages,
Norwegian and Icelandic**

Language	Active ingredient	Indication
English	Autologous tumour-derived gp96 heat shock protein-peptide complex	Treatment of glioma
Bulgarian	Автоложен gp96 топлинен шок протеин –пептид комплекс, получен от тумор	Лечение на глиома
Czech	Autologní, z tumoru derivovaný gp96 komplex peptidů a proteinů tepelného šoku	Léčba gliomů
Danish	Autogent tumoraflødt gp96 varmekok-protein-peptidkomplex	Behandling af gliom
Dutch	Autoloog tumoreus afgeleid gp96 hiteshok-protéïne - peptidecomplex	Behandeling van glioma
Estonian	Autoloogiline kasvajaletatud gp96 kuumashoki valgupeptiidi kompleks	Glioomi ravi
Finnish	Autologinen, kasvainperäinen, gp96- lämpösokkiproteiini-peptidi-kompleksi	Gliooman hoito
French	Complexe de protéine-peptide de choc thermique gp96, dérivé de cellules tumorales autologues	Traitement des gliomes
German	Autologer, aus Tumorzellen gewonnener gp96 Hitzeshock-Protein-Peptidkomplex	Behandlung von Gliomen
Greek	Αυτόλογο πρωτεϊνικό-πεπτιδικό σύμπλεγμα θερμικού πλήγματος gp96, προερχόμενο από νεόπλασμα	Θεραπεία του γλοιώματος
Hungarian	Autológ tumor-eredetű gp96 hőshock fehérje-peptid komplex	Glioma kezelése
Italian	Complesso proteina gp96-peptide da shock termico derivato da tumore autologo	Trattamento del glioma
Latvian	Autologs, no audzēja atvasināts gp96 karstumšoka olbaltumvielu-peptīdu komplekss	Gliomas ārstēšana
Lithuanian	Autologinis navikinės kilmės gp96 šiluminio streso baltymų ir peptidų kompleksas	Gliomos gydymas
Maltese	Kumpless ta' proteina-peptide gp96 b'xokk termiku imnissel minn tumor awtologuż	Kura tal-glioma
Polish	Otrzymywany z tkanki nowotworowej autologiczny kompleks polipeptydów gp96 białek szoku cieplnego	Leczenie glejaka
Portuguese	Complexo de proteínas/péptidos gp96 obtido por choque térmico, derivado de tumor autólogo	Tratamento do glioma
Romanian	Complex de proteine-peptide de șoc termic gp 96 derivat din celule tumorale autologe	Tratamentul gliomului
Slovak	Autologový, z tumoru získaný gp96 komplex peptidov a proteínov tepelného šoku	Liečba gliómu
Slovenian	Avtologni, iz tumorskih celic s toplotnim šokom pridobljen gp96 proteinsko-peptidni kompleks	Zdravljenje glioma
Spanish	Complejo péptido- proteína gp96 del shock térmico derivado de tumor autólogo	Tratamiento del glioma
Swedish	Autogott tumörderiverat gp96 värmechock protein-peptidkomplex	Behandling av gliom
Norwegian	Autogott tumor-derivert gp96- varmesjokkprotein-peptidkompleks	Behandling av gliom
Icelandic	Samkynja gp96 hitalostmyndað prótínpeptíð samband úr æxli	Meðferð á glíóma