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 anti epidermal growth factor receptor antibody h-R3 for the treatment of glioma

On 2 September 2004, orphan designation (EU/3/04/220) was granted by the European Commission to Oncoscience AG, Germany, for anti epidermal growth factor receptor antibody h-R3 (cimazumab) for the treatment of glioma.

What is 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 being gliomas, which begin in the glial (supportive) tissue.
Gliomas represent a potentially debilitating and life-threatening condition. Patients affected by gliomas can suffer from severe symptoms of the nervous system, depending on where in the brain the tumour develops.

What are the methods of treatment available?
Treatment for gliomas depends on a number of factors and encompasses several methods such as surgery, radiotherapy (using high-dose x-rays or other high-energy rays to kill cancer cells) or chemotherapy (using drugs to kill cancer cells), as well as some symptomatic treatments. Symptomatic treatments include certain steroid hormones (corticosteroids) to control the effects of raised pressure within the skull, and medication to help control seizures, as required. Methods of treatment of glioma were authorised in the Community at the time of submission of the application for orphan designation.
Cimazumab might be of potential significant benefit for the treatment of gliomas. The main reason is that cimazumab may offer a new way of killing the cancer cells and stopping tumour growth in these patients. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

What is the estimated number of patients affected by the condition?
According to the information provided by the sponsor, glioma was considered to affect about 46,000 persons in the European Union.

How is this medicinal product expected to act?
Antibodies are proteins in the body that target specific shapes on the surface of foreign entities, such as bacteria and virus, but also body cells including cancer cells. Epidermal growth factor receptor (EGFR) is a protein that can be found on the surface of certain normal cells, the so-called epithelial cells. It can also be found in a higher proportion on the surface of some tumour cells such as gliomas and in this particular case, seems to be associated with a higher tendency to become a more invasive tumour. Cimazumab is an antibody that specifically recognises and binds to these EGFR proteins. Once cimazumab is linked to EGFR, the biological reactions associated to EGFR are blocked, and in

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particular the one that has an important role in the survival and multiplication of the cancer cells. Cimazumab might, by inhibiting these activities, help in slowing down or stopping the further growth of the glioma cells and might help in the destruction of these cells.

What is the stage of development of this medicinal product?
The effects of cimazumab were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with glioma were ongoing.

Cimazumab was not marketed anywhere worldwide for glioma or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 22 July 2004 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

For more information:
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*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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

Language	**Active Ingredient**	**Indication**
English	Anti epidermal growth factor receptor antibody h-R3	Treatment of glioma
Czech	Protilátka h-R3 proti receptoru epidermálního růstovéhofaktoru	Léčba gliomu
Danish	Anti-epidermal vækstfaktorreceptor-antistof h-R3	Behandling af gliom
Dutch	Anti epidermale groeifactor receptor antilichaam h-R3	Behandeling van glioma
Estonian	Epidermaalse kasvufaktori retseptori vastane antikeha h-R3	Glioomi ravi
Finnish	h-R3, epidermaalisen kasvutekijän reseptorin vasta-aine	Gliooman hoito
French	Anticorps h-R3 anti-récepteur du facteur de croissance épidermique	Traitement des gliomes
German	Anti epidermaler Wachstumsfaktor Rezeptor Antikörper h-R3	Behandlung des Glioms
Greek	Αντίσωμα h-R3 αντι- υποδοχέα του επιδερμικού αυξητικού παράγοντα	Θεραπεία του γλοιώματος
Hungarian	h-R3, anti-epidermalis növekedési faktor receptor elleni antitest	Glioma kezelése
Italian	Anticorpo anti-recettore del fattore di crescita epiteliale h-R3	Trattamento del glioma
Latvian	Antiepidermālā augšanas faktora receptoru antiviela h-R3	Gliomas ārstēšana
Lithuanian	Antiepiderminio augimo faktoriaus receptoriaus antikūnis h-R3	Gliomos gydymas
Maltese	Anti epidermal growth factor receptor antibody h-R3	Treatment of glioma
Polish	Przeciwciała h-R3 przeciw receptorowi nabłonkowego czynnika wzrostu	Leczenie glejaka
Portuguese	Anticorpo h-R3 do receptor do factor de crescimento anti-epidérmico	Tratamento do glioma
Slovak	Protilátka h-R3 proti receptoru epidermálneho rastového faktora	Liečba gliómu
Slovenian	Protitelo h-R3 proti receptorju epidermalnega rastnega faktorja	Zdravljenje glioma
Spanish	Anticuerpo humanizado R3 contra el receptor del factor de crecimiento epidérmico	Tratamiento del glioma
Swedish	Antiepidermal tillväxtfaktorreceptor antikropp h-R3	Behandling av gliom
Norwegian	Anti-epidermalt vekstfaktor-reseptor antistoff h-R3	Behandling av gliom
Icelandic	Mótefni h-R3 gegn vaxtarþáttarviðtaka húðþekju	Meðferð gegn tróðæxli