



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

16 December 2011
EMA/COMP/793868/2011 Rev 1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

L-cysteine, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyl]-complex with keyhole limpet haemocyanin for the treatment of glioma

On 27 October 2011, orphan designation (EU/3/11/923) was granted by the European Commission to Orphix Consulting GmbH, Germany, for L-cysteine, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyl]-complex with keyhole limpet haemocyanin (also known as rindopepimut) 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 severe damage to the brain which 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 approximately 1.2 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 61,000 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).



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 and radiotherapy (treatment with radiation), as well as 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 this medicine might be of significant benefit for patients with glioma because it works in a different way to existing treatments and might be used in combination with existing methods to improve the treatment of patients. 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?

The medicine is a 'cancer vaccine'. It is expected to work by activating the patient's immune system (the body's natural defences) so that it attacks and destroys the tumour cells of the glioma.

This vaccine is based on a peptide (a short chain of amino acids) which is specific to a variant of the epidermal growth factor receptor known as EGFRvIII which is involved in the growth and spread of cancer cells and is found on the tumour cells in some glioma patients. To prepare this vaccine, the peptide is produced in a laboratory. It is attached to a carrier, called 'keyhole limpet haemocyanin' (a protein prepared from a sea snail), which acts as an immune stimulant to enhance the response of the body to the EGFRvIII peptide in the vaccine. When this vaccine is given, the patient's immune system is expected to recognise the EGFRvIII peptide as 'foreign'. This is expected to stimulate an immune response against the glioma cells containing this peptide, resulting in the immune system attacking and destroying these cells, but leaving other cells in the body unharmed.

What is the stage of development of this medicine?

The effects of the medicinal product have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicinal product in patients with glioma were ongoing.

At the time of submission, the medicinal product was not authorised anywhere in the EU for glioma. Orphan designation of the medicinal product had been granted in the United States for glioblastoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 September 2011 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 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:

Orphix Consulting GmbH

Steinsdorfstraße 19

80538 Munich

Germany

tel: +49 89 44 42 94 97

fax: +49 89 44 48 94 93

e-mail: info@orphix.com

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	L-cysteine, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyl]-complex with keyhole limpet haemocyanin	Treatment of glioma
Bulgarian	L-цистеин, L-левцил-L-алфа-глутамил-L-алфа-глутамил-L-лизил-L-лизилглицил-L-аспарагинил-L-тирозил-L-валил-L-валил-L-треонил-L-алфа-аспартил-L-хистидил-S-[1-[(4-карбоксициклохексил)метил]-2,5-диоксо-3-пирролидинил]-, комплекс с хемоцианин от <i>Megathura crenulata</i>	Лечение на глиома
Czech	L-cystein, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyl]-, komplex s hemocyanin klíště klíčovou dírkou	Léčba gliomů
Danish	L-cystein, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartylprotease-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyl]-, kompleks med nøglehul limpet hemocyanin	Behandling af gliom
Dutch	L-cysteïne, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyl]-, complex met sleutelgat (keyhole) limpet hemocyanine	Behandeling van glioma
Estonian	L-tsüsteiin, L-leucyl-L-alpha-glutamüül-L-alpha-glutamüül-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)metüül]-2,5-diokso-3-pyrrolidinyl]-, kompleksi lukuauku Maljakotilo hemocyanin	Glioomi ravi
Finnish	L-kysteiini, L-leusyyli-L-alfa-glutamyyli-L-alfa-glutamyyli-L-lysyli-L-lysyyliglysyli-L-asparaginyli-L-tyrosyyli-L-valyyli-L-valyyli-L-treonyyli-L-alfa-aspartyyli-L-histidyyli-S-[1-[(4-karboksisikloheksyyli)metyyli]-2,5-diokso-3-pyrrolidinyli]-, kompleksi KLH (keyhole limpet hemocyanin):n kanssa	Gliooman hoito
French	L-cystéine, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginy-L-tyrosyl-L-valyl-L-valyl-L-thréonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)méthyl]-2,5-dioxo-3-pyrrolidinyl]-, complexe avec l'hémocyanine de patelle	Traitement des gliomes

¹ At the time of designation

Language	Active ingredient	Indication
German	L-Cystein, L-Leucyl-L-alpha-Glutamyl-L-alpha-Glutamyl-L-Lysyl-L-lysylglycyl-L-asparaginyL-L-Tyrosyl-L-Valyl-L-Valyl-L-Threonyl-L-alpha-Aspartyl-L-Histidin-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-PyrrolidinyGruppe]-Komplex mit Schluesselloch-Napfschnecken-Hämocyanin	Behandlung von Gliomen
Greek	L-κυστεΐνη, L-λευκυλ-L-α-γλουταμυλ-L-α-γλουταμυλ-L-λυσυλ-L-λυσυλογλυκυλ-L-ασπαραγινυλ-L-τυροσυλ-L-βαλυλ-L-βαλυλ-L-θρεονυλ-L-α-ασπαρτυλ-L-ιστιδυλ-S-[1-[(4-καρβοξυκυκλοεξυλ)μεθυλο]-2,5-διοξο-3-πυρολιδινυλ]-, σύμπλεγμα με την αιμοκυανίνη του <i>Megathura crenulata</i> .	Θεραπεία του γλοιώματος
Hungarian	L-cisztein, L-metionil-leucil-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginyL-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aszpartil-L-hisztidin-S-[1-[(4-carboxycyclohexyl)metil]-2,5-dioxo-3-pirrolidil]-, komplexum kulcslyukon tapadó tengeri csiga hemocyanin	Glioma kezelése
Italian	L-cistein, L-leucil-L-alpha-glutamyl-L-alpha-glutamyl-L-lisil-L-lysylglycyl-L-asparaginyL-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartil-L-istidil-S-[1-[(4-carboxycyclohexyl)metil]-2,5-diosso-3-pirrolidinile]-, complesso con emocianina da <i>Megathura crenulata</i>	Trattamento del glioma
Latvian	L-cisteīna, L-leucil-L-alpha-glutamyl-L-alpha-glutamyl-L-lizil-L-lizilglicil-L-asparaginil-L-tirozil-L-valil-L-valil-L-treonil-L-alpha-aspartil-L-histidil-S-[1-[(4-karboksicikloheksil)metil]-2,5-diokso-3-pirrolidinil]-, komplekss ar pieeju hemocianīnam	Gliomas ārstēšana
Lithuanian	L-cisteinas, L-leucil-L-alfa-glutamyl-L-alfa-glutamyl-L-lizil-L-lizilglycil-L-asparaginil-L-tirozil-L-valil-L-valil-L-treonil-L-alfa-aspartil-L-histidil-S-[1-[(4-karboksicikloheksil)metil]-2,5-diokso-3-pirolidinil]-, kompleksas su raktiniu atitikimu hemocianinui	Gliomos gydymas
Maltese	L-cysteine, L-leucyl-L-alpha-glutamyl-L-alpha-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginyL-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-alpha-aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyL]-, kumpleks mal-emoċjanina ta' <i>Megathura crenulata</i> (keyhole limpet)	Kura tal-glioma
Polish	L-cysteiny, L-leucylo-L-alfa-glutamylo-L-alfa-glutamylo-L-lizyno-L-lizynoglicylo-L-asparaginylo-L-tyrozylo-L-walino-L-walino-L-treonino-L-alfa-aspartylo-L-histydylo-S-[1-[(4-carboksycykloheksyl)metylo]-2,5-diokso-3-pirolidynylo]-, kompleks z hemocyjaniną skałoczezu	Leczenie glejaka
Portuguese	Complexo L-cisteína, L-leucil-L-alpha-glutamyl-L-alpha-glutamyl-L-lisil-L-lisilglicil-L-asparaginil-L-tirosina, L-valil-L-valil-L-threonil-L-alpha-aspartil-L-histidil-S-[1-[(4-carboxiciclohexil)metil]-2,5-dioxo-3-pirrolidinila]-, com sitio de ligação de forte afinidade para hemocianina	Tratamento do glioma

Language	Active ingredient	Indication
Romanian	L-cisteină, L-leucil-L-alfa-glutamyl-L-alfa-glutamyl-L-lizil-L-lizilglicil-L-asparaginil-L-tirozil-L-valil-L-valil-L-treonil-L-alfa-aspartil-L-histidil-S-[1-[(4-carboxiciclohexil)metil]-2,5-dioxo-3-pirolidinil]-, complex cu hemocianină din <i>Megathura crenulata</i> (keyhole limpet)	Tratamentul gliomului
Slovak	L-cysteín, L-leucyl-L-alfa-glutamyl-L-alfa-glutamyl-L-lyzyl-L-lyzylglycyl-L-asparaginyL-L-tyrozyl-L-valyl-L-valyl-L-treonyl-L-alfa-aspartyl-L-histidyl-S-[1-[(4-karboxycyklohexyl)metyl]-2,5-dioxo-3-pyrrolidinyl]-, komplex s hemocyanínom z <i>Megathura crenulata</i>	Liečba gliómu
Slovenian	L-cistein, L-leucil-L-alfa-glutamyl-L-alfa-glutamyl-L-lisil-L-lisilglicil-L-asparaginil-L-tirosil-L-valil-L-valil-L-treonil-L-alfa-aspartil-L-histidil-S-[1-[(4-karboksicikloheksil)metil]-2,5-diokso-3-pirolidinil]-, kompleks s hemocianinom orjaške strešice	Zdravljenje glioma
Spanish	Complejo de L-cisteína, L-leucil-L-alpha-glutamyl-L-alpha-glutamyl-L-lisil-L-lysylglycyl-L-asparaginil-L-tirosilo-L-valil-L-valil-L-treonil-L-alfa-aspartil-L-histidina-S-[1-[(4-carboxyciclohexyl)metil]-2,5-dioxo-3-pirrolidinilo]-, y hemocianina de <i>Megathura crenulata</i>	Tratamiento del glioma
Swedish	L-cystein, L-leucyl-L-alfa-glutamyl-L-alfa-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginyL-L-tyrosyl-L-valyl-L-valyl-L-treonyl-L-alfa-aspartyl-L-histidyl-S-[1-[(4-carboxycycloheksyl)metyl]-2,5-diokso-3-pyrrolidinyl]-, komplex med nyckelhål limpet hemocyanin	Behandling av gliom
Norwegian	L-cystein, L-leucyl-L-alfa-glutamyl-L-alfa-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginyL-L-tyrosyl-L-valyl-L-valyl-L-treonyl-L-alfa-aspartyl-L-histidyl-S-[1-[(4-carboxycycloheksyl)metyl]-2,5-diokso-3-pyrrolidinyl]-, kompleks med nøkkelhull limpet hemocyanin	Behandling av gliom
Icelandic	L-sýsteín, L-leucýl-L-alfa-glútamýl-L-alfa-glútamýl-L-lýsýl-L-lýsýlglýcýl-L-asparagínýl-L-týrósfýl-L-valýl-L-valýl-L-threónýl-L-alfa-aspartýl-L-histidýl-S-[1-[(4-carboxýcýclóhexýl)metýl]-2,5-díoxó-3-pýrrólidínýl]-, samstæðameð skráargat sæsniglahemóc+yaníni	Meðferð á glíóma