30 March 2015
EMA/COMP/26647/2015
Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## Recombinant human glutamate oxaloacetate transaminase 1 for the treatment of glioma



On 12 February 2015, orphan designation (EU/3/15/1443) was granted by the European Commission to Impasara Ltd, United Kingdom, for recombinant human glutamate oxaloacetate transaminase 1 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 one 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 the severe damage to the brain, and 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 less than 2.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 128,000 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?

At the time of designation, several medicines were authorised for the treatment of glioma in the EU. Treatments included surgery, radiotherapy (treatment with radiation), and chemotherapy (medicines

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

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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 the medicine might be of significant benefit for patients with glioma because studies in experimental models showed that the medicine, when given with another medicine for glioma, temozolomide, might improve the survival of patients with the condition. 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?

In glioma patients, the glioma cells release high levels of glutamate into some parts of the brain. Glutamate is a substance important for brain function but if too much is present it can cause death of nerve cells and thus promote the growth of glioma cells. The medicine is made up of 'glutamate oxaloacetate transaminase', an enzyme normally found in the blood that transforms glutamate into another compound that is not toxic to the brain. By reducing the levels of glutamate in the blood the levels of glutamate in the brain are also expected to decrease. This is expected to slow down the growth of the glioma.

The glutamate oxaloacetate transaminase in this medicine is made by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced that makes them able to produce the protein. The medicine is to be delivered by injection under the skin.

## What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with glioma had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for glioma or designated as an 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 9 January 2015 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.

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 | Recombinant human glutamate oxaloacetate transaminase 1 | Treatment of glioma |
| Bulgarian | Рекомбинантен човешка глутамат оксалацетат-трансаминаза 1 | Лечение на глиома |
| Croatian | Rekombinantna ljudska glutamat-oksaloacetatna transaminaza 1 | Liječenje glioma |
| Czech | Rekombinantní lidský glutamát oxaloacetát transamináz 1 | Léčba gliomů |
| Danish | Rekombineret humant glutamat oxaloacetat transaminase 1 | Behandling af gliom |
| Dutch | Recombinant humaan glutamaat oxaloacetaat transaminase 1 | Behandeling van glioma |
| Estonian | Rekombinantne inimese glutamaat oksaloatsetaat transaminaas 1 | Glioomi ravi |
| Finnish | Rekombinantti ihmisen glutamaatti oksalostaasetaatti transaminaasi 1 | Gliooman hoito |
| French | Glutamate oxaloacétate transaminase 1 recombinante humaine | Traitement des gliomes |
| German | Rekombinante humane Glutamat oxaloacetat–Transaminase 1 | Behandlung von Gliomen |
| Greek | Ανασυνδυασμένηανθρώπινη γλουταμινική οξαλοξεική τρανσαμινάση 1 | Θεραπεία του γλοιώματος |
| Hungarian | Rekombináns humán glutamát-oxálacetát-transzamináz 1 | Glioma kezelése |
| Italian | Glutammato-ossalacetato transaminasi 1 umana ricombinante | Trattamento del glioma |
| Latvian | Rekombinanta cilvēka glutamāta oksalacetāta transaminācze 1 | Gliomas ārstēšana |
| Lithuanian | Rekombinantinė žmogaus glutamato oksaloacetato transaminazė 1 | Gliomos gydymas |
| Maltese | Glutamate oxaloacetate transaminase 1 uman rikombinanti | Kura tal-glioma |
| Polish | Rekombinowana ludzka transaminaza glutaminianowo-szczawiooctanowa 1 | Leczenie glejaka |
| Portuguese | Glutamato-oxaloacetato-transaminase 1 humana recombinante | Tratamento do glioma |
| Romanian | Transaminaza glutamat oxaloacetat 1 umană recombinantă | Tratamentul gliomului |
| Slovak | Rekombinantný ľudský glutamát-oxalacetát transaminázy 1 | Liečba gliómu |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Slovenian | Rekombinantna humana glutamatoksaloacetatna transaminaza 1 | Zdravljenje glioma |
| Spanish | Glutamato-oxaloacetato-transaminasa 1 humana recombinante | Tratamiento del glioma |
| Swedish | Recombinant humant glutamat oxaloacetat – transaminas 1 | Behandling av gliom |
| Norwegian | Rekombinant human glutamat oksaloacetat transaminase 1 | Behandling av gliom |
| Icelandic | Raðbrigða mannaglútamat oxalóasetat transamínasi 1 | Meðferð á glíóma |