10 November 2014
EMA/COMP/553420/2014
Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## Recombinant human bone morphogenetic protein 4 for the treatment of glioma

On 15 October 2014, orphan designation (EU/3/14/1348) was granted by the European Commission to Stemgen S.p.A., Italy, for recombinant human bone morphogenetic protein 4 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 approximately 1.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 92,000 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 511,100,000 (Eurostat 2014).

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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 'recombinant human bone morphogenetic protein 4' might be of significant benefit for patients with glioma because studies in experimental models showed that the medicine might reduce tumour growth and 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?

This medicine is made up of a protein called 'bone morphogenetic protein 4', which belongs to a group of proteins that stimulate immature dividing cells called stem cells to become fully mature cells. Gliomas are thought to arise from so-called 'glioma stem cells', which divide uncontrollably and are thought to be responsible for glioma growth. This medicine is expected to reduce glioma growth by making glioma stem cells become fully mature cells, thus reducing their growth. Fully mature glioma cells would also be more sensitive to cancer treatment.

The bone morphogenetic protein 4 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 directly into the brain by a catheter (tube).

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

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, 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 4 September 2014 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 bone morphogenetic protein 4 | Treatment of glioma |
| Bulgarian | Рекомбинантен човешки костен морфогенетичен протеин 4 | Лечение на глиома |
| Croatian | Rekombinantni ljudski koštani morfogenetski protein 4 | Liječenje glioma |
| Czech | Rekombinantní lidský kostní morfogenetický protein 4 | Léčba gliomů |
| Danish | Rekombinant humant knoglemorfogenetisk protein 4 | Behandling af gliom |
| Dutch | Recombinant humaan botmorfogenetisch proteïne 4 | Behandeling van glioma |
| Estonian | Inimese rekombinantne morfogeneetiline valk 4 | Glioomi ravi |
| Finnish | Rekombinantti ihmisen luun morfogeneettinen proteiini 4 | Glioman hoito |
| French | Protéine 4 humaine recombinante morphogénétique osseuse | Traitement des gliomes |
| German | Rekombinantes humanes Knochen-morphogenetisches Protein 4 | Behandlung von Gliomen |
| Greek | Ανασυνδυασμένη ανθρώπινη οστεομορφογενετική πρωτεΐνη 4 | Θεραπεία του γλοιώματος |
| Hungarian | 4-es számú rekombináns humán csont morfogenetikus fehérje | Glioma kezelése |
| Italian | proteina umana ricombinante morfogenetica dell'osso 4 | Trattamento del glioma |
| Latvian | Rekombinants cilvēka kaulu morfoģenētiskais proteīns 4 | Gliomas ārstēšana |
| Lithuanian | Rekombinantinis žmogaus kaulų morfogenetinis baltymas 4 | Gliomos gydymas |
| Maltese | Proteina 4 morfoġenetika tal-għadam uman rikombinanti | Kura tal-glioma |
| Polish | Rekombinowane ludzkie białko morfogenetyczne kości 4 | Leczenie glejaka |
| Portuguese | Proteína-4 morfogenética óssea humana recombinante | Tratamento do glioma |
| Romanian | Proteină morfogenetică osoasă 4 umană recombinantă | Tratamentul gliomului |
| Slovak | Rekombinantný ľudský kostný morfogenetický protein 4 | Liečba gliómu |
| Slovenian | Rekombinantni humani kostni morfogenetski protein 4 | Zdravljenje glioma |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Spanish | Proteína morfogenética ósea 4 humana recombinante | Tratamiento del glioma |
| Swedish | Rekombinant humant benmorfogenesprotein 4 | Behandling av gliom |
| Norwegian | Rekombinant humant beinmorfogent protein 4 | Behandling av gliom |
| Icelandic | Raðbrigða mannabeinaformvaka prótein 4 | Meðferð á glíóma |