16 October 2017
EMA/507448/2017

Public summary of opinion on orphan designation

Salmonella typhi Ty21a strain transfected with a plasmid vector encoding the human vascular endothelial growth factor receptor 2 for the treatment of glioma

On 23 August 2017, orphan designation (EU/3/17/1909) was granted by the European Commission to Vaximm GmbH, Germany, for *Salmonella typhi* Ty21a strain transfected with a plasmid vector encoding the human vascular endothelial growth factor receptor 2 (also known as VXM01) 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 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 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 134,000 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 28), Norway, Iceland and Liechtenstein. This represents a population of 515,700,000 (Eurostat 2017).

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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 (treatment with radiation), and 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 early data show improvement in patients whose disease came back after standard therapy including authorised treatments. 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 stimulates the patient's immune (defence) system to target and destroy cells with a receptor (target) called VEGFR-2. These receptors are involved in the development of new blood vessels and are found in high numbers on glioma cells.

The medicine is made of *Salmonella* bacteria which contain genetic material (plasmid). When given to patients, the bacteria release the plasmid in the body causing the body's cells to produce VEGFR-2. This leads the immune system to regard cells with VEGFR-2 as 'foreign' and destroy them. By removing cells with VEGFR-2, the medicine is expected to prevent development of blood vessels to the glioma and so starve the cancer cells of oxygen and nutrients.

The *Salmonella* bacteria have been attenuated (weakened) so that they do not cause disease and cannot multiply in the body.

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, clinical trials with the medicine in patients with glioma were ongoing.

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 13 July 2017 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	*Salmonella typhi* Ty21a strain transfected with a plasmid vector encoding the human vascular endothelial growth factor receptor 2	Treatment of glioma
Bulgarian	Щам Ty21a на *Salmonella typhi*, трансфектиран с плазмиден вектор, кодиращ рецептор 2 за човешкия съдов ендотелен растежен фактор	Лечение на глиома
Croatian	*Salmonella typhi* Ty21a soj transfektiran s plazmidnim vektorom koji kodira za ljudski receptor 2 vaskularnog endotelnog faktora rasta	Liječenje glioma
Czech	Kmen *Salmonella typhi* Ty21a transfektovaný plazmidovým vektorem kódujícím receptor typu 2 pro humánní cévní endoteliální růstový faktor	Léčba gliomů
Danish	*Salmonella typhi* Ty21a stamme transficeret med en plasmid vektor, der koder for den humane vaskulære endoteliale vækstfaktorreceptor 2	Behandling af gliom
Dutch	Stam van *Salmonella typhi* Ty21a, getransfecteerd met een plasmide vector die codeert voor de humane vaatendotheel-groeifactorreceptor 2	Behandeling van glioma
Estonian	Inimese veresoonte endoteeli kasvufaktori 2. tüüpi retseptorit kodeeriva plasmiidvektoriga transfekteeritud *Salmonella typhi* Ty21a tüvi	Glioomi ravi
Finnish	*Salmonella typhi* Ty21a -kanta, johon on transfektoitu ihmisen endoteelikasvutekijäreseptoria 2 koodaava plasmidivektori	Glioman hoito
French	Souche Ty21a de *Salmonella typhi* transfectée par un vecteur plasmidique codant pour le récepteur de type 2 du facteur de croissance de l'endothélium vasculaire humain	Traitement des gliomes
German	*Salmonella typhi* Ty21a Stamm, der mit einem Plasmidvektor transfiziert ist , der den humanen vaskulären endothelialen Wachstumsfaktor kodiert	Behandlung von Gliomen
Greek	Στέλεχος Ty21a της σαλμονέλας του τύφου που έχει διαμολυνθεί με πλασμιδιακό φορέα που κωδικοποιεί για τον υποδοχέα 2 του ανθρώπινου αγγειακού ενδοθηλιακού αυξητικού παράγοντα	Θεραπεία του γλοιώματος
Hungarian	Humán endoteliális növekedési faktor receptor 2-t kódoló plazmid vektorral transzfektált *Salmonella typhi* Ty21a törzs	Glioma kezelése
Italian	*Salmonella typhi* ceppo Ty21a transfettato con un vettore plasmidico che codifica per il recettore 2 del fattore di crescita vascolare endoteliale umano	Trattamento del glioma
Latvian	*Salmonella typhi* Ty21a celms, kas transfekcijas ceļā pārveidots ar plazmīdu vektoru, kas kodē cilvēka asinsvadu endotēlija augšanas faktora receptoru 2	Gliomas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	*Salmonella typhi* Ty21a štamas, transfekuotas su plazmidės vektoriumi, koduojančiu žmogaus kraujagyslių endotelio augimo faktoriaus receptorių 2	Gliomos gydymas
Maltese	Razza ta' *Salmonella typhi* Ty21a trasfettata ma' vettur ta' plasmid li jenkowdja r-riċettur 2 tal-fattur tat-tkabbir tal-endotelju vaskulari uman	Kura tal-glioma
Polish	Szczep *Salmonella typhi* Ty21a transfekowany wektorem plazmidowym kodującym receptor 2 dla ludzkiego naczyniowo-śródbłonkowego czynnika wzrostu	Leczenie glejaka
Portuguese	Estirpe Ty21a da *Salmonella typhi* transfetada com um vetor plasmídico que codifica o receptor 2 do fator de crescimento endotelial vascular humano	Tratamento do glioma
Romanian	Tulpină Ty21a de *Salmonella typhi* transfectată cu un vector plasmidic care codifică pentru receptorul 2 al factorului de creştere endotelial vascular uman	Tratamentul gliomului
Slovak	Kmeň *Salmonella Typhi* Ty21a transfektovaný plazmidovým vektorom kódujúcim receptor 2 ľudského cievneho endotelového rastového faktora	Liečba gliómu
Slovenian	Sev *Salmonella typhi* Ty21a, transfekciran s plazmidnim vektorjem, kodiranim za receptor humanega vaskularnega endotelijskega rastnega faktorja 2	Zdravljenje glioma
Spanish	Cepa de *Salmonella typhy* Ty21a transformada con un plásmido que contiene el gen que codifica para el receptor 2 del factor de crecimiento endotelial vascular humano.	Tratamiento del glioma
Swedish	*Salmonella typhi* Ty21a-stam transfekterad med en plasmidvektor som kodar för human vaskulär endoteltillväxtfaktorreceptor 2	Behandling av gliom
Norwegian	*Salmonella typhi* Ty21a stamme transfektert med en plasmid vektor som koder for human vaskulær endotelial vekstfaktor reseptor 2	Behandling av gliom
Icelandic	*Salmonella typhi* Ty21a stofn innleiddur með plasmíð-genaferju fyrir viðtaka 2 fyrir manna vaxtarþátt æðaþels (VEGF)	Meðferð á glíóma