13 November 2020
EMADOC-628903358-2753

Public summary of opinion on orphan designation

Autologous CD34+ cells transduced with a lentiviral vector encoding glucosylceramidase beta for the treatment of Gaucher disease

On 21 August 2020, orphan designation EU/3/20/2326 was granted by the European Commission to Clinical Technology Centre (Ireland) Limited, Ireland, for autologous CD34+ cells transduced with a lentiviral vector encoding glucosylceramidase beta (also known as AVR-RD-02) for the treatment of Gaucher disease.

What is Gaucher disease?

Gaucher disease is an inherited disorder that is caused by the lack of an enzyme called glucocerebrosidase beta. This enzyme normally breaks down a fatty waste product called glucocerebroside. Without the enzyme, glucocerebroside builds up in the body, typically in the liver, spleen and bone marrow. This causes a wide range of symptoms, including anaemia (low red blood cell counts), tiredness, easy bruising and a tendency to bleed, an enlarged spleen and liver, and bone pain and fractures. Some severe forms of the disease affecting children also involve the brain, which may cause problems such as abnormal eye and head movements and seizures (fits).

Gaucher disease is a long-term debilitating and life-threatening disease that is associated with a reduced life expectancy if left untreated.

What is the estimated number of patients affected by the condition?

At the time of designation, Gaucher disease affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 31,000 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, four medicines (eliglustat, imiglucerase, miglustat and velaglucerase alfa) were authorised for the treatment of Gaucher disease in the EU. Imiglucerase and velaglucerase alfa

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

are 'enzyme replacement therapies' that work by replacing the missing enzyme. Eliglustat and miglustat block the production of glucocerebroside.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Gaucher disease because laboratory results showed that the medicine significantly increased levels of glucocerebrosidase beta in spleen, liver and bone marrow. 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 made up of 'haematopoietic stem cells' that are taken from the patient. Haematopoietic stem cells are cells that can develop into different types of blood cell. To make this medicine, the cells are modified by a virus that carries normal copies of the gene for glucocerebrosidase beta (the enzyme that is missing in patients with Gaucher disease) into the cells. When these modified stem cells are given back to the patient, they are expected to produce the missing enzyme, thus restoring the body's ability to break down glucocerebroside.

The type of virus used in this medicine (‘lentivirus') is modified so that it does not cause disease in humans.

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 Gaucher disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of Gaucher disease. Orphan designation of the medicine had been granted in the United States for Gaucher disease.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 16 July 2020, 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

Contact details of the current sponsor for this orphan designation can be found on EMA website.

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	Autologous CD34+ cells transduced with a lentiviral vector encoding glucosylceramidase beta	Treatment of Gaucher disease
Bulgarian	Автоложни CD34+ клетки, трансдуцирани с лентивирусен вектор, кодиращ бета-глюкозилцерамидаза	Лечение на болест на Гоше
Croatian	Autologne CD34+ ćelije stanice transducirane lentivirusnim vektorom koji kodira glukozilceramidazu beta	Liječenje Gaucherove bolesti
Czech	Autologní CD34+ buňky transdukované s lentivirovým vektorem kódujícím β-glukosylceramidázu	Léčba Gaucherovy choroby
Danish	Autologe CD34+ celler overført med en lentiviralt vektor kodende for beta-glucosylceramidase	Behandling af Gauchers sygdom
Dutch	Autologe CD34+ cellen getransduceerd met een lentivirale vector die glucosylceramidase-beta codeert	Behandeling van de ziekte van Gaucher
Estonian	Beetaglükosüültseramidaasi kodeeriva lentiviirusvektoriga transdutseeritud autoloogsed CD34+ rakud	Gaucher' tõve ravi
Finnish	Beeta-glukosyyliseramidaasia koodaavalla lentivirusvektorilla transfektoidut autologiset CD34+-solut	Gaucherin taudin hoito
French	Cellules autologues CD34+ transduites par un vecteur lentiviral codant pour la glucosylcéramidase bêta	Traitement de la maladie de Gaucher
German	Autologe CD34-positive Zellen, welche mit einem Beta-Glucosylceramidase kodierenden, lentiviralen Vektor transduziert wurden	Behandlung der Gaucher-Krankheit
Greek	Αυτόλογα κύτταρα CD34+ διαμολυσμένα με λεντι-ιικό φορέα που κωδικοποιεί τη β-γλυκοσυλκεραμιδάση	Θεραπευτική αγωγή για την νόσο του Gaucher
Hungarian	Glükozilceramidáz béta enzimet kódoló lentivirális vektorral transzdulált autológ CD34+ sejtek	Gaucher-kór kezelése
Italian	Cellule CD34+ autologhe trasdotte con un vettore lentivirale che codifica l'enzima beta-glucosilceramidasi	Trattamento della malattia di Gaucher

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Autologas CD34+ šūnas, kas transducētas ar lentivīrusa vektoru, kas kodē bēta glikozilkeramidāzi	Gošē slimības ārstēšana
Lithuanian	Autologinės CD34+ ląstelės, transdukuotos su lentiviruso vektoriumi, koduojančiu beta gliukozilceramidazę	Gošė ligos gydymas
Maltese	Ċelloli awtologi CD34+ trasdotti b'vettur lentivirali li jikkodifika l-glukosilċeramidaży beta	Kura tal-marda ta' Gaucher
Polish	Komórki autologiczne CD34+ transdukowane wektorem lentiwiralnym kodującym kwaśną beta-glukozydazę	Leczenie choroby Gaucher'a
Portuguese	Células CD34+ autólogas transduzidas com um vetor lentiviral que codifica a beta-glicosilceramidase	Tratamento da doença de Gaucher
Romanian	Celule CD34+ autologe transduse cu un vector lentiviral care codifică beta-glucozilceramidaza	Tratamentul bolii Gaucher
Slovak	Autológne bunky CD34+ transdukované lentivírusovým vektorom kódujúcim beta-glykozylceramidázu	Liečba Gaucherovej choroby
Slovenian	Avtologne celice CD34+, transducirane z lentivirusnim vektorjem, ki kodira glukozilceramidazo beta	Zdravljenje Gaucherove bolezni
Spanish	Células CD34+ autólogas transducidas con un vector lentiviral que codifica la glucosilceramidasa beta	Tratamiento de la enfermedad de Gaucher
Swedish	Autologa CD34+ celler transducerade med en lentiviral vektor som kodar för beta-glukosylceramidas	Behandling av Gauchers sjukdom
Norwegian	Autologe CD34+ celler transdusert med en lentiviral vektor som koder for glukosylceramidase beta	Behandling av Gauchers sykdom
Icelandic	Samgena CD34 + frumur veiruleiddar með lentiveiruferju sem kóðar fyrir glúkósýlseramíðasa beta	Meðferð á Gauchersveiki