European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of autologous haematopoietic stem cells transduced with lentiviral vector encoding the human beta-globin gene for the treatment of beta thalassaemia major and intermedia

On 29 April 2009, orphan designation (EU/3/09/623) was granted by the European Commission to EGT San Rocco Italia SRL, Italy, for autologous haematopoietic stem cells transduced with lentiviral vector encoding the human beta-globin gene for the treatment of beta thalassaemia major and intermedia.

What are beta thalassaemia major and intermedia?

Beta thalassaemia is an inherited disease in which patients are unable to make enough haemoglobin, the protein found in red blood cells that carries oxygen around the body. Beta thalassaemia major is a severe form of the disease in which patients need frequent blood transfusions. Beta thalassaemia intermedia is a less severe form, which may get worse with age.
Beta thalassaemia intermedia and major are caused by abnormalities in a gene that is responsible for the production of beta globin. Beta globin is one of the proteins that make up haemoglobin.
Beta thalassaemia intermedia and major are debilitating diseases that are long lasting and may be life threatening because of the anaemia (the lack of haemoglobin), the need for repeated blood transfusions and the risk of complications associated with them.

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

At the time of designation, beta thalassaemia major and intermedia affected approximately 1 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 50,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, blood transfusion was used to treat the symptoms of beta thalassaemia intermedia and major. This was usually combined with iron chelators, medicines used to reduce the high iron levels in the body caused by repeated blood transfusions.
In some cases, bone marrow transplantation was used to cure the disease. This is a complex procedure in which the bone marrow of the patient is destroyed and replaced with bone marrow from a matched donor, to allow the patient to produce red blood cells with normal levels of haemoglobin.
The sponsor has provided sufficient information to show that this medicine might be of significant benefit for the patients, particularly because it may represent an alternative to bone marrow

[*]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 504,800,000 (Eurostat 2009).

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transplantation. 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 '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 so that they contain normal copies of the beta-globin gene. When these modified cells are transplanted back into the patient, they are expected to start producing beta globins that can be assembled into haemoglobin, avoiding the need for blood transfusion or bone marrow transplantation. 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 this medicine have been evaluated in experimental models.
At the time of submission of the application for orphan designation, no clinical trials in patients with beta thalassaemia intermedia or major had been started.
At the time of submission, this medicine was not authorised anywhere in the EU for beta thalassaemia intermedia and major. Orphan designation of this medicine had been granted in United States of America for these conditions.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 4 March 2009 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 Community) 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.

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Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Autologous haematopoietic stem cells transduced with lentiviral vector encoding the human beta-globin gene	Treatment of beta-thalassaemia intermedia and major
Bulgarian	Автоложни хемопоетични стволови клетки трансдуцирани с лентивирусен вектор кодиращ човешкия бета-глобин ген.	Лечение на бета таласемия интермедия и майор
Czech	Autologní hematopotické buňky transdukované lentivirálním vektorem kódujícím lidský gen beta-globinu	Léčení beta thalasémie intermedia a major
Danish	Autologe hæmatopoietiske stamceller transduceret med lentiviral vektor som koder for humant beta-globin gen	Behandling af beta-thalassæmia intermedia og major
Dutch	Autologe haematopoiëtische stamcellen getransudeerd met lentivirale vector die het humane bètaglobine-gen codeert	Behandeling van bètathalassemie intermedia en major
Estonian	Lentiviraalne vektor, mis kodeerib inimese beetaglobiini geeni	Keskmise ja raske beetatalasseemia ravi
Finnish	Ihmisen beta-globiinigeeniä koodaavalla lentivirusvektorilla muunnettuja autologisia hematopoieettisia kantasoluja	Beetatalassemia intermedia- ja major-tyypin hoito
French	Cellules souches autologues transformées par un vecteur lentiviral codant pour le gène de la bêta-globine humaine	Traitement de la bêta-thalassémie intermédiaire et majeure
German	Autologe hämatopoetische Stammzellen , die mit einem lentiviralen Vektor transduziert sind, der das humane Betaglobingen kodiert	Behandlung der Beta-Thalassämie (Intermediäre und Major-Form)
Greek	Αυτολόγα αιματοποιητικά βλαστοκύτταρα γενετικά τροποποιημένα από λεντικό φορέα ιού ο οποίος κωδικοποιεί το ανθρώπινο γονίδιο της β-σφαιρίνης	Θεραπεία της β-μεσογειακής αναιμίας, ενδιάμεσης και μείζονος
Hungarian	A humán béta-globin gént kódoló lentivirális vectorral transzdukált autológ hematopoietikus őssejtek	Béta-talasszémia intermedia és major kezelése
Italian	Cellule staminali ematopoietiche autologhe transdotte con un vettore lentivirale codificante il gene della beta-globina umana	Trattamento della beta-talassemia intermedia e major
Latvian	Autologas hematopoētiskas climes šūnas transducētas ar lentivīrusa vektoru, kas kodē cilvēka beta globīna gēnu	Vidēji izteiktas un izteiktas bēta talasēmijas ārstēšana
Lithuanian	Autologinės hemopoetinės kamieninės	Vidutinio sunkumo ir sunkios β-

	ląstelės pakeistos lentivirusiniu vektoriumi, koduojančiu žmogaus beta-globino geną	talasemijos gydymas
Maltese	Ċelluli steminali ematopojetiċi awtologużi trasformati permezz ta' vettur lentivirali li jikkodifika il-ġene uman tal-beta-golbulin	Kura tal-beta talassemija intermedja u maġġuri
Polish	Autologiczne hematopoetyczne komórki macierzyste transdukowane wektorem lentiwirusowym kodującym ludzki gen beta-globiny	Leczenie talasemii beta- intermedia i major
Portuguese	Células estaminais hematopoiéticas autólogas transduzidas com vector lentoviral contendo o gene da beta – globolina humana	Tratamento da beta talassémia intermédia e major
Romanian	Celule stem hematopoietice autologe obţinute prin transducţie cu vector lentiviral ce codează gena beta-globinei umane	Tratamentul beta talasemiei intermediare şi majore
Slovak	Autológne hematopoetické kmeňové bunky transdukované lentivírusovým vektorom kódujúcim ľudský beta-globínový gén	Liečba stredne závažnej a závažnej beta talasémie
Slovenian	Autologne hematopoetične matične celice transducirane z lentivirusnim vektorjem, ki enkodira humani gen za beta globin	Zdravljenje srednje in velike talasemije beta
Spanish	Células hematopoyéticas pluripotenciales autólogas transducidas con un vector lentivírico que contiene el gen de la beta-globina humana	Tratamiento de la beta talasemia intermedia y mayor
Swedish	Autologa stam celler transfekterade med lentivirusvektor som innehåller humant beta-globin gen	Behandling av beta-thalassaemia intermedia och major
Norwegian	Autologe hematopoetiske stamceller transdusert med lentiviral vektor som inneholder genet for humant beta-globin	Behandling av beta-thalassemia intermedia og beta-thalassemia major
Icelandic	Samgena blóðstofnfrumur, fluttar með lentiveiru ferju, sem kóða fyrir manna beta-glóbín geni	Meðferð á meðalbráðu Beta-Miðjarðarhafsblóðleysi og bráðu Beta-Miðjarðarhafsblóðleysi