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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human *beta $^{A\text{-}T87Q}$-globin* gene for treatment of beta-thalassaemia intermedia and major

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Rev.1: sponsor's change of address	4 February 2014
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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 24 January 2013, orphan designation (EU/3/12/1091) was granted by the European Commission to bluebird bio France, France, for autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human *beta $^{A\text{-}T87Q}$-globin* gene for treatment of beta-thalassaemia intermedia and major.

What is beta-thalassaemia intermedia and major?

Beta thalassaemia is an inherited disease in which patients are unable to make enough haemoglobin, the protein found in red blood cells that carry 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 severe anaemia (the lack of haemoglobin), the need for repeated blood transfusions and the risk of complications associated with them.

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

At the time of designation, beta-thalassaemia intermedia and major affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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, the main treatments for beta-thalassaemia intermedia and major were blood transfusion and the use of iron chelators (medicines for reducing 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 patients because, as a gene therapy, it offers the possibility of curing the genetic defect in the bone marrow cells that cause beta thalassaemia in contrast to transfusion and iron chelators, which only manage the effects of the disease. 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 that carries normal copies of the *beta-globin* gene into the cells. When these modified cells are transplanted back into the patient, they are expected to develop into healthy red blood cells that produce 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 (a '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 medicinal product have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicinal product in patients with beta-thalassaemia intermedia and major had been started.

At the time of submission, the medicinal product was not authorised anywhere in the EU for beta-thalassaemia intermedia and major or designated as an orphan medicinal product elsewhere for these conditions.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 December 2012 recommending the granting of this designation.

[*]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.
At the time of designation, this represented a population of 512,200,000 (Eurostat 2013).

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	Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human *beta^{A-T87Q}-globin* gene	Treatment of beta-thalassaemia intermedia and major
Bulgarian	Автоложни CD34+ хематопоетични стволови клетки, трансдуцирани с лентижирусен вектор, кодиращ човешки *beta^{A-T87Q}* глобин ген	Лечение на бета таласемия интермедия и майор
Czech	Autologní CD34+ hematopoetické buňky transdukované lentivirálním vektorem kódujícím lidský gen *beta^{A-T87Q}-globinu*	Léčení beta thalasémie intermedia a major
Danish	Autologe CD34+ hæmatopoietiske stamceller transduceret med lentiviral vektor som koder for humant beta^{A-T87Q} -globin gen	Behandling af beta-thalassæmia intermedia og major
Dutch	Autologe CD34+ haematopoiëtischestamcellen getransudeerd met lentivirale vector die het humane *bèta^{A-T87Q} globine*-gen codeert	Behandeling van bètathalassemie intermedia en major
Estonian	Autoloogsed CD34+ hematopoeetilised tüvirakud, mis sisaldavad lentiviraalset vektorit , mis kodeerib inimese *beeta^{A-T87} -globiini* geeni	Keskmise ja raske beetatalasseemia ravi
Finnish	Ihmisen *beeta^{A-T87Q}*-globiinigeeniäkoodaavalla lentivirusvektorillamuunnettuja autologisia CD34+hematopoieettisia kantasoluja	Beetatalassemia intermedia- ja major-tyypin hoito
French	Cellules souches hematopoiétiques autologues CD34+ transduites par le vecteur lentiviral codant pour le gène de la *bêta^{A-T87Q}-globine* humaine	Traitement de la bêta-thalassémie intermédiaire et majeure
German	Autologe CD34+ hämatopoetische Stammzellen, die mit einem lentiviralen Vektor transduziert sind, der für das humane *Beta^{A-T87Q}-globin* Gen kodiert	Behandlung der Beta-Thalassämie (Intermediäre und Major-Form)
Greek	Αυτόλογα CD34+ αιμοποιητικά βλαστικά κύτταρα διαμολυσμένα με λεντι-ιικό φορέα που κωδικοποιεί το ανθρώπινο γονίδιο *β^{A-T87Q} σφαιρίνης*	Θεραπεία της β-μεσογειακής αναιμίας, ενδιάμεσης και μείζονος
Hungarian	Humán *béta^{A-T87Q}-globin* gént kódoló lentivirális vectorral transzdukált autológ CD34+ hematopoietikus őssejtek	Béta-talasszémia intermedia és major kezelése

[1] At the time of designation

Language	Active ingredient	Indication
Italian	Cellule staminali ematopoietiche autologhe CD34+ transdotte con un vettore lentivirale codificante il gene della *beta^{A-T87Q}-globina* umana	Trattamento della beta-talassemia intermedia e major
Latvian	Autologas CD34+ hematopoētiskas climes šūnas transducētas ar lentivīrusa vektoru, kas kodē cilvēka beta^{A-T87Q} globīna gēnu	Vidēji izteiktas un izteiktas bēta talasēmijas ārstēšana
Lithuanian	Autologinės CD34+ hemopoetinės kamieninės ląstelės pakeistos lentivirusiniu vektoriumi, koduojančiu žmogaus *beta^{A-T87Q}-globino* geną	Vidutinio sunkumo ir sunkios β-talasemijos gydymas
Maltese	Ċelluli steminali ematopojetiċi CD34+ awtologużi trasformati permezz ta' vettur lentivirali li jikkodifika il-ġene uman *beta^{A-T87Q}-globina*	Kura tal-beta talassemija intermedja u maġġuri
Polish	Autologiczne hematopoetyczne komórki macierzyste CD34+ transdukowane wektorem lentiwirusowym kodującym ludzki gen beta^{A-T87Q} -globiny	Leczenie talasemii beta- intermedia i major
Portuguese	Células estaminais hematopoiéticas autólogas CD34+ transduzidas com um vetor lentoviral que codifica o gene da *beta^{A-T87Q} – globolina* humana	Tratamento da beta talassémia intermédia e major
Romanian	Celule stem hematopoietice autologe CD34+ obţinute prin transducţie cu vector lentiviral care codează gena umană *beta^{A-T87Q}-globină*	Tratamentul beta talasemiei intermediare şi majore
Slovak	Autológne CD34+ hematopoetické kmeňové bunky transdukované lentivírusovým vektorom kódujúcim ľudský *beta^{A-T87Q}-globínový* gén	Liečba stredne závažnej a závažnej beta talasémie
Slovenian	Autologne CD34+ hematopoetične matične celice transducirane z lentivirusnim vektorjem, ki enkodira humani gen za beta^{A-T87Q}-globin	Zdravljenje srednje in velike talasemije beta
Spanish	Células hematopoiéticas CD34+autólogas transducidas con un vector lentivírico que contiene el gen de la *beta^{A-T87Q} –globina* humana	Tratamiento de la beta talasemia intermedia y mayor
Swedish	Autologa CD34+ hematopoetiska stamceller transfekterade med lentivirusvektor innehållande den mänskliga *beta^{A-T87Q}-globin* genen	Behandling av beta-thalassaemia intermedia och major
Norwegian	Autologe CD34+ hematopoetiske stamceller transdusert med lentiviral vector som inneholder genet for humant *beta^{A-T87Q}-globin*	Behandling av beta-thalassemia intermedia og beta-thalassemia major

Language	Active ingredient	Indication
Icelandic	Samgena blóðstofnfrumur, fluttar með lentiveiru ferju, sem kóða fyrir manna *beta*$^{A\text{-}T87Q}$*-glóbín* geni	Meðferð á meðalbráðu Beta-Miðjarðarhafsblóðleysi og bráðu Beta-Miðjarðarhafsblóðleysi