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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-T87Q-globin gene for the treatment of sickle cell disease

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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 29 April 2014, orphan designation (EU/3/14/1263) was granted by the European Commission to bluebird bio France SARL, France, for autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human beta A-T87Q-globin gene for the treatment of sickle cell disease.

What is sickle cell disease?

Sickle cell disease is a genetic disease in which the red blood cells become rigid and sticky, and change from being disc-shaped to being crescent-shaped (like a sickle). The change in shape is caused by the presence of an abnormal form of haemoglobin, the protein in red blood cells that carries oxygen around the body. In patients with sickle cell disease, the abnormal red blood cells attach to the walls of blood vessels and block them, restricting the flow of oxygen-rich blood to the internal organs such as the heart, lungs and spleen. Because the abnormal red blood cells have a shorter life span, they release haemoglobin into the blood circulation rather than carrying it to the internal organs where it is needed. As a result, the disease causes severe pain and damage to these organs as well as repeated infections and anaemia (low red-blood-cell counts).

Sickle cell disease is a severe disease that is long-lasting and may be life-threatening because of damage to the heart and the lungs, anaemia and infections.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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

At the time of designation, sickle cell disease affected approximately 2.16 in 10,000 people in the European Union (EU). This was equivalent to a total of around 110,000 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 only medicine authorised in the EU to treat sickle cell disease was hydroxycarbamide. The main treatment for sickle cell disease was blood transfusion. This was usually combined with 'iron chelators' (medicines used to reduce the high iron levels in the body caused by repeated blood transfusions), which are necessary in patients with long-term anaemias such as sickle cell disease. In some cases, haematopoietic (blood) stem cell transplantation was used (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow) to allow the patient to produce red blood cells containing normal haemoglobin.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with sickle cell disease because it works in a different way to existing treatments and early studies show that it might provide an alternative for patients who are intolerant or do not respond to hydroxycarbamide. 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 patient's stem cells are modified in the laboratory by a virus that carries healthy copies of the gene that is defective in patients with sickle cell disease (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 containing normal haemoglobin, and thereby avoid the need for blood transfusion, bone marrow transplantation or other treatments.

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 medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, preliminary clinical trials with the medicine in patients with sickle cell disease had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of sickle cell disease. Orphan designation of the medicine had been granted in the United States for this condition, and in the EU and the United States for the treatment of beta-thalassaemia intermedia and major.

*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).

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 March 2014 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

Sponsor's contact details:

bluebird bio France
155 rue du Faubourg Saint-Denis
75010 Paris
France
Tel. +33 1 82 88 00 56
Fax +33 1 82 88 00 91
E-mail: patient.advocacy@bluebirdbio.com

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 sickle cell disease
Bulgarian	Автоложни CD34 + хематопоетични стволови клетки, трансдуцирани с лентивирусен вектор, кодиращ човешки β*A-T87Q-глобин* ген	Лечение на сърповидно-клетъчна анемия
Croatian	Autologne CD34+ hematopoetske matične stanice transducirane lentivirusnim vektorom koji kodira gen za ljudski beta *A-T87Q-globin*	Liječenje bolesti srpastih stanica
Czech	Autologní CD34+ hematopotické buňky transdukované lentivirálním vektorem kódujícím lidský gen beta*A-T87Q-globinu*	Léčba srpkovité anémie
Danish	Autologe CD34+ hæmatopoietiske stamceller transduceret med lentiviral vektor som koder for humant beta *A-T87Q-globin* gen	Behandling af seglcellesygdom
Dutch	Autologe CD34+ haematopoiëtische stamcellen getransudeerd met lentivirale vector die het humane bèta *A-T87Q-globine* en codeert	Behandeling van sikkelcelaandoening
Estonian	Autoloogsed CD34+ hematopoeetilised tüvirakud koos lentiviraalse vektoriga, mis kodeerib inimese beeta *A-T87Q-globiini* geeni	Sirprakulise aneemia ravi
Finnish	Ihmisen beta *A-T87Q*-globiinigeeniäkoodaavalla lentivirusvektorilla muunnettuja autologisia CD34+hematopoieettisia kantasoluja	Sirppisolusyndrooman hoito
French	Cellules souches hématopoiétiques autologues CD34+ transduites par le vecteur lentiviral codant pour le gène de la bêta *A-T87Q-globine* humaine	Traitement de la drépanocytose
German	Autologe CD34+ hämatopoetische Stammzellen, die mit einem lentiviralen Vektor transduziert sind, der das humane Beta*A-T87Q-Globingen* kodiert	Behandlung der Sichelzellenanämie
Greek	Αυτόλογα CD34+ αιμοποιητικά βλαστικά κύτταρα διαμολυσμένα με λεντι-ιικό φορέα που κωδικοποιεί το ανθρώπινο γονίδιο της *βA-T87Q-σφαιρίνης*	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	Humán beta *A-T87Q-globin* gént hordozó lentivirus vektorral transzdukált autológ CD34+ hematopoetikus őssejtek	Sarlósejtes anaemia kezelése
Italian	Cellule staminali ematopoietiche autologhe transdotte con un vettore lentivirale codificante il gene della beta *A-T87Q-globina* umana	Trattamento dell'anemia falciforme

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Ar cilvēka beta *A-T87Q globīna* gēnu kodējošu lentivīrusa vektoru transducētas autologas CD34+ šūnas	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	Autologinės CD34+ hemopoetinės kamieninės ląstelės pakeistos lentivirusiniu vektoriumi, koduojančiu žmogaus beta *A-T87Q-globino* geną	Siklemijos gydymas
Maltese	Ċelluli steminali ematopojetiċi awtologużi trasformati permezz ta' vettur lentivirali li jikkodifika il-ġene uman beta *A-T87Q-globina*	Kura tal-marda taċ-ċelluli sura ta' minġel
Polish	Autologiczne hematopoetyczne komórki macierzyste transdukowane wektorem lentiwirusowym kodującym ludzki gen beta *A-T87Q-globiny*	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	Células estaminais hematopoiéticas autólogas CD34+ transduzidas com vector lentoviral contendo o gene da beta*A-T87Q–globolina* humana	Tratmento do sindrome das células falciformes
Romanian	Celule stem hematopoietice autologe CD34+ obţinute prin transducţie cu vector lentiviral ce codează gena beta *A-T87Q-globinei* umane	Tratamentul anemiei cu celule falciforme
Slovak	Autológne CD34+ hematopoetické kmeňové bunky transdukované lentivírusovým vektorom kódujúcim ľudský beta *A-T87Q-globínový* gén	Liečba kosáčikovej anémie
Slovenian	Autologne CD34+hematopoetične matične celice transducirane z lentivirusnim vektorjem, ki enkodira humani gen za beta *A-T87Q -globin*	Zdravljenje bolezni srpastih celic
Spanish	Células hematopoiéticas pluripotenciales autólogas transducidas con un vector lentivírico que contiene el gen de la beta *A-T87Q-globina* humana	Tratamiento de la anemia drepanocítica
Swedish	Autologa CD34+ hematopoetiska stamceller transducerade med en lentivirusvektor som uttrycker den mänskliga genen för beta *A-T87Q-globin*	Behandling av sickle cell syndrom
Norwegian	Autologe CD34+ hematopoetiske stamceller transdusert med lentiviral vektor som inneholder genet for humant beta *A-T87Q-globin*	Behandling av sigdcellesykdom
Icelandic	Samgena blóðstofnfrumur, fluttar með lentiveiru ferju, sem kóða fyrir manna *beta A-T87Q-glóbín* geni	Meðferð sigðkornablóðleysis