18 June 2013
EMA/COMP/277074/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous CD34+ cells transduced with a lentiviral vector containing the human *ADA* gene for the treatment of adenosine-deaminase-deficient severe combined immunodeficiency

On 7 June 2013, orphan designation (EU/3/13/1134) was granted by the European Commission to Prof. Bobby Gaspar, United Kingdom, for autologous CD34+ cells transduced with a lentiviral vector containing the human *ADA* gene for the treatment of adenosine-deaminase-deficient severe combined immunodeficiency.

What is adenosine-deaminase-deficient severe combined immunodeficiency?

Adenosine-deaminase-deficient severe combined immunodeficiency (SCID) is an inherited disorder where the patients are unable to fight infections due to defective white blood cells called lymphocytes.

It is caused by a defect in the gene for adenosine deaminase, an enzyme that helps cells to clear waste products and is particularly important for cells such as lymphocytes which multiply rapidly and produce more waste. As a consequence, waste accumulates in the lymphocytes and damages them. Patients therefore do not have enough white blood cells to fight infections and are highly susceptible to bacterial, fungal and viral infections. The main symptoms usually occur in the first six months of life, and include pneumonia, diarrhoea and a failure to grow and develop normally.

Adenosine-deaminase-deficient SCID is a long-term debilitating and life-threatening condition due to repeated and long-lasting infections. If left untreated the disease is usually fatal in the first two years of life, while it can lead to various health problems in the longer term, including developmental disorders, hearing loss, skeletal dysplasia (dwarfism) and liver and kidney problems.

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

At the time of designation, adenosine-deaminase-deficient SCID affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 people*, and is

*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 509,000,000 (Eurostat 2013).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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, no satisfactory methods were authorised in the European Union for the treatment of adenosine-deaminase-deficient SCID. In some patients, allogeneic haematopoietic (blood) stem cell transplantation was used. This is a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow.

How is this medicine expected to work?

This medicine is made up of immature bone marrow cells (called CD34+ cells) that are taken from the patient. These cells are able to develop into different types of blood and immune cells. To make this medicine, the CD34+ cells are modified by a virus that contains the gene for the adenosine deaminase enzyme, so that this gene is carried into the cells. When these modified cells are transplanted back into the patient, they are expected to populate the bone marrow and produce healthy blood and immune cells that produce the adenosine deaminase enzyme, which is lacking in patients with adenosine-deaminase-deficient SCID, and thereby help to relieve the symptoms of the disease.

The type of virus used in this medicine ('lentivirus') is modified in order not to cause disease in humans.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with adenosine deaminase-deficient SCID had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for adenosine-deaminase-deficient SCID 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 17 April 2013 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:

Prof Bobby Gaspar,
UCL Institute of Child Health
30 Guilford Street
London WC1N 1EH
United Kingdom
Telephone: +44 207 905 2319
Telefax: +44 207 905 2810
E-mail: h.gaspar@ucl.ac.uk

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 containing the human *ADA* gene	Treatment of adenosine deaminase-deficient-severe combined immunodeficiency
Bulgarian	Автоложни CD34+ клетки, трансдуцирани с лентивирусен вектор, съдържащ човешки аденозин деаминаза ген	Лечение на тежък комбиниран имунодефицит с аденозин деаминазна недостатъчност
Czech	Autologní buňky CD34+ transdukované lentivirálním vektorem obsahujícím lidský gen *ADA*	Léčba deficitu adenosinové deaminázy - závážného kombinovaného imunodeficitu.
Danish	Autologe CD34+ celler transduceret (omdannet) med en lentivirus vektor der indeholder humant *ADA*-gen	Behandling af adenosinedeaminase manglende-svært kombineret immundefekt
Dutch	Autologe CD34+ cellen getransduceerd met een lentivirale vector die het humane *ADA*-gen bevat	Behandeling van adenosinedeaminasedeficiënte ernstige gecombineerde, immunodeficiëntie
Estonian	Autoloogsed CD34+ rakud transdukteeritud lentiviraalse vektoriga, mis sisaldab inimese *ADA*-geeni	Adenosiindeaminaasi defitsiidist t tingitud raske kombineeritud immuunpuudulikkuse ravi
Finnish[2]	Autologisia CD34+_soluja, jotka kuljetetaan ihmisen *ADA*-geenin sisältävällä lentivirusvektorilla	Adenosiinideaminaasin puutteen, johon liittyy vakava immuunivajaus, hoito
French	Cellules CD34+ autologues transduites avec un vecteur lentiviral contenant le gène humain *ADA*	Traitement de l'immunodeficience combinée sévère adénosine désaminase
German	Autologe CD34+ Zellen, transfiziert mit lentiviralen Vektoren, die das menschliche ADA-Gen enthalten	Behandlung des schweren kombinierten Immuneffekts der durch Adenosindeaminase-Mangel hervorgerufen wird
Greek	Αυτόλογα κύτταρα CD34+ διαμολυσμένα με φορέα λεντι-ιού που περιέχει το ανθρώπινο γονίδιο *ADA* (απαμινάση της αδενοσίνης)	Θεραπεία της βαριάς συνδυασμένης ανοσοανεπάρκειας που οφείλεται στην ανεπάρκεια της απαμινάσης της αδενοσίνης
Hungarian	Humán *ADA* gént hordozó lentivirusvektorral transzdukált autológ CD34+ sejtek	Adenozindezamináz (ADA) hiány okozta súlyos kombinált immunhiány kezelése ~~(ADA)-hiány~~
Italian	Cellule CD34+ autologhe trasdotte con un vettore lentivirale contenente il gene umano *ADA*	Trattamento della immunodeficienza grave combinata da deficit di adenosina deaminasi
Latvian	Autologās CD34+ šūnas, kas nodotas ar cilvēka *ADA* gēnusaturošu lentivīrusa vektoru	Adenozīna deaminācijas deficīta izraisīta smaga kombinēta imūndeficīta ārstēšana

[1] At the time of designation
2 Correction of Finnish text of active ingredient

Language	Active ingredient	Indication
Lithuanian	Autologinės CD34+ ląstelės, pakeistos lentivirusiniu vektoriumi, turinčiu žmogaus *ADA* geną	Ūminio sunkaus kombinuoto imunodeficito dėl adenozino deaminazės trūkumo gydymas
Maltese	Ċelluli CD34+ awtologi trasformati b'vettur lentivirali li fih il-ġene *ADA* uman	Kura ta' immunodefiċjenza magħquda severa minħabba nuqqas ta' adenosine deaminase
Polish	Autologiczne komórki CD34+ transfekowanewektorem lentiwirusowym zawierającym ludzki gen *ADA*	Leczenie niedoboru deaminazy adenozynowej - ciężkiego złożonego niedoboru odporności
Portuguese	Células CD34+ autólogas transduzidas com um vetor lentiviral que contém o gene *ADA* humano	Tratamento da imunodeficiência combinada grave por défice de adenosina desaminase
Romanian	Celule autologe CD34+ transduse cu un vector lentiviral conţinând gena umană *ADA*	Tratamentul imunodeficienţei combinate severe produse de deficitul de adenozin-desaminază
Slovak	Autológne CD34+ bunky transfektované lentivírusovým vektorom, ktorý obsahuje ľudský *ADA* gén	Liečba ťažkej kombinovanej imunodeficiencie spôsobenej deficitom adenosín dezaminázy
Slovenian	Avtologne CD34 + celice, transducirane s pomočjo lentivirusnega vektorja, ki vsebuje človeški *ADA* gen	Zdravljenje hude imunske pomanjkljivosti, povezane s pomanjkanjem deaminaze adenozina
Spanish	Células CD34+ autólogas transfectadas con un vector lentivírico que contiene el gen humano de la *ADA*	Tratamiento del la inmunodeficiencia severa combinada por déficit de adenosina deaminasa
Swedish	Autologa CD34+ celler transducerade med en lentivirusvektor innehållande den mänskliga *ADA*-genen	Behandling av svår kombinerad immunbrist med adenosindeaminasbrist
Norwegian	Autologe CD34+ celler transdusert med lentiviral vektor som inneholder det humane *ADA*-genet	Behandling av alvorlig kombinert immunsvikt som skyldes adenosindeaminasemangel
Icelandic	Samgena CD34 + frumur sem manna *ADA*-gen hefur verið flutt í me lentiveiru genaferju	Meðferð á adenósín-deamínasaskorts - alvarlegum, samsettum ónæmisbresti