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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous CD34+ cells transfected with retroviral vector containing adenosine deaminase gene for the treatment of severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency

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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 26 August 2005, orphan designation (EU/3/05/313) was granted by the European Commission to Fondazione Telethon, Italy, for autologous CD34+ cells transfected with retroviral vector containing adenosine deaminase gene for the treatment of severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency.

The sponsorship was transferred to Glaxo Group Limited, United Kingdom, in June 2011 and subsequently to GlaxoSmithKline Trading Services Limited, Ireland, in July 2014.

What is severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency?

Severe combined immunodeficiency, or SCID, is a group of inherited disorders characterized by little or no body's defence (immune) response due to the total or partial lack of those specilised white cells (lymphocytes) which are normally part of the body's defense system. A form of SCID is caused by a lack of adenosine deaminase (ADA), an enzyme (a protein that speeds up the conversion of certain substances into other substances) which helps the cell to clear the waste products it generates during proliferation. This enzyme is important in every cell of the body but in particular in those cells which proliferate rapidly, like the lymphocytes. As a consequence of the adenosine deaminase (ADA) deficiency, lymphocytes, which proliferate greatly during their maturation, are injured by these

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accumulation of toxic metabolites. This deficiency usually results in the onset of one or more serious infections within the first few months of life. The symptoms of this type of SCID include an increased susceptibility to a variety of infections, including ear infections, lung infections and diarrhea. Because children with SCID experience multiple infections, they fail to grow and to gain weight as expected. Severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency is chronically debilitating and life-threatening.

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

At the time of designation, severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency affected approximately 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of around 900 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 the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of submission of the application for the orphan drug designation there were no products authorised in the European Union. Treatment of severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency included compatible donor (heterologous) bone-marrow transplantation to replace the defective cells.

How is this medicine expected to work?

The gene coding for the adenosine deaminase enzyme, carried by a so-called “retroviral vector”, is inserted (transfected) into the patient’s own progenitor bone marrow cells (so-called CD34+ cells), previously isolated. It is assumed that, once admininistrated back to the patient, these CD34+ cells transfected with the adenosine deaminase gene will be able to produce their own genetic material (nucleosides) in a normal way and thus actively proliferate in order to restore the normal number of functional white blood cells (lymphocytes).

What is the stage of development of this medicine?

The effects of autologous CD34+ cells transfected with retroviral vector containing adenosine deaminase gene were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency were ongoing.

Autologous CD34+ cells transfected with retroviral vector containing adenosine deaminase gene was not authorised anywhere worldwide for the treatment of severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 July 2005 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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 466,600,000 (Eurostat 2005).

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 European Union) 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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http://ie.gsk.com/ie/contact-us

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 transfected with retroviral vector containing adenosine deaminase gene	Treatment of severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency
Bulgarian	Автоложни CD34+ клетки, трансфектирани с ретровирусен вектор, съдържащ аденозин деаминазен ген	Лечение на тежък комбиниран имунодефицит (SCID) в следствие на аденозин деаминазна недостатъчност
Croatian	Autologne CD34+ stanice transficirane retrovirusnim vektorom koji sadrži gen za adenozin deaminazu	Liječenje teške kombinirane imunodeficijencije (SCID) uslijed manjka adenozin deaminaze (ADA).
Czech	Autologní CD 34+ buňky s retrovirálním vektorem obsahující gen adenosin deaminázy	Léčba těžké kombinované imunodeficience (SCID) způsobené deficitem adenosin deaminázy
Danish	Autologe CD 34 + transfekterede med retroviral vektor indeholdende adenosin deaminase gen	Behandling af svær kombineret immundefekt (SCID) forårsaget af mangel på adenosin-deaminase (ADA)
Dutch	Autologe CD34+ cellen getransfecteerd met retrovirale vector welke het adenosine deaminase gen bevat	Behandeling van ernstige gecombineerde immuundeficiëntie(SCID) als gevolg van een adenosine deaminise (ADA) deficiëntie
Estonian	Autoloogsed CD34+ rakud transfekteeritud retroviirusvektoriga, mis sisaldab adenosiindeaminaasi cDNA	Adenosiindeaminaasi (ADA) defitsiidist tingitud raske kombineeritud immuundefitsiidi ravi
Finnish	Autologisia CD34+ soluja, jotka ovat transfektoituja retroviraalivektorilla, joka sisältää adenosiinideaminaasigeenin	Adenosiinideaminaasin (ADA) puutteesta johtuvan vakavan sekamuotoisen immuunivajavuuden (SCID) hoito
French	Cellules CD34+ autologues transfectées du vecteur rétroviral contenant le gène de l'adénosine désaminase	Traitement de l'immunodéficience combinée sévère (SCID) due à la déficience en adénosine désaminase (ADA)
German	Autologe CD34+ Zellen, transfiziert mit einem retroviralen Vektor, der das humane Adenosingen enthält	Behandlung des schweren kombinierten Immundefizits (SCID) verursacht durch ein Adenosindeaminasedefizit
Greek	Αυτόλογα κύτταρα CD34+ επιμολυσμένα με ρετροϊικό φορέα που περιέχει το γονίδιο της ανθρώπινη απαμινάσης αδενοσίνης	Θεραπεία σοβαρής Συνδυασμένης Ανοσοανεπάρκειας (SCID) που οφείλεται σε ανεπάρκεια απαμινάσης αδενοσίνης (ADA)
Hungarian	Adenozin dezamináz gént hordozó autológ CD34+ sejtekkel egyesített retrovirus vektor	Adenozin deamináz (ADA)-hiány okozta súlyos kombinált immunhiány kezelése

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Italian	Cellule CD34+ autologhe transfettate con vettore retrovirale contenente il gene codificante l'adenosina deaminasi	Trattamento della sindrome da immunodeficienza grave combinata (SCID) causata dalla carenza di adenosina deaminasi (ADA)
Latvian	Autologas CD34+ šūnas ar ievadītu adenozīna deaminācēs gēnu saturošu retrovirālu vektoru	Adenozīna deaminācēs (ADA) deficīta izraisīta smaga kombinēta imūndeficīta (SCID) ārstēšana
Lithuanian	Autologinės CD34+ ląstelės transfekuotos su retroviruso vektoriumi, turinčiu adenozino deaminazės geną	Ūmaus kombinuoto imunodeficito (ŪKI) dėl adenozino deaminazės (ADA) stokos gydymas
Maltese	Ċelluli awtologi CD34+ transfettati b'vettur retrovirali li fih il-ġene adenosine deaminase	Kura ta' immunodefiċjenza magħquda serja (SCID) minħabba defiċjenza ta' adenosine deaminase (ADA)
Polish	Autologiczne komórki CD34+ z wprowadzonym wektorem retrowirusowym zawierającym gen dezaminazy adenozynowej	Leczenie ciężkiego złożonego niedoboru odporności (SCID) wywołanego niedoborem dezaminazy adenozynowej (ADA)
Portuguese	Células CD34+ autólogas transfectadas com o vector retroviral que contem o gene da adenosina desaminase	Tratamento da Imunodeficiência Combinada Grave(IDCG) por deficiência de adenosina desaminase (ADA)
Romanian	Celule autolog CD34+ transfectate cu vector retroviral ce conţine gena pentru adenozin dezaminază	Tratamentul imunodeficienţei severe combinata (SCID) datorata deficienţei de adenozin dezaminază (ADA)
Slovak	Autológové CD34+ bunky transfektované s retrovírovým vektorom, ktorý obsahuje gén adenozín deaminázy	Liečba závažnej kombinovanej imunodeficiencie (SCID) spôsobenej nedostatkom adenozín deaminázy (ADA)
Slovenian	Avtologne CD34+ celice, transficirane z retroviralnim vektorjem, ki vsebuje gen adenozin deaminaze	Zdravljenje hude kombinirane imunodeficience (SCID) zaradi pomanjkanja adenozin deaminaze (ADA)
Spanish	Células CD34 positivas transfectadas por con un vector retrovírico que contiene el gen de la adenosina desaminasa	Tratamiento de la Inmunodeficiencia Combinada Grave (ICG) causada por déficit de adenosina desaminasa
Swedish	Autologa CD34+ celler trasnfekterade med retroviral vektor som innehåller humant adenosindeaminas gen	Behandling av svår kombinerad immunbrist (SCID) som beror på adenosindeaminasbrist (ADA-brist)
Norwegian	Autologe CD34+ celler transfektert med retroviral vektor som inneholder gen for adenosindeaminase	Behandling av alvorlig kombinert immunsvikt (SCID) som skyldes adenosindeaminasemangel
Icelandic	Samgena CD34+ frumur fluttar með retroveiru ferju sem inniheldur adenósín deamínasa gen	Meðferð við samsettum ónæmisbresti (SCID) sem stafar af adenósín deamínasa (ADA) skorti