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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Human donor haematopoietic stem and progenitor cells that have been treated ex vivo with the protein transduction domain of the HIV-1 transactivation protein fused to MYC transcription factor for treatment in haematopoietic stem cell transplantation

On 12 January 2017, orphan designation (EU/3/16/1817) was granted by the European Commission to Coté Orphan Consulting UK Limited, United Kingdom, for human donor haematopoietic stem and progenitor cells that have been treated ex vivo with the protein transduction domain of the HIV-1 transactivation protein fused to MYC transcription factor (also known as TBX-1400) for treatment in haematopoietic stem cell transplantation.

What is haematopoietic stem cell transplantation?

Haematopoietic stem cell transplantation is a procedure where the patient's bone marrow is cleared of cells and replaced by stem cells (cells that can develop into different types of cell) to form new bone marrow that produces healthy blood cells. It can be used to treat serious diseases of the blood and immune system such as leukaemia.

Haematopoietic stem cell transplantation can be a debilitating and life-threatening procedure due to the risk of severe infections and developing graft-versus-host disease (when the transplanted cells regard the patient's body as 'foreign' and attack the patient's organs, leading to organ damage).

What is the estimated number of patients receiving haematopoietic stem cell transplants?

At the time of designation, approximately 0.5 in 10,000 people in the European Union (EU) have haematopoietic stem cell transplantation per year. This was equivalent to a total of around 26,000 people per year*, and is below the ceiling for orphan designation. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

*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 513,700,000 (Eurostat 2016).

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What treatments are available?

At the time of designation, several medicines were authorised in the EU for patients undergoing haematopoietic stem cell transplants. These included radiation treatment or intensive treatment with cancer medicines such as busulfan to clear the bone marrow of existing cells, medicines to help restore the immune system, such as filgrastim, immunoglobulin replacement therapy and Zalmoxis, and medicines to reduce the risk of infections, such as antiviral and antifungal medicines. Medicines that suppress the immune system, such as ciclosporin and corticosteroids, were used for the treatment of graft-versus-host disease.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients undergoing haematopoietic stem cell transplantation because experimental studies showed that the medicine may increase the success of 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?

The medicine is made of donated stem cells and immature blood cells ('haematopoietic stem and progenitor cells') that are to be used in haematopoietic stem cell transplantation. These cells are treated with a specially engineered protein that is made by joining two smaller proteins. One part of the engineered protein enables it to easily enter the cells. Once in the cells, the other part, called MYC protein, transiently stimulates the genes that control the survival and multiplication of stem cells. The medicine when transplanted into a patient is thus expected to increase the production of blood cells and improve success of the transplant.

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, no clinical trials with the medicine in patients receiving haematopoietic stem cell transplantation had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for haematopoietic stem cell transplantation. Orphan designation of the medicine had been granted in the United States for the enhancement of cell engraftment in patients receiving haematopoietic stem cell transplantation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 December 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Human donor haematopoietic stem and progenitor cells that have been treated ex vivo with the protein transduction domain of the HIV-1 transactivation protein fused to MYC transcription factor	Treatment in haematopoietic stem cell transplantation
Bulgarian	Човешки донорни хематопоетични стволови и прогениторни клетки, третирани ex vivo с протеиновия трансдукционен домейн на трансактивационния протеин на HIV-1, свързани с MYC транскрипционен фактор	Лечение при трансплантация на хемопоетични стволови клетки
Croatian	Hematopoetske matične stanice i prastanice ljudskog donora tretirane *ex vivo* domenom transdukcije proteina transaktivacijskog proteina virusa HIV-1 proteinom fuzioniranim na transkripcijski faktor MYC	Liječenje u transplantaciji hematopoetskih matičnih stanica
Czech	Hematopoetické kmenové a progenitorové buňky od lidského dárce ošetřené ex-vivo proteinovou transdukční doménou transaktivačního proteinu HIV-1 fúzovanou na MYC transkripční factor	Léčba transplantace hemopoetickými zárodečnými buňkami
Danish	Humane donor hæmatopoietiske stam-og-progenitorceller, som er blevet behandlet ex vivo med proteintransduktionsdomænet af HIV-1-transaktiveringsproteinet sammensmeltet med MYC-transkriptionsfaktor	Behandling i hæmatopoietisk stamcelletransplantation
Dutch	Humane donor hematopoëtische stamcellen en progenitorcellen die ex vivo behandeld zijn met het eiwittransductiedomein van het hiv-1-transactivatie-eiwit gefuseerd aan MYC-transcriptiefactor	Behandeling in haematopoiëtische stemceltransplantatie
Estonian	Inimdoonori hematopoeetilised tüvi- ja eellasrakud, mida on *ex vivo* töödeldud HIV-1 transaktivatsioonivalgu valgu transduktsiooni domeeniga, mis on liidetud transkriptsioonifaktori MYC külge	Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis
Finnish	Ihmisperäisen luovuttajan hematopoieettisia kanta- ja esisoluja, jotka on käsitelty ex vivo HIV-1-transaktivaatioproteiinin proteiinitransduktiodomeenilla, joka on fuusioitu MYC-transkriptiotekijään	Hoito hematopoeettisen kantasolusiirron yhteydessä

[1] At the time of designation

Language	Active ingredient	Indication
French	Cellules souches et cellules progénitrices hématopoïétiques de donneur humain ayant été traitées *ex vivo* avec le domaine de transduction protéique de la protéine de transactivation du VIH-1, fusionné au facteur de transcription MYC	Traitement dans la greffe de moëlle osseuse
German	Von Humanspendern gewonnene, hämatopoetische Stammzellen und Vorläuferzellen, ex vivo behandelt mit der Proteintransduktionsdomäne des HIV-1-Transaktivierungsproteins, welches an den MYC-Transkriptionsfaktor fusioniert ist	Behandlung in hämatopoetischer Stammzelltransplantation
Greek	Αρχέγονα και προγονικά αιμοποιητικά κύτταρα ανθρώπου τα οποία έχουν υποβληθεί σε επεξεργασία ex vivo με την περιοχή πρωτεϊνικής μεταγωγής της πρωτεΐνης διενεργοποίησης του HIV-1 συντηγμένη στον παράγοντα μεταγραφής MYC	θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων
Hungarian	Humán donortól származó hemopoetikus ős- és progenitorsejtek, amelyeket *ex vivo* a HIV-1 transzaktivációs fehérje fehérjetranszdukciós doménjével, a TAT-tal kezeltek, amelyhez MYC transzkripciós faktort kapcsoltak	Hematopoietikus őssejt-transzplantáció esetén alkalmazandó
Italian	Cellule staminali e progenitrici ematopoietiche di donatore umano trattate ex vivo con il dominio di trasduzione proteica della proteina transattivante del virus HIV-1 fusa con fattore di trascrizione MYC	Trattamento nel trapianto di cellule staminali ematopoietiche
Latvian	Cilvēka donora asinsrades cilmes un celma šūnas, kas *ex vivo* apstrādātas ar HIV-1 transaktivācijas proteīna proteīnu transdukcijas domēnu, kas sapludināts ar MYC transkripcijas faktoru	Ārstēšanai hematopoētisko cilmes šūnu transplantācijā
Lithuanian	Žmogaus donorinės hematopoetinės kamieninės ir pirminės ląstelės, apdorotos *ex vivo* transdukcijos domeno baltymu nuo ŽIV-1 transaktyvacijos baltymo , sulieto su MYC transkripcijos faktoriumi	Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme
Maltese	Ċelloli steminali u proġenituri ematopojetiċi ta' donatur uman li ġew ikkurati ex vivo bid-dominju ta' trasduzzjoni ta' proteina tal-proteina ta' transattivazzjoni ta' HIV-1, infuża għal ma' fattur ta' traskrizzjoni ta' MYC	Kura fi trapjant ta' ċelloli staminali ematopojetiċi
Polish	Pochodzące od ludzkiego dawcy komórki macierzyste i progenitorowe, które ex vivo poddano działaniu domeny transdukcji białkowej białka transaktywacji HIV-1, połączonego z czynnikiem transkrypcji MYC	Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych
Portuguese	Células estaminais e progenitoras hematopoiéticas de dador humano que foram tratadas ex vivo com o domínio de transdução proteica da proteína de transativação do VIH-1 fundida com o fator de transcrição MYC	Tratamento em transplantes de células estaminais hematopoiéticas

Language	Active ingredient	Indication
Romanian	Celule stem şi celule progenitoare hematopoietice (HSPC) de la donator uman care au fost tratate ex vivo cu domeniul de transducţie proteică al proteinei transactivatoare a HIV-1 fuzionată cu factorul de transcripţie MYC	Tratament în transplantul de celule stem hematopoetice
Slovak	Krvotvorné kmeňové a progenitorové bunky od ľudského darcu, ktoré boli ošetrené ex vivo transdukciou domény proteínu HIV-1, transaktivačným proteínom, transkripčným faktorom fúzovaným s MYC	Liečba pri transplantácii hematopoietických kmeňových buniek
Slovenian	Humane darovane hematopoetske matične in progenitorske celice, ki so bile obdelane *ex vivo* s tj. domeno za beljakovinsko transdukcijo transaktivacijske beljakovine virusa HIV-1, ki je združena s transkripcijskim faktorjem	Zdravljenje pritransplantaciji hematopoetskih matičnih celic
Spanish	Células madre y progenitoras hematopoiéticas tratadas *ex vivo* con una proteína que combina el dominio de transducción de la proteína TAT del VIH-1 -1 fusionada con el factor de transcripción MYC	Tratamiento en el trasplante de células madre hematopoyéticas
Swedish	Humana hematopoetiska stam- och progenitorceller, vilka behandlats ex vivo med transduktionsdomänen från HIV-1-transaktiveringsproteinet fuserat med MYC-transkriptionsfaktor	Behandling vid hematopoetisk stamcellstransplantation
Norwegian	Hematopoietiske stam-og progenitorceller fra human donor som er behandlet ex vivo med proteintransduksjonsdoment fra HIV-1-transaktiveringsprotein fusjonert med MYC-transkripsjonsfaktor	Behandling ved hematopoetisk stamcelletransplantasjon
Icelandic	Manna blóðmyndandi stofnfrumur og forverafrumur sem hafa verið meðhöndlaðar utan lifandi líkama með próteingenaleiðslusvæði HIV 1 transvirkjunarpróteinsins tengdu við MYC umritunarþáttinn	Meðferð á stofnfrumublóðfrumu ígræðslu