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Public summary of opinion on orphan designation

Allogeneic umbilical cord blood CD34+ cells cultured ex vivo with Notch ligand Delta1 for treatment in haematopoietic stem cell transplantation

On 17 January 2018, orphan designation (EU/3/17/1958) was granted by the European Commission to Voisin Consulting S.A.R.L, France, for allogeneic umbilical cord blood CD34+ cells cultured ex vivo with Notch ligand Delta1 (also known as NLA101) for treatment in haematopoietic stem cell transplantation.

What is haematopoietic stem cell transplantation?

Haematopoietic stem cell transplantation (HSCT) 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) from a donor 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.

HSCT 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 affected by the condition?

At the time of designation, approximately 1 in 10,000 people receive HSCT every year in the European Union (EU). This was equivalent to a total of around 52,000 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).

What treatments are available?

At the time of designation, several medicines were authorised in the EU for patients undergoing HSCT. 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

*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 515,700,000 (Eurostat 2017).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
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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 the medicine might be of significant benefit for patients undergoing HSCT because early studies show that it can improve success of the transplantation and reduce graft-versus-host 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?

The medicine consists of CD34+ cells (a type of stem cells) collected from the umbilical cord blood of several donors. CD34+ cells are very effective at multiplying and developing into different types of blood cells when transplanted into the patient. The CD34+ cells in this medicine are cultivated in a laboratory to increase their number. Cord blood cells are less likely than adult stem cells to cause rejection or graft-versus-host disease. The medicine is used off-the-shelf and is given to patients during a HSCT. The CD34+ cells provide a rapid, but short-term, increase in the levels of different blood cells until healthy blood cells are produced by the new bone marrow. This is expected to improve survival in patients undergoing HSCT.

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, clinical trials with the medicine in patients undergoing HSCT were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for HSCT 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 7 December 2017 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:

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	Allogeneic umbilical cord blood CD34+ cells cultured ex vivo with Notch ligand Delta1	Treatment in haematopoietic stem cell transplantation
Bulgarian	Алогенни CD34+ клетки от умбиликална кръв, култивирани ex vivo с Notch лиганд Делта1	Лечение при трансплантация на хемопоетични стволови клетки
Croatian	Alogene CD34+ stanice iz krvi pupkovine kultivirane ex vivo s Notch ligandom Delta1	Liječenje u transplantaciji hematopoetskih matičnih stanica
Czech	Allogenní CD34+ buňky pupečníkové krve kultivované ex vivo s Notch ligantem Delta1	Léčba transplantace hemopoetickými zárodečnými buňkami
Danish	Allogen navlestrengsblod CD34+celler, dyrket ex-vivo med Notch ligand Delta 1	Behandling i hæmatopoietisk stamcelletransplantation
Dutch	Allogene navelstrengbloed CD34+ cells gekweekt ex-vivo met Notch ligand Delta1	Behandeling in haematopoiëtische stemceltransplantatie
Estonian	Allogeensed nabaväädivere CD34+ rakud , mida on kultureeritud ex vivo koos Notch ligand Delta 1	Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis
Finnish	Allogeeniset napaveren CD34+-solut, jotka on ex vivo kasvatettu yhdessä Notch ligand Delta1:n kanssa	Hoito hematopoeettisen kantasolusiirron yhteydessä
French	Cellules CD34+ allogéniques de sang de cordon ombilical cultivées ex vivo avec le ligand Notch Delta 1	Traitement dans la greffe de moëlle osseuse
German	Allogene CD34+ Nabelschnurblutzellen kultiviert ex vivo mit Notch Ligand Delta1	Behandlung in hämatopoetischer Stammzelltransplantation
Greek	Αλλογενή CD34+ κύτταρα αίματος ομφαλίου λώρου καλλιεργημένα ex vivo παρουσία Notch προσδέματος Delta1	θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων
Hungarian	Notch ligand Delta1-el ex vivo tenyésztett allogén köldökzsinórvér CD34+ sejtek	Hematopoietikus őssejt-transzplantáció esetén alkalmazandó
Italian	Cellule allogeniche CD34+ dal sangue del cordone ombelicale, coltivate ex vivo con ligando Notch Delta1	Trattamento nel trapianto di cellule staminali ematopoietiche
Latvian	Allogēnas nabas saites asins CD34+ šūnas, kas kultivētas ex vivo ar Notch ligandu Delta1	Ārstēšanai hematopoētisko cilmes šūnu transplantācijā
Lithuanian	Alogeninės virkštelės kraujo CD34+ ląstelės augintos ex vivo su Notch ligandu Delta1	Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme
Maltese	Ċelloli tad-demm CD34+ alloġeniku tal-kurdun ombelikali kkulturati ex vivo b'Notch ligand Delta1	Kura fi trapjant ta' ċelloli staminali ematopojetiċi

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Alogeniczne komorki CD34+ z krwi pępowinowej namnożone ex vivo z Notch ligandem Delta 1	Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych
Portuguese	Células CD34 + do sangue do cordão umbilical alogénicas cultivadas ex vivo com o ligando Notch Delta1	Tratamento em transplantes de células estaminais hematopoiéticas
Romanian	Celule CD34+ alogenice provenite din sângele cordonului ombilical, cultivate ex vivo cu notch ligandul Delta-1	Tratament în transplantul de celule stem hematopoetice
Slovak	Alogenické CD34+ bunky z pupočníkovej krvi kultivované ex vivo s Notch ligandom Delta 1	Liečba pri transplantácii hematopoietických kmeňových buniek
Slovenian	Alogene CD34+ popkovnične krvne celice kultivirane ex vivo z "notch" ligandom delta1	Zdravljenje pritransplantaciji hematopoetskih matičnih celic
Spanish	Sangre alogénico del cordon umbilical cultivadas ex vivo con Notch ligand Delta1	Tratamiento en el trasplante de células madre hematopoyéticas
Swedish	Allogena CD34+navelsträngsblodceller odlade ex vivo med Notch ligand Delta1	Behandling vid hematopoetisk stamcellstransplantation
Norwegian	Allogene CD34+ celler fra navlestrengsblod dyrket ex vivo med Notch-ligand Delta1	Behandling ved hematopoetisk stamcelletransplantasjon
Icelandic	Osamgena naflastrengs CD34+ frumur ræktaðar ex vivo með Notch ligand Delta1	Meðferð á stofnfrumublóðfrumu ígræðslu