



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Allogeneic peripheral blood mononuclear cells incubated ex-vivo with 16, 16-dimethyl prostaglandin E2 and dexamethasone for treatment in haematopoietic stem cell transplantation

On 18 November 2016, orphan designation (EU/3/16/1774) was granted by the European Commission to Fate Therapeutics Ltd, United Kingdom, for allogeneic peripheral blood mononuclear cells incubated ex-vivo with 16, 16-dimethyl prostaglandin E2 and dexamethasone (also known as ProTmune) 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 recognise 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 1 in 10,000 people in the European Union (EU) have haematopoietic stem cell transplants per year. This was equivalent to a total of around 51,000 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 (European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).



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 immunoglobulin replacement therapy, 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 reduce graft-versus-host disease and improve success of the transplant and survival. 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 consists of white blood cells, including stem cells, extracted from a donor for use as a transplant. These cells are to be given to the patient to form new bone marrow that produces healthy blood cells. Before they are given to the patient, the cells are mixed with medicines (16, 16-dimethyl prostaglandin E2 and dexamethasone) so that the cells produce more of a protein called CXCR4. This improves the ability of the cells to find their way to the bone marrow and start to grow once transplanted. The cells are also less likely to recognise the patient's body as foreign, and fewer cells able to cause graft-versus-host disease are produced.

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 haematopoietic stem cell transplantation were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for use in haematopoietic stem cell transplantation or designated as an orphan medicinal product elsewhere.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 October 2016 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Allogeneic peripheral blood mononuclear cells incubated ex vivo with 16, 16-dimethyl prostaglandin E2 and dexamethasone	Treatment in haematopoietic stem cell transplantation
Bulgarian	Алогенни периферни кръвни мононуклеарни клетки инкубирани ex vivo с 16, 16-диметил простагландин E2 и дексаметазон	Лечение при трансплантация на хемopoетични стволови клетки
Croatian	Alogene mononuklearne stanice periferne krvi inkubirane ex vivo 16, 16-dimetil prostaglandinom E2 i deksametazonom	Liječenje u transplantaciji hematopoetskih matičnih stanica
Czech	Allogenní mononukleární buňky periferní krve inkubované ex vivo s 16,16- dimethyl prostaglandinem E2 a dexamethasonem	Léčba transplantace hemopoetickými zárodečnými buňkami
Danish	Allogene perifere blod-mononukleære celler inkuberet ex vivo med 16,16-dimethyl prostaglandin E2 og dexamethason	Behandling i hæmatopoietisk stamcelletransplantation
Dutch	Allogene perifere bloed mononucleaire cellen geïncubeerd ex-vivo met 16, 16-dimethyl prostaglandine E2 en dexamethasone	Behandeling in haematopoëtische stemceltransplantatie
Estonian	Allogeensed perifeerse vere mononukleaarsed rakud, mida on inkubeeritud ex vivo 16, 16-dimetüül prostaglandiin E2 ja dexametasooniga	Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis
Finnish	Allogeeniset perifeerisen veren mononukleaariset solut inkuboituna ex vivo yhdessä 16, 16-dimetyyli prostaglandiini E2:n ja deksametasonin kanssa	Hoito hematopoeettisen kantasolusiirron yhteydessä
French	Cellules mononucléaires allogéniques de sang périphérique incubées ex-vivo avec 16, 16-diméthyl prostaglandine E2 et dexaméthasone	Traitement dans la greffe de moëlle osseuse
German	Allogene mononukleäre Zellen des peripheren Blutes, ex vivo inkubiert mit 16, 16-Dimethyl-Prostaglandin E2 und Dexamethason	Behandlung in hämatopoetischer Stammzelltransplantation
Greek	Αλλογενή μονοκύτταρα περιφερικού αίματος επωασμένα ex vivo με 16, 16-διμεθυλο προσταγλανδίνη E2 και δεξαμεθαζόνη	θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων
Hungarian	16, 16-dimetil prosztaglandin E2-vel és dexamethazonnal ex vivo inkubált allogén periferális mononukleáris vérsejtek	Hematopoietikus őssejt-transzplantáció esetén alkalmazandó
Italian	Cellule ematiche mononucleari allogeniche incubate ex vivo con 16, 16-dimetil prostaglandina E2 e dexametasone	Trattamento nel trapianto di cellule staminali ematopoietiche
Latvian	Alogēnas perifēro asiņu mononukleārās šūnas, kas inkubētas ex vivo ar 16, 16-dimetil prostaglandīnu E2 un deksametazonu	Ārstēšanai hematopoētisko cilmes šūnu transplantācijā

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	Alogeninės periferinio kraujo mononuklearinės ląstelės, inkubuotos su 16, 16-dimetilprostaglandinu E2 ir deksametazonu <i>ex vivo</i>	Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme
Maltese	Ċelloli tad-demmm mononukleari periferali alloġeneiċi inkubati <i>ex vivo</i> b'16, b'16-dimetil prostaglandina E2 u deksametażon	Kura fi trapjant ta' ċelloli staminali ematopojetiči
Polish	Allogeniczne mononuklearne komórki krwi obwodowej inkubowane <i>ex vivo</i> z 16, 16-dimetyl prostaglandyną E2 oraz deksametazonem	Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych
Portuguese	Células mononucleares alogénicas do sangue periférico incubadas <i>ex vivo</i> com 16, 16-dimetil prostaglandina E2 e dexametasona	Tratamento em transplantes de células estaminais hematopoiéticas
Romanian	Celule mononucleare alogene din sângele periferic incubate <i>ex vivo</i> cu 16, 16-dimetil prostaglandina E2 și dexametazonă	Tratament în transplantul de celule stem hematopoetice
Slovak	Alogénne periférne krvné mononukleárne bunky inkubované <i>ex vivo</i> s 16,16-dimetylprostaglandínom E2 a dexametazónom	Liečba pri transplantácii hematopoietických kmeňových buniek
Slovenian	Alogene mononuklearne celice periferne krvi inkubirane <i>ex vivo</i> s 16, 16 dimetilprostaglandinom E2 in deksametazonom	Zdravljenje pritransplantaciji hematopoetskih matičnih celic
Spanish	Celulas perifericas mononucleares alogenicas incubadas <i>ex vivo</i> en dexametasona y 16,16 dimetil prostglandina E2.	Tratamiento en el trasplante de células madre hematopoyéticas
Swedish	Allogena periferä mononukleära blodceller inkuberade <i>ex vivo</i> med 16, 16-dimetyl prostaglandin E2 och dexametason	Behandling vid hematopoetisk stamcellstransplantation
Norwegian	Allogene perifere mononuklære celler fra blod inkubert <i>ex vivo</i> med 16, 16-dimetyl prostaglandin E2 og deksametason	Behandling ved hematopoetisk stamcelletransplantasjon
Icelandic	Ósamgena útlægar einkjarna blóðfrumur sem eru inkúberaðar <i>ex vivo</i> með 16, 16-dímethýl prostaglandíni E2 og dexamethasóni	Meðferð á stofnfrumublóðfrumu ígræðslu