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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Donor T lymphocytes depleted ex vivo of host alloreactive T cells using photodynamic treatment for treatment in haematopoietic stem cell transplantation

On 27 June 2016, orphan designation (EU/3/16/1678) was granted by the European Commission to Kiadis Pharma Netherlands B.V., the Netherlands, for donor T lymphocytes depleted ex vivo of host alloreactive T cells using photodynamic treatment (also called ATIR) for treatment in haematopoietic stem cell transplantation.

What is haematopoietic stem cell transplantation?

Haematopoietic stem cell transplantation involves a patient receiving stem cells (cells that can develop into different types of cell) to help the bone marrow produce healthy blood cells. It can be used to treat serious diseases of the blood and immune system. A stem cell transplant in which the patient receives cells from a healthy donor is called an allogeneic transplant. Before receiving the transplant, the patient's own bone marrow is cleared of cells. The patient then receives the donor stem cells, which multiply and develop into healthy blood cells.

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 (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 medicines to help restore the immune system, such as immunoglobulin replacement therapy, and 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 early studies showed that its use improved overall survival and transplantation-related mortality. 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?

For many patients who require haematopoietic stem cell transplantation, it is often difficult to find a fully matched donor. When the donor is partly matched to the patient (e.g. a close relative), the risk of the patient developing graft-versus-host disease is increased.

This medicine is made of T cells, a type of white blood cell, extracted from a donor who is partly matched to the patient. Before being injected into the patient, a specific group of T cells (known as alloreactive T cells) that is known to attack the patient's cells is first removed. The remaining T cells are then injected into the patient after the patient has received a haematopoietic stem cell transplant depleted of T cells from the same partly matched donor. The injected T cells are expected to help the patient to fight off viral infections while their immune system is being restored with the transplanted stem cells, without attacking the patient's own cells.

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. Orphan designation of the medicine had been granted in the EU for prevention of graft-versus-host disease and for treatment of acute myeloid leukaemia, and in the United States for treatment of immune reconstitution and prevention of graft-versus-host disease following bone marrow transplantation and for reduction of transplant-related mortality caused by graft-versus-host disease and/or infections following mismatched (haploidentical) allogenic haematopoietic stem cell transplantation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 May 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Donor T lymphocytes depleted ex vivo of host alloreactive T cells using photodynamic treatment	Treatment in haematopoietic stem cell transplantation
Bulgarian	Донорски Т лимфоцити, освободени ex vivo от алореактивни към реципиента Т клетки с помощта на фотодинамично третиране	Лечение при трансплантация на хемопоетични стволови клетки
Croatian	T limfociti davatelja na kojima je fotodinamičkim tretmanom ex vivo izvršena deplecija T stanica aloreaktivnih na primatelja	Liječenje u transplantaciji hematopoetskih matičnih stanica
Czech	Dárcovské T lymfocyty po depleci ex vivo hostitelských alloreaktivních T buněk pomocí fotodynamické léčby	Léčba transplantace hemopoetickými zárodečnými buňkami
Danish	Alloreaktive T celler rettet mod værten fjernes fra donorens T lymfocytter ex vivo ved brug af fotodynamisk behandling.	Behandling i hæmatopoietisk stamcelletransplantation
Dutch	Donor T lymfocyten welke ex vivo zijn gedepleteerd van alloreactieve T cellen tegen de gastheer met gebruikmaking van fotodynamische behandeling	Behandeling in haematopoiëtische stemceltransplantatie
Estonian	Doonori T lümfotsüüdid, millest on ex vivo fotodünaamilise töötlemisega peremehe vastu suunatud alloreaktiivsed T rakud eemaldatud	Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis.
Finnish	Luovuttajan T lymfosyytit, joista isäntää vastaan kohdistetut alloreaktiiviset T solut on poistettu ex vivo fotodynaamisella hoidolla	Hoito hematopoeettisen kantasolusiirron yhteydessä
French	Lymphocytes T de donneur obtenus après élimination des lymphocytes T alloréactifs dirigés contre le receveur par traitement photodynamique ex vivo	Traitement dans la greffe de moëlle osseuse
German	Spender T-Lymphozyten, bei denen ex-vivo mittels photodynamischer Therapie gegen den Empfänger alloreaktive T-Zellen entfernt wurden	Behandlung in hämatopoetischer Stammzelltransplantation
Greek	Τ λεμφοκύτταρα δότη μετά από αφαίρεση ex vivo των αλλοαντιδραστικών Τ κυττάρων κατά του ξενιστή με χρήση φωτοδυναμικής θεραπείας	θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων
Hungarian	A recipiensre alloreaktív T-sejtektõl ex vivo, fotodinámiás kezeléssel mentesített donor T limfociták	Hematopoietikus őssejt-transzplantáció esetén alkalmazandó

[1] At the time of designation

Language	Active ingredient	Indication
Italian	Linfociti T da donatore sottoposti a deplezione ex vivo delle cellule T alloreattive dirette contro l'ospite mediante trattamento fotodinamico	Trattamento nel trapianto di cellule staminali ematopoietiche
Latvian	Donora T limfocīti, kas ex vivo attīrīti no saimniekam aloreaktīvām T šūnām, izmantojot fotodinamisko metodi	Ārstēšanai hematopoētisko cilmes šūnu transplantācijā
Lithuanian	Fotodinamine terapija nuo šeimininko aloreaktyvių T ląstelių *ex vivo* išvalyti donoro T limfocitai	Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme
Maltese	Limfoċiti tat-tip T minn donatur li tneħħewlhom ċelloli alloreattivi tat-tip T b'mod ex vivo permezz ta' kura fotodinamika	Kura fi trapjant ta' ċelloli staminali ematopojetiċi
Polish	Limfocyty T dawcy pozbawione limfocytów T alloreaktywnych wobec gospodarza uzyskane metodą fotodynamiczną w warunkach ex vivo	Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych
Portuguese	Linfocitos T do dador com eliminação das células T aloreativas contra o hospedeiro, obtidos por tratamento fotodinâmico *ex vivo*	Tratamento em transplantes de células estaminais hematopoiéticas
Romanian	Limfocite T de la donator obţinute după eliminarea ex vivo a celulelor T aloreactive direcţionate împotriva gazdei prin tratament fotodinamic	Tratament în transplantul de celule stem hematopoetice
Slovak	Darcovské T lymfocyty zbavené pomocou fotodynamickej liečby ex vivo T buniek aloreaktívnych voči hostiteľovi	Liečba pri transplantácii hematopoietických kmeňových buniek
Slovenian	T limfociti, usmerjeni proti gostitelju, so ex vivo odstranjeni iz dajalčevih aloreaktivnih celic T z uporabo fotodinamične obdelave T Donorski T limfociti po ex-vivo depleciji dajalčevih aloreaktivnih celic T, usmerjenih proti gostitelju, z uporabo fotodinamične obdelave	Zdravljenje pri transplantaciji hematopoetskih matičnih celic
Spanish	Linfocitos T de donantes desprovistos ex vivo de las células T alorreactivas dirigidas contra el anfitrión por medio de tratamiento fotodinámico	Tratamiento en el trasplante de células madre hematopoyéticas
Swedish	T lymfocyter från donator som har tömts ex vivo på patientinriktade alloreaktiva T celler med hjälp av fotodynamisk behandling	Behandling vid hematopoetisk stamcellstransplantation
Norwegian	Donor T lymfocytter der alloreaktive T celler rettet mot verten blir fjernet ex vivo ved hjelp av fotodynamisk behandling	Behandling ved hematopoetisk stamcelletransplantasjon
Icelandic	T eitilfrumur úr gjafa þar sem T frumum hýsils sem svara ósamgena áreiti hefur verið eytt ex vivo með ljóshrifameðferð	Meðferð í blóðstofnfrumu ígræðslu