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Public summary of opinion on orphan designation

Allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured for treatment in haematopoietic stem cell transplantation

On 21 August 2020, orphan designation EU/3/20/2317 was granted by the European Commission to Smart Immune, France, for allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured (also known as HTLPs) 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). Additionally, in some patients the stem cells do not establish themselves and are unable to form new bone marrow.

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

At the time of designation, approximately 1 in 10,000 people in the European Union (EU) received HSCT per year. 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

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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filgrastim and 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 the medicine might be of significant benefit for patients with haematopoietic stem cell transplantation because early laboratory results suggest it might speed up the formation of new healthy blood cells needed to restore the immune system.

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?

After HSCT it can take up to 2 years for the patient's immune system to be fully restored, leaving them temporarily vulnerable to severe infections. The medicine consists of the precursor (early-stage) cells that produce T-cells, a specific form of white blood cell with important roles in the immune system. The precursor cells are derived from blood given by a donor and are grown in the laboratory to increase their number. When they are given to a patient who has just had HSCT, they are expected to migrate to the thymus, an organ just above the breastbone, where they will develop into new T-cells specific to the patient. This is expected to speed up the restoration of a functioning immune system.

What is the stage of development of this medicine?

The effects of allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine were ongoing.

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

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 16 July 2020, 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

Contact details of the current sponsor for this orphan designation can be found on EMA website.

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 T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured	Treatment in haematopoietic stem cell transplantation
Bulgarian	Алогенни прекурсори на Т-клетки, получени от мобилизирана периферна кръв, култивирани ex vivo	Лечение при трансплантация на хемопоетични стволови клетки
Croatian	Alogeni prekursori T-stanica, izvedeni iz mobilizirane periferne krvi, uzgojeni *ex vivo*	Liječenje u transplantaciji hematopoetskih matičnih stanica
Czech	Alogenní prekurzory T-buněk, derivované z periferní krve, ex vivo kultivované	Léčba transplantace hemopoetickými zárodečnými buňkami
Danish	Allogene T-prækursor-celler, mobiliseret og afledt af perifert blod, ex vivo dyrket	Behandling ved hæmatopoietisk stamcelletransplantation
Dutch	Allogenene T-cell precursoren, gemobiliseerd uit perifeer bloed-afgeleid, ex vivo gekweekt	Behandeling in haematopoiëtische stemceltransplantatie
Estonian	Mobiliseeritud perifeersest verest saadud ja *ex vivo* kasvatatud allogeensed T-rakkude eellasrakud	Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis.
Finnish	Allogeeniset T-solujen prekursorit, mobilisoidut perifeerisestä verestä peräisin, ex vivo viljellyt	Hoito hematopoeettisen kantasolusiirron yhteydessä
French	Précurseurs de cellules T allogéniques, dérivés du sang périphérique mobilisés, cultivés ex vivo	Traitement dans la greffe de moëlle osseuse
German	Allogene T-Zell Vorläufer, mobilisiert aus peripherem Blut, ex vivo kultiviert	Behandlung in hämatopoetischer Stammzelltransplantation
Greek	Αλλογενή προδρομα Τ-κύτταρα, απομονωμένα από κινητοποιημένο περιφερικό αίμα, καλλιεργημένα ex vivo	θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων
Hungarian	Mobilizált, perifériás vérből származó, ex vivo tenyésztett allogen T-sejt prekurzorok	Hematopoietikus őssejt-transzplantáció esetén alkalmazandó

[1] At the time of designation

Language	Active ingredient	Indication
Italian	Precursori di cellule T allogeniche, derivate da sansgue periferico mobilizzato, cultivate ex vivo	Trattamento nel trapianto di cellule staminali ematopoietiche
Latvian	No mobilizētām perifērām asinīm iegūti un ex vivo kultivēti allogēni T-šūnu prekursori	Ārstēšanai hematopoētisko cilmes šūnu transplantācijā
Lithuanian	Iš periferinio kraujo išskirti, mobilizuoti, *ex vivo* pagausinti alogeniniai T ląstelių pirmtakai	Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme
Maltese	Prekursuri taċ-ċellola T alloġeneiċi, derivati mid-demm periferali mobbli, ikkultivati ex vivo	Kura fi trapjant ta' ċelloli staminali ematopojetiċi
Polish	Allogeniczne prekursory komórek T, mobilizowane, pozyskane z krwi obwodowej, namnożone ex vivo	Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych
Portuguese	Células T precursoras alogénicas, derivadas de sangue periférico, cultivadas *ex vivo*	Tratamento em transplantes de células estaminais hematopoiéticas
Romanian	Precursori de celule T alogenice, derivati din sange periferic mobilizat, cultivaţi ex vivo	Tratament în transplantul de celule stem hematopoetice
Slovak	Alogenické prekurzory T-buniek, mobilizované z periférnej krvi, kultivované ex vivo	Liečba pri transplantácii hematopoietických kmeňových buniek
Slovenian	Alogeni prekurzorji T-celic, pridobljenih ex vivo iz periferne krvi	Zdravljenje pritransplantaciji hematopoetskih matičnih celic
Spanish	Celulas precursoras movilizadas alogenicas derivadas de sangre cultivadas ex vivo.	Tratamiento en el trasplante de células madre hematopoyéticas
Swedish	Allogena T-precursorceller mobiliserade från preifert blood och ex-vivo odlade	Behandling vid hematopoetisk stamcellstransplantation
Norwegian	Allogene T-celleforløpere, fra mobilisert perifert blod, kultivert ex vivo	Behandling ved hematopoetisk stamcelletransplantasjon
Icelandic	Samgena T-frumuforverar, losaðir, unnir úr útæðablóði, ræktaðir *ex vivo*	Meðferð við ígræðslu blóðmyndandi stofnfrumna