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Public summary of opinion on orphan designation

Allogeneic $CD4^+$ and $CD25^+$ T lymphocytes ex vivo incubated with GP120 for the treatment in haematopoietic stem cell transplantation

On 22 February 2018, orphan designation (EU/3/18/1976) was granted by the European Commission to Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Germany, for allogeneic $CD4^+$ and $CD25^+$ T lymphocytes ex vivo incubated with GP120 for the 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 receiving haematopoietic stem cell transplantation?

At the time of designation, approximately 1 in 10,000 people receive HSCT per 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

*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 517,400,000 (Eurostat 2018).

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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 HSCT. This is because laboratory studies showed that the medicine may reduce graft-versus-host disease. Furthermore, the treatment is expected to be used in a different way to other authorised treatments in HSCT including Zalmoxis. 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 a type of white blood cells called regulatory T cells extracted from a donor. Regulatory T cells suppress the activity of other T cells that are responsible for graft-versus-host disease. The cells are treated with a protein called GP120 before being given to the patient along with or after stem cell transplantation. The GP120 treatment helps activate the regulatory T cells and thus reduces the chance of graft-versus-host disease occurring.

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 had been carried out with the medicine in patients undergoing HSCT.

At the time of submission, the medicine was not authorised anywhere in the EU for use in patients undergoing 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 18 January 2018 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	Allogeneic CD4+ and CD25+ T lymphocytes ex vivo incubated with GP120	Treatment in haematopoietic stem cell transplantation
Bulgarian	Алогенни CD4+ и CD25+ Т лимфоцити ex vivo инкубирани с GP120	Лечение при трансплантация на хемопоетични стволови клетки
Croatian	Alogeni CD4+ i CD25+ T limfociti inkubirani ex vivo s GP120	Liječenje u transplantaciji hematopoetskih matičnih stanica
Czech	Allogení CD4+ a CD25+ T lymfocyty inkubované ex vivo s GP120	Léčba transplantace hemopoetickými zárodečnými buňkami
Danish	Allogen CD4+ og CD25+ T-lymfocyt ex vivo inkuberet med GP120	Behandling i hæmatopoietisk stamcelletransplantation
Dutch	Allogene CD4+ and CD25+ T lymphocytes ex vivo geïncubeerd met GP120	Behandeling in haematopoiëtische stemceltransplantatie
Estonian	*Ex vivo* koos GP120 inkubeeritud allogeensed CD4+ ja CD25+ T-lümfotsüüdid	Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis
Finnish	Allogeeniset CD4+ ja CD25+ T-lymfosyytit, *ex vivo* inkuboituna yhdessä GP120:n kanssa	Hoito hematopoeettisen kantasolusiirron yhteydessä
French	Lymphocytes T CD4 + et CD25 + allogéniques incubés ex vivo avec GP120	Traitement dans la greffe de moëlle osseuse
German	Allogene CD4+ und CD25+ T-Lymphozyten ex vivo inkubiert mit GP120	Behandlung in hämatopoetischer Stammzelltransplantation
Greek	Αλλογενή CD4+ και CD25+ Τ λεμφοκύτταρα ex vivo επωασμένα με GP120	θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων
Hungarian	GP120-al ex vivo inkubált allogén CD4+ és CD25+ T limfociták	Hematopoietikus őssejt-transzplantáció esetén alkalmazandó
Italian	Linfociti T CD4 + e CD25 + allogeneici incubati ex vivo con GP120	Trattamento nel trapianto di cellule staminali ematopoietiche
Latvian	Alogēni CD4+ un CD25+ T limfociti, kas *ex vivo* inkubēti ar GP120	Ārstēšanai hematopoētisko cilmes šūnu transplantācijā
Lithuanian	Alogeniniai CD4+ ir CD25+ T limfocitai *ex vivo* inkubuoti su GP120	Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme
Maltese	Limfoċiti T CD4+ u CD25+ alloġeniċi ex vivo inkubati b'GP120	Kura fi trapjant ta' ċelloli staminali ematopojetiċi
Polish	Allogeniczne limfocyty T typu CD4+ i CD25+ inkubowane ex vivo z GP120	Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych
Portuguese	Linfócitos T CD4+ e CD25+ alogénicos incubados *ex vivo* com GP120	Tratamento em transplantes de células estaminais hematopoiéticas
Romanian	Limfocite T alogenice CD4+ şi CD25+ incubate ex vivo cu GP120	Tratament în transplantul de celule stem hematopoetice
Slovak	Alogenické CD4+ a CD25+ T lymfocyty inkubované ex vivo s GP120	Liečba pri transplantácii hematopoietických kmeňových buniek

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Alogenski CD4+ and CD25+ T limfociti ex vivo inkubirani z GP120	Zdravljenje pritransplantaciji hematopoetskih matičnih celic
Spanish	Celulas T alogenicas CD4+ y CD25+incubadas ex vivo en GP120	Tratamiento en el trasplante de células madre hematopoyéticas
Swedish	Allogena CD4+ och CD25+ T-lymfocyter inkuberade ex vivo med GP120	Behandling vid hematopoetisk stamcellstransplantation
Norwegian	Allogene CD4+ og CD25+ T lymfocytter inkubert ex vivo med GP120	Behandling ved hematopoetisk stamcelletransplantasjon
Icelandic	Ósamgena CD4+ og CD25+ T eitilfrumur inkúberað ex vivo með GP120	Meðferð á stofnfrumublóðfrumu ígræðslu