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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Allogeneic CD4+ and CD8+ T lymphocytes ex vivo incubated with synthetic peptides of the viral antigens of cytomegalovirus, adenovirus and Epstein-Barr virus for the treatment of cytomegalovirus infection following haematopoietic stem cell transplantation

On 12 February 2015, orphan designation (EU/3/15/1439) was granted by the European Commission to Miltenyi Biotec GmbH, Germany, for allogeneic CD4+ and CD8+ T lymphocytes ex vivo incubated with synthetic peptides of the viral antigens of cytomegalovirus, adenovirus and Epstein-Barr virus for the treatment of cytomegalovirus infection following haematopoietic stem cell transplantation.

What is cytomegalovirus infection?

Cytomegalovirus is a common virus that usually only causes mild infection such as a sore throat. Most people get infected at some stage during their lifetime but are very often unaware of it. After infection, the virus usually remains in the body in a 'latent' (inactive) state and becomes active if the immune system (the body's natural defences) is weakened.

Cytomegalovirus is therefore a risk in patients with weakened immune systems such as patients who have undergone haematopoietic (blood) stem cell transplantation. Patients undergoing blood stem cell transplantation have their immune systems weakened so that the body does not reject the donor cells. A delay in the recovery of the immune system can cause a reactivation of the latent cytomegalovirus.

Cytomegalovirus infection following haematopoietic stem cell transplantation is a life-threatening and long-term debilitating condition that affects different organs and indirectly affects the immune system, increasing the risk of other infections and the risk of the body rejecting the donor cells.

What is the estimated number of patients affected by the condition?

At the time of designation, cytomegalovirus infection following haematopoietic stem cell transplantation affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 people[*], and is below the ceiling for orphan designation,

[*]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 512,900,000 (Eurostat 2015).

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which is 5 people in 10,000. 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 antiviral medicines were authorised in the EU for the treatment of cytomegalovirus disease in patients with weakened immune systems (cidofovir, foscarnet, ganciclovir, valaciclovir and valganciclovir).

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for the treatment of cytomegalovirus infection following haematopoietic stem cell transplantation as the medicine has been shown to clear the virus and improve survival in patients who did not respond to previous treatment. 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 is made from immune cells, known as T lymphocytes, from the same donor that supplied the blood stem cells for the transplant. These immune cells are first incubated with proteins that match those from cytomegalovirus. When the medicine is then given to the patients, the immune cells are expected to start attacking the cytomegalovirus in the patient and thereby help cure the patient of the infection.

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 with the medicine in patients with cytomegalovirus infection following haematopoietic stem cell transplantation had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the condition 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 9 January 2015 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:

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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 CD8+ T lymphocytes ex vivo incubated with synthetic peptides of the viral antigens of cytomegalovirus, adenovirus and Epstein-Barr virus	Treatment of cytomegalovirus infection following haematopoietic stem cell transplantation
Bulgarian	Алогенни CD4+ и CD8+ Т лимфоцити екс виво инкубирани със синтетични пептиди на вирусните антигени на цитомегаловирус, аденовирус и вирус на Епщайн-Бар	Лечение на цитомегаловирусна инфекция след трансплантация на хемопоетични стволови клетки
Croatian	Alogeni CD4+ i CD8+ T limfociti ex vivo inkubirani sa sintetičkim peptidima virusnih antigena citomegalovirusa, adenovirusa i Epstein-Barrovog virusa	Liječenje citomegalovirusne infekcije nakon transplantacije hematopoetskih matičnih stanica
Czech	Alogenní CD4+ a CD8+ T lymfocyty ex vivo inkubované se syntetickými peptidy virových antigenů cytomegaloviru, adenoviru a viru Epstein-Barrové	Léčba cytomegalové infekce po transplantaci hematopoetickými zárodečnými buňkami
Danish	Allogeniske CD4+ og CD8+ T lymfocytter ex vivo inkuberet med syntetiske peptider fra de virale antigener cytomegalovirus, adenovirus og Epstein-Barr virus	Behandling af cytomegalovirusinfektion efter transplantation af hæmatopoietiske stamceller
Dutch	Allogeneïsche CD4+ en CD8+ T lymfocyten ex vivo geïncubeerd met synthetische peptiden van de virale antigenen van cytomegalovirus, adenovirus en het Epstein-Barr virus	Behandeling van cytomegalovirusinfecties na hematopoëtische stamceltransplantaties
Estonian	Allogeensed CD4+ ja CD8+ T lümfotsüüdid, mida on organismiväliselt inkubeeritud tsütomegaloviiruse, adenoviiruse ja Epstein-Barr viiruse viiruslike antigeenide peptiididega	Tsütomegaloviirusinfektsioonide ravi peale hematopoeetiliste tüvirakkude siirdamist
Finnish	Sytomegaloviruksen, adenoviruksen ja Epstein-Barrin viruksen virusinfektioiden synteettisten peptidien kanssa kehon ulkopuolella viljeltyjä allogeenisiä CD4+ ja CD8+ T-lymfosyyttejä	Hematopoieettisen kantasolusiirron jälkeisen sytomegalovirusinfektion hoito

[1] At the time of designation

Language	Active ingredient	Indication
French	Lymphocytes T allogénéiques CD4+ et CD8+ incubés ex vivo avec des peptides synthétiques des antigènes viraux du cytomégalovirus, de l'adénovirus et du virus d'Epstein-Barr	Traitement de l'infection à cytomégalovirus suivant une greffe de cellules souches hématopoïétiques
German	Allogene CD4- und CD8-positive T-Lymphozyten, die ex vivo mit synthetischen Peptiden von Zytomegalievirus-, Adenovirus- und Epstein-Barr-Virus-Antigenen inkubiert werden	Behandlung von Cytomegalievirusinfektionen nach hämatopoietischer Stammzellentransplantation
Greek	Αλλογενή Τ λεμφοκύτταρα CD4+ και CD8+ επωασμένα ex vivo με συνθετικά πεπτίδια των ιικών αντιγόνων κυτταρομεγαλοϊού, αδενοϊού και ιού Epstein–Barr	Θεραπεία λοιμώξεων από κυτταρομεγαλοϊό, μετά από μεταμόσχευση αιμοποιητικών βλαστοκυττάρων
Hungarian	Allogenikus CD4+ és CD8+ T limfociták, ex vivo inkubálva citomegalovírus, adenovírus és Epstein-Barr vírus virális antigénjeinek szintetikus peptidjeivel	Haematopoietikus őssejt transzplantációt követő citomegalovirus infekciók kezelésére
Italian	Linfociti T CD4+ e CD8+ allogenici incubati ex vivo con peptidi sintetici degli antigeni virali di citomegalovirus, adenovirus e virus di Epstein-Barr	Trattamento di infezioni da citomegalovirus conseguenti a trapianti di cellule staminali ematopoietiche
Latvian	Alogēnie CD4+ un CD8+ T limfocīti, ex vivo inkubēti ar citomegalovīrusa, adenovīrusa un Epšteina-Barra vīrusa antigēnu sintētiskajiem peptīdiem	Citomegālijas vīrusa infekcijas ārstēšana pēc hematopoētisko cilmes šūnu transplantācijas
Lithuanian	Alogeniniai CD4 + ir CD8 + T limfocitai *ex vivo* inkubuoti su sintetiniais peptidais citomegalo viruso, adenoviruso ir Epstein-Barr viruso virusinių antigenų	Citomegalo virusinės infekcijos po hemapoetinių kamieninių ląstelių transplantacijos gydymas
Maltese	Limfoċiti tat-tip T CD4+ u CD8+ alloġeniċi inkubati ex vivo ma' peptidi sintetiċi tal-antiġeni virali ta' ċitomegalovirus, adenovirus u l-virus Epstein-Barr	Kura ta' infezzjoni minn ċitomegalovirus wara trapjant ta' ċelluli staminali ematopojetiċi
Polish	Allogeniczne limfocyty T CD4+ oraz CD8+ inkubowane *ex vivo* z syntetycznymi peptydami antygenów wirusowych wirusa cytomegalii, adenowirusa oraz wirusa Epsteina-Barr	Leczenie zakażeń wirusem cytomegalii po przeszczepach hematopoetycznych komórek macierzystych

Language	Active ingredient	Indication
Portuguese	Linfócitos CD4 + e CD8 + T alogénicos *ex vivo* incubados com os péptidos sintéticos dos antigénios virais de cito megalovírus, adenovírus e vírus de Epstein-Barr	Tratamento da infecção por citomegalovirus em transplantes de células estaminais hematopoiéticas
Romanian	Limfocite T alogenice CD4+ şi CD8+ incubate ex vivo cu peptide sintetice ale antigenelor virale ale citomegalovirusului, adenovirusului şi virusului Epstein-Barr	Tratamentul infecţiilor cu citomegalovirus post transplant de celule stem hematopoietice
Slovak	Alogénne lymfocyty CD4+ a CD8+ T, inkubované ex vivo so syntetickými pepmidmi vírusových antigénov cytomegalovírusu, adenovírusu a vírusu Epsteina-Barrovej	Liečba cytomegalovírusových infekcií po hematopoetickej transplantácii kmeňových buniek
Slovenian	Alogenski limfociti CD4+ in CD8+ T, ex vivo inkubirani s sintetičnimi peptidi virusnih antigenov citomegalovirusa, adenovirusa in virusa Epstein-Barr	Zdravljenje citomegalovirusne okužbe po transplantaciji krvotvornih matičnih celic
Spanish	Linfocitos T CD4+ y CD8+ alogénicos ex vivo incubados con péptidos sintéticos de los antígenos virales del citomegalovirus, del adenovirus y del virus de Epstein-Barr	Tratamiento de infecciones virales citomegalo en en transplantes de células madre hematopoieticas
Swedish	Allogena CD4+ och CD8+ T lymfocyter som framställts ex vivo med syntetiska peptider av virusantigener från cytomegalovirus, adenovirus och Epstein-Barr virus	Behandling av cytomegalovirusinfektion efter hematopoetisk stamcellstransplantation
Norwegian	Allogene CD4+ - og CD8+ -T-lymfocytter inkubert ex vivo med syntetiske peptider av virusantigener fra cytomegalovirus, adenovirus og Epstein-Barr-virus	Behandling av cytomegalovirusinfeksjon etter hematopoetisk stamcelletransplantasjon
Icelandic	Ósamgena CD4+ og CD8+ T-eitilfrumur ræktaðar ex vivo með tilbúnum peptíðum veirumótefnavaka úr stórfrumuveiru, adenóveiru og Epstein-Barr-veiru	Meðferð við stórfrumuveirusýkingum eftir ósamgena blóðstofnfrumuígræðslu