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EMA/COMP/55791/2015
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 Epstein-Barr virus infection following haematopoietic stem cell transplantation

On 19 March 2015, orphan designation (EU/3/15/1440) 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 Epstein-Barr virus, adenovirus and Epstein-Barr virus for the treatment of Epstein-Barr virus infection following haematopoietic stem cell transplantation.

What is Epstein-Barr virus infection?

Epstein-Barr virus is a common virus that usually causes mild illness and is mostly known for causing glandular fever. 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 body's immunity is weakened.

Epstein-Barr virus 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 Epstein-Barr virus.

Epstein-Barr virus infection following haematopoietic stem cell transplantation is life threatening and long-term debilitating because it can cause inflammation of the intestines, ulcers, hepatitis (liver inflammation), encephalitis (inflammation of the brain) and enlarged lymph nodes.

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

At the time of designation, Epstein-Barr virus 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, no satisfactory methods were authorised for treatment of Epstein-Barr virus infection in the European Union.

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 the Epstein-Barr virus. When the medicine is then given to the patients, the immune cells are expected to recognise virus proteins as foreign and start attacking the Epstein-Barr virus in the patient, thereby helping to 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 Epstein-Barr virus infection following haematopoietic stem cell transplantation had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Epstein-Barr virus infection or designated as an orphan medicinal product elsewhere for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 February 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 Epstein-Barr virus 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 Епщайн-Бар вирусна 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 infekcije Epstein-Barrovim virusom 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 infekce virem Epstein-Barrové 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 Epstein-Barr-virusinfektion 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 Epstein-Barr virusinfecties na hematopoëtische stamceltransplantaties
Estonian	Allogeensed CD4+ ja CD8+ T lümfotsüüdid, mida on organismiväliselt inkubeeritud tsütomegaloviiruse, adenoviiruse ja Epstein-Barr viiruse viiruslike antigeenide sünteetiliste peptiididega.	Epstein-Barri viirusinfektsioonide 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 Epstein–Barrin virusinfektion 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 au virus d'Epstein Barr 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 Epstein-Barr Virus-Infektionen 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 ιό Epstein-Barr, μετά από μεταμόχευση 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 Epstein-Barr virus 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 Epstein-Barr virus conseguenti a trapianti di cellule staminali ematopoietiche
Latvian	Alogēni CD4+ un CD8+ T limfocīti, kas inkubēti *ex vivo* ar citomegalovīrusa, adenovīrusa un Epšteina-Barra vīrusa antigēnu sintētiskajiem peptīdiem	Epšteina-Barra vīrusa infekcijas ārstēšana pēc hematopoētisko cilmes šūnu transplantācijas
Lithuanian	Alogeniniai CD4 + ir CD8 + T limfocitai, inkubuoti *ex vivo* su sintetiniais peptidais iš virusinių citomegalo viruso, adenoviruso ir Epstein-Barr viruso antigenųantigen	*Epstein-Barr* virusinės infekcijos po hemopoetinių 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 mill-virus Epstein-Barr 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 Epsteina-Barr po przeszczepach hematopoetycznych komórek macierzystych

Language	Active ingredient	Indication
Portuguese	Linfócitos CD4 + e CD8 + T alogénicos dos incubados com os péptidos sintéticos dos antigénios virais de citomegalovírus, adenovírus e vírus de Epstein-Barr	Tratamento da infecção por vírus Epstein-Barr 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 virusul Epstein-Barr post transplant de celule stem hematopoietice
Slovak	Alogénne CD4+ a CD8+ T lymfocyty, inkubované ex vivo so syntetickými peptidmi vírusových antigénov cytomegalovírusu, adenovírusu a vírusu Epsteina-Barrovej	Liečba infekcií vírusu Epstein-Barrovej 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 okužbe z virusom Epstein-Barr po presaditvi 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 Epstein-Barr en transplantes de células madre hematopoieticas
Swedish	Allogena CD4+ och CD8+ T lymfocyter som framställts ex vivo med syntetiska peptider av virusantigen från cytomegalovirus, adenovirus och Epstein-Barr virus	Behandling av Epstein Barr-virusinfektion 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 Epstein-Barr-virusinfeksjon 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 Epstein-Barr veirusýkingum hjá sjúklingum eftir ósamgena blóðstofnfrumuígræðslu