



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public summary of opinion on orphan designation

Allogeneic multi-virus specific T lymphocytes targeting BK virus, cytomegalovirus, human herpesvirus-6, Epstein Barr virus and adenovirus for treatment in haematopoietic stem cell transplantation

On 24 March 2020, orphan designation EU/3/20/2260 was granted by the European Commission to TMC Pharma (EU) Limited, Ireland, for allogeneic multi-virus specific T lymphocytes targeting BK virus, cytomegalovirus, human herpesvirus-6, Epstein Barr virus and adenovirus 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 cells 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 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 affected by the condition?

At the time of designation, approximately 1 in 10,000 people received HSCT every year in the European Union (EU). This was equivalent to a total of around 52,000 people\*, and is below the ceiling for orphan designation, 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 medicines were authorised in the EU for patients undergoing HSCT. These included radiation treatment or intensive treatment with cancer medicines such as busulfan to

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\*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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clear the bone marrow of existing cells, medicines to help restore the immune system, such as 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 the medicine might be of significant benefit for patients undergoing HSCT. Early studies show that it can improve the condition of patients with viral haemorrhagic cystitis (an infection of the bladder), which is a complication of HSCT.

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?**

Patients undergo HSCT to replace their bone marrow cells, which include the white blood cells (called T cells) that fight infection. Before the new bone marrow cells are fully functional, the patients are therefore at risk of infections, such as viral haemorrhagic cystitis.

This medicine is made up of white blood cells from a donor which have been activated to target viruses that can cause viral haemorrhagic cystitis and other serious viral infections in patients who have undergone HSCT. When these white blood cells are injected into the patients, they are expected to provide protection against these viruses while the patient's immune system is being restored.

## **What is the stage of development of this medicine?**

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients who had viral haemorrhagic cystitis after undergoing haematopoietic stem cell transplantation 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 for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 20 February 2020, 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](#).

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Allogeneic multi-virus specific T lymphocytes targeting BK virus, cytomegalovirus, human herpesvirus-6, Epstein-Barr virus and adenovirus	Treatment in haematopoietic stem cell transplantation
Bulgarian	Алогенни мулти-вирусни специфични Т-лимфоцити, насочени към ВК вирус, цитомегаловирус, човешки херпес вирус тип 6, вирус на Epstein Barr и аденовирус	Лечение при трансплантация на хемопоетични стволови клетки
Croatian	Alogeni multi-virus specifični T limfociti koji ciljaju BK virus, citomegalovirus, humani herpes virus-6, virus Epstein Barr i adenovirus	Liječenje u transplantaciji hematopoetskih matičnih stanica
Czech	Alogenní multi-virové specifické T lymfocyty cílené na virus BK, cytomegalovirus, lidský herpes virus-6, virus Epstein Barrové a adenovirus	Léčba transplantace hemopoetickými zárodečnými buňkami
Danish	Allogen multivirus-specifikke T-lymfocytter rettet mod BK-virus, cytomegalovirus, human herpesvirus-6, Epstein-Barr-virus og adenovirus	Behandling i hæmatopoietisk stamcelletransplantation
Dutch	Allogene multivirus-specifieke T-lymfocyten gericht op BK-virus, cytomegalovirus, humaan herpesvirus-6, Epstein Barr-virus en adenovirus	Behandeling in haematopoiëtische stemceltransplantatie
Estonian	Allogeensed mitme viiruse spetsiifilised T-lümfotsüüdid, mis on suunatud BK-viirusele, tsütomegaloviirusele, inimese herpesviirusele-6, Epstein Barri viirusele ja adenoviirusele	Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis.
Finnish	Allogeeniset monivirusspesifiset T-lymfosyytit, jotka kohdistuvat BK-virukseen, sytomegalovirukseen, ihmisen herpesvirukseen-6, Epstein Barr-virukseen ja adenovirukseen	Hoito hematopoeettisen kantasolusiirron yhteydessä
French	Lymphocytes T allogéniques spécifiques à plusieurs virus ciblant le virus BK, le cytomégalovirus, le virus de l'herpès humain-6, le virus d'Epstein Barr et l'adénovirus	Traitement dans la greffe de moëlle osseuse

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
German	Allogene multi-virus-spezifische T-Lymphozyten, die auf das BK-Virus, das Cytomegalievirus, das humane Herpes-6-Virus, das Epstein-Barr-Virus und das Adenovirus abzielen	Behandlung in hämatopoetischer Stammzelltransplantation
Greek	Αλλογενή Τ λεμφοκύτταρα ειδικά έναντι πολλαπλών ιών που στοχεύουν τον ιό BK, τον κυτταρομεγαλοϊό, τον ιό του ανθρώπινου έρπητα -6, τον ιό Epstein Barr και τον αδενοϊό	θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων
Hungarian	A BK vírust, citomegalovírust, humán herpesz-6, Epstein Barr vírust és adenovírust célzó, allogén multi-vírusspecifikus T-limfociták	Hematopoietikus őssejt-transzplantáció esetén alkalmazandó
Italian	Linfociti T specifici allogenici multi-virus diretti verso virus BK, citomegalovirus, herpes virus-6 umano, virus di Epstein Barr e adenovirus	Trattamento nel trapianto di cellule staminali ematopoietiche
Latvian	Alogēni multi-vīrusiem specifiski T limfocīti, kas vērsti pret BK vīrusu, citomegalovīrusu, cilvēka herpes vīrusu-6, Epšteina Barra vīrusu un adenovīrusu	Ārstēšanai hematopoētisko cilmes šūnu transplantācijā
Lithuanian	Alogeniniai keliems virusams specifiniai T limfocitai, nukreipti į BK virusą, citomegalo virusą, žmogaus herpes virusą-6, Epstein Barr virusą ir adenovirusą	Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme
Maltese	Limfoċiti T alloġeniċi speċifiċi għal diversi viruses li huma mmirati lejn il-Virus BK, iċ-ċitomegalovirus, il-virus tal-herpes uman 6, il-virus Epstein Barr u l-adenovirus	Kura fi trapjant ta' ċelloli staminali ematopojetiči
Polish	Allogeniczne limfocyty T specyficzne dla wielu wirusów atakujące wirus BK, wirus cytomegalii, ludzki wirus opryszczki-6, wirus Epsteina Barra i adenowirus	Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych
Portuguese	Linfócitos T alogênicos específicos de múltiplos vírus, direcionados ao vírus BK, ao citomegalovírus, ao vírus do herpes humano-6, ao vírus Epstein Barr e ao adenovírus	Tratamento em transplantes de células estaminais hematopoiéticas
Romanian	Limfocitele T alogene, multi-virus specifice, care vizează virusul BK, citomegalovirusul, virusul herpes uman-6, virusul Epstein Barr și adenovirusul	Tratament în transplantul de celule stem hematopoetice

Language	Active ingredient	Indication
Slovak	Alogénne viacvírusové špecifické T lymfocyty zamerané na BK vírus, cytomegalovírus, ľudský herpes vírus-6, vírus Epstein Barrovej a adenovírus	Liečba pri transplantácii hematopoietických kmeňových buniek
Slovenian	Alogenski multi virus specifični T-limfociti, ki ciljajo na BK virus, citomegalovirus, humani herpes virus-6, virus Epstein Barr in adenovirus	Zdravljenje pritransplantaciji hematopoetskih matičnih celic
Spanish	Linfocitos T alogénicos específicos de múltiples virus dirigidos al virus BK, citomegalovirus, virus herpes humano-6, virus Epstein Barr y adenovirus	Tratamiento en el trasplante de células madre hematopoyéticas
Swedish	Allogena multivirus-specifika T-lymfocyter riktade mot BK Virus, cytomegalovirus, humant herpesvirus-6, Epstein Barr-virus och adenovirus	Behandling vid hematopoetisk stamcellstransplantation
Norwegian	Allogene multivirus-spesifikke T-lymfocytter rettet mot BK-virus, cytomegalovirus, humant herpesvirus-6, Epstein-Barr-virus og adenovirus	Behandling ved hematopoetisk stamcelletransplantasjon
Icelandic	Ósamgenaðar fjölveirusértækar T-eitilfrumur sem beinast gegn BK Veiru, frumufrumuveiru, herpes vírus-6, Epstein Barr vírus og adenovirus	Meðferð við ígræðslu blóðmyndandi stofnfrumna