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Public summary of opinion on orphan designation

Allogeneic anti-Epstein Barr virus cytotoxic T lymphocytes expanded ex vivo for the treatment of post-transplant lymphoproliferative disorder

On 26 February 2019, orphan designation (EU/3/19/2138) was granted by the European Commission to Common Services Agency (National Health Services - Scotland), United Kingdom, for allogeneic anti-Epstein Barr virus cytotoxic lymphocytes expanded ex vivo for the treatment of post-transplant lymphoproliferative disorder.

What is post-transplant lymphoproliferative disorder?

Post-transplant lymphoproliferative disorder is a group of disorders that cause rapid growth of a type of white blood cell called B cells after transplantation. Following a transplant, patients receive medicines that weaken their immune system (the body's natural defences) to prevent rejection of the transplant. However, a weakened immune system also makes patients vulnerable to infection with viruses such as the Epstein-Barr virus. The Epstein-Barr virus is a common virus which can infect B cells. After transplantation, the virus may cause changes to the infected blood cells leading to cancer.

Post-transplant lymphoproliferative disorder is a life-threatening condition and is debilitating due to weight loss, fever and organ dysfunction.

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

At the time of designation, post-transplant lymphoproliferative disorder affected approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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, various cancer medicines were authorised in the EU for the treatment of lymphomas in patients with post-transplant lymphoproliferative disorder.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with post-transplant lymphoproliferative disorder. Early studies showed that

[*]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 518,400,000 (Eurostat 2019).

patients whose condition did not respond to standard treatments responded completely to this medicine and had improved survival. 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 contains certain cells of the immune system called cytotoxic T cells, which kill infected or abnormal cells. To make this medicine, cytotoxic T cells obtained from healthy donors are exposed to protein fragments from the Epstein-Barr virus, so that they can recognise B cells infected with the virus and attack them. When the medicine is given to the patient, the T cells are expected to attack and kill the patient's own infected B cells, helping to control cancers associated with the virus.

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, a clinical trial with the medicine in patients with post-transplant lymphoproliferative disorder had finished.

At the time of submission, the medicine was not authorised anywhere in the EU for post-transplant lymphoproliferative disorder 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 24 January 2019 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

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on the 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 anti-Epstein Barr virus cytotoxic T lymphocytes expanded ex vivo	Treatment of post-transplant lymphoproliferative disorder
Bulgarian	Алогенни цитотоксични Т-лимфоцити, култивирани ex vivo, насочени срещу вируса на Епщайн Бар	Лечение на посттрансплантационно лимфопролиферативно заболяване
Croatian	Allogeni anti-Epstein Barr virus citotoksični T limfociti ekspandirani ex vivo	Liječenje post-transplancijskog limfoproliferativnog poremećaja
Czech	Alogenní cytotoxické T-lymfocyty specifické pro virus Epstein-Barrové, expandované ex vivo	Léčba posttransplančních lymfoproliferací
Danish	Allogen anti-Epstein Barr virus cytotoksiske T-lymphocytter expanderet ex vivo	Behandling af transplantationsrelateret lymfomsygdom
Dutch	Allogenene anti-Epstein Barr virus cytotoxische T lymphocyten, geëexpandeerd ex vivo	Behandeling van post-transplant lymphoproliferatieve aandoening
Estonian	*Ex vivo* paljundatud allogeensed Epstein-Barr viiruse vastased tsütotoksilised T-lümfotsüüdid	Siirdamisjärgsete lümfoproliferatiivsete haiguste ravi
Finnish	Allogeeniset ex-vivo laajennetut, sytotoksiset t-lymfosyytit Ebstein-Barrin virusta vastaan	Elinsiirron jälkeisen lymfoproliferatiivisen sairauden hoito
French	Lymphocytes T cytotoxiques allogéniques anti- virus Epstein Barr expansés ex-vivo	Traitement des désordres lymphoprolifératifs post-transplantation
German	Allogene, ex vivo expandierte, Anti-Epstein Barr Virus zytotoxische T-Lymphozyten	Behandlung des Lymphoproliferativen Syndroms nach Transplantation
Greek	Αλλογενή, κυταροτοξικά Τ λεμφοκύτταρα έναντι το ιού Epstein Barr, καλλιεργημένα ex vivo	Θεραπεία της λεμφοϋπερπλαστικής διαταραχής μετά από μεταμόσχευση
Hungarian	Ex-vivo tenyésztett, allogén, Epstein Barr virus ellenes citotoxikus T limfociták	Poszt-transzplantációs limfoproliferatív megbetegedés kezelése
Italian	Linfociti T citotossici allogenici anti-virus Epstein Barr espansi ex-vivo	Trattamento del disordine linfoproliferativo post-trapianto
Latvian	*Ex vivo* pavairoti, alogēni, pret Epšteina-Barra vīrusu vērsti citotoksiskie T limfocīti	Pēctransplantācijas limfoproliferatīvo traucējumu ārstēšana
Lithuanian	Alogeniniai citotoksiniai T limfocitai, prieš-*Epstein Barr* virusą, išskirti *ex vivo*	Potransplantacinės limfoproliferacinės ligos gydymas
Maltese	Virus alloġeniku anti-Epstein Barr tal-linfoċiti T ċitotossiċi ex vivo estiżi	Kura tal-marda limfoproliferattiva ta' wara t-trapjant
Polish	Allogeniczne cytotoksyczne limfocyty T przeciw wirusowi Epstein-Barra nahodowane ex vivo	Leczenie poprzeszczepowej choroby limfoproliferacyjnej
Portuguese	Linfócitos T citotóxicos alogênicos do vírus anti-Epstein-Barr expandidos ex vivo	Tratamento da doença linfoproliferativa pós-transplante

[1] At the time of designation

Romanian	Limfocite T citotoxice alogenice anti virusul Epstein-Barr, expandate ex viivo	Tratamentul tulburării limfoproliferative post-transplant
Slovak	Alogenické anti- Epstein Barr vírus cytotoxické T-lymfocyty expandované ex vivo	Liečba posttransplantačnej lymfoproliferatívnej poruchy
Slovenian	Alogenični citotoksični T limfociti proti virusu Epstein Barr, ekspandirani ex vivo	Zdravljenje potransplantacijske limfoproliferativne motnje
Spanish	Linfocitos T citotoxicos alogenicos del vírus anti-Epstein-Barr expandidos ex vivo	Tratamiento del trastorno post-transplante limfoproliferativo
Swedish	Allogena anti-Epstein Barr virus cytotoxiska T-lymfocyter expanderade ex vivo	Behandling av post-transplantation lymfoproliferativ sjukdom
Norwegian	Allogene anti-Epstein-Barr-virus cytotoksiske T lymfocytter ekspandert ex vivo	Behandling av post-transplantasjon lymfoproliferativ sykdom
Icelandic	Ósamgena frumudrepandi T-eitilfrumur sértækar gegn Epstein-Barr veiru, fjölgað *ex vivo*	Meðferð áeitilfrumuoffjölgunar kvilla eftir líffæraígræðslu