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Public summary of opinion on orphan designation

Autologous T cells transduced with lentiviral vector containing a tandem chimeric antigen receptor directed against CD20 and CD19 for the treatment of diffuse large B-cell lymphoma

On 21 August 2020, orphan designation EU/3/20/2327 was granted by the European Commission to Miltenyi Biomedicine GmbH, Germany, for autologous T cells transduced with lentiviral vector containing a tandem chimeric antigen receptor directed against CD20 and CD19 (also known as MB-CART2019.1) for the treatment of diffuse large B-cell lymphoma.

What is diffuse large B-cell lymphoma?

Diffuse large B-cell lymphoma is a type of blood cancer and the most common form of a group of blood cancers known as non-Hodgkin lymphomas.

Diffuse large B-cell lymphoma affects a type of white blood cells called B lymphocytes, or B cells. In patients with this cancer, the B cells multiply quickly and live for too long, so there are too many of them in the lymph nodes. The first sign of the disease is usually a lump in the neck, under the arm or in the groin area, which is caused by an enlarged lymph node. Patients with diffuse large B-cell lymphoma may also have fever, tiredness, night sweats or weight loss that have no obvious cause.

Although some people with diffuse large B-cell lymphoma can be cured, it remains a serious and life-threatening disease, particularly when the disease is diagnosed late or has come back after treatment.

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

At the time of designation, diffuse large B cell lymphoma affected approximately 4.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 234,000 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).

*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).



What treatments are available?

At the time of designation, several medicines were authorised for the treatment of diffuse large B-cell lymphoma in the EU. The main treatment was chemotherapy (medicines to treat cancer) usually in combination with medicines called monoclonal antibodies and sometimes with radiotherapy (treatment with radiation). The gene therapy medicines axicabtagene ciloleucel and tisagenlecleucel, also called CAR-T cells, were used when other cancer medicines had not worked.

Autologous haematopoietic (blood) stem-cell transplantation was also used in patients at risk of the disease coming back after treatment. This procedure involves replacing the patient's bone marrow with the patient's own stem cells to form new bone marrow that produces healthy blood cells.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with diffuse large B cell lymphoma because laboratory results suggest that the way the medicine works by targeting 2 proteins could provide better results than CAR-T cell medicines that have one target. In addition, early results in patients whose cancer did not respond to previous treatments or had come back indicate that they may benefit from treatment with the medicine. 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?

The cancer cells in patients with diffuse large B cell lymphoma produce proteins on their surface called CD19 and CD20.

The medicine is made from the patient's own T cells. T cells are cells of the immune system (the body's natural defences) that can kill cancer cells. The T cells have been modified in the laboratory by a virus that carries a gene into the cells, enabling them to produce a receptor that targets CD19 and CD20. When given back to the patient, with this receptor on their surface the modified cells, called CAR-T cells, are expected to attach to CD19 and CD 20 on the cancer cells and kill them, thus reducing the growth and spread of the tumour.

The virus used in this medicine ('lentivirus') is modified so that it does not cause disease in humans.

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, clinical trials with the medicine in patients with diffuse large B cell lymphoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of diffuse large B cell lymphoma 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 16 July 2020, 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

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Autologous T cells transduced with lentiviral vector containing a tandem chimeric antigen receptor directed against CD20 and CD19	Treatment of diffuse large B-cell lymphoma
Bulgarian	Автоложни Т клетки, трансдуцирани с лентивирален вектор, съдържащ tandem химерен антигенен рецептор, насочен срещу CD20 и CD19.	Лечение на дифузен В-едроклетъчен лимфом
Croatian	Autologne T-stanice transducirane lentivirusnim vektorom koji sadrži tandemski himerni antigenski receptor usmjeren protiv CD20 in CD19	Liječenje difuznog limfoma velikih B-stanica
Czech	Autologní T buňky transdukované s lentivirovým vektorem obsahujícím tandemový chimérický antigenní receptor namířený proti CD20 a CD19	Léčba velkobuněčného difuzního B-lymfomu
Danish	Autologe T-celler transduceret med lentiviral vektor indeholdende en tandem-kimær antigenreceptor rettet mod CD20 og CD19	Behandling af diffust storcellet B-celle lymfom
Dutch	Autologe T-cellen getransduceerd met lentivirale vector die een tandem-chimere antigeenreceptor bevat gericht tegen CD20 en CD19	Behandeling van diffuus grootcellig B-cel-lymfoom
Estonian	Autoloogsed T-rakud, mida on transdutseeritud lentiviirusvektoriga, mis sisaldab CD20 ja CD19 vastu suunatud tandemkimäärset antigeeni retseptorit.	Diffuusse suure β-rakulise lümfoomi ravi
Finnish	Autologiset T-solut transduoituna lentiviraalivektorilla, joka sisältää kimeerisen antigeenin tandemreseptorin, jonka kohteena on CD20 ja CD19	Diffuusin suurisoluisen B-solulymfooman hoito
French	Cellules T autologues transduites avec un vecteur lentiviral contenant un récepteur antigénique chimérique tandem dirigé contre CD20 et CD19	Traitement du lymphome diffus à grandes cellules B
German	Autologe T-Zellen, transduziert mit einem lentiviralen Vektor, der einen gegen CD20 und CD19 gerichteten chimären Tandemantigenrezeptor enthält.	Behandlung des diffusen großzelligen B-Zell-Lymphoms
Greek	Αυτόλογα Τ-κύτταρα διαμολυσμένα με λεντι-ϊικό φορέα, ο οποίος φέρει διπλό υποδοχέα χιμαϊρικού αντιγόνου κατά των CD20 και CD19	Θεραπεία του διάχυτου μεγαλοκυτταρικού λεμφώματος Β-κυττάρου (DLBCL)

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	CD20 és CD19 ellen irányított tandem kiméra antigénreceptort tartalmazó, lentivirális vektorral transzdukált autológ T-sejtek.	Diffúz nagy B-sejtes lymphoma kezelése
Italian	Cellule T autologhe trasdotte con vettore lentivirale contenente un recettore chimerico per l'antigene in tandem diretto contro CD20 e CD19	Terapia del Linfoma non-Hodgkin diffuso a grandi cellule di tipo B (DLBCL)
Latvian	Autologās T šūnas, kas transducētas ar pret CD20 un CD19 vērstu tandēma himēriskā antigēna receptoru saturošu lentivīrusu vektoru	Difūzas lielo B šūnu limfomas ārstēšana
Lithuanian	Autologinės T ląstelės, transdukuotos lentivirusiniu vektoriumi, turinčiu prieš CD20 ir CD19 nukreiptą tandeminį chimerinį antigeno receptorių	Difuzinės stambiųjų B ląstelių limfomos gydymas
Maltese	Ċelloli T awtologi trasdotti b'vettur lentivirali li fih riċettur ta' antigen kimeriku f'tandem dirett kontra CD20 u CD19	Kura tal-limfoma taċ-ċelluli tat-tip B kbar mxerrda
Polish	Autologiczne limfocyty T poddane transdukcji wektorem lentiwirusowym zawierającym tandemowy chimeryczny receptor antygenowy skierowany przeciwko CD20 i CD19.	Leczenie rozlanego chłoniaka z dużych limfocytów B
Portuguese	Células T autólogas transduzidas com vetor lentiviral contendo um recetor de antígeno quimérico tandem dirigido contra CD20 e CD19	Tratamento do linfoma difuso de grandes células B
Romanian	Celule T autologe transduse cu vector lentiviral conținând un receptor de antigen himeric în tandem direcționat împotriva CD20 și CD19.	Tratamentul limfomului difuz cu celule B mari
Slovak	Autológne T-lymfocyty transdukované lentivírovým vektorom, obsahujúce tandemový chimérický antigénový receptor namierený proti CD20 a CD19.	Liečba difúzneho veľkobunkového lymfómu z buniek B
Slovenian	Autologne T celice, transducirane z lentivirusnim vektorjem, ki vsebuje tandem himernega antigenskega receptorja, usmerjenega proti CD19 in CD20	Zdravljenje razširjenega limfoma velikih B celic
Spanish	Células T autólogas transducidas con vector lentiviral que contienen un receptor antígeno quimérico en tándem contra CD20 y CD19	Tratamiento del linfoma difuso de células B grandes
Swedish	Autologa T-celler transducerade med lentivirusvektor innehållande en tandemchimär antigenreceptor riktad mot CD20 och CD19	Behandling av diffusa storcelliga B-cells lymfom
Norwegian	Autologe T celler transdusert med lentiviral vektor som inneholder en tandem kimær antigenreseptor rettet mot CD20 og CD19	Behandling av diffust storcellet B-celle lymfom

Language	Active ingredient	Indication
Icelandic	Samgena T-frumur veiruleiddar með lentiveirufurju sem inniheldur raðtengdan blendingsvakaviðtaka sem beinist gegn CD20 og CD19	Til meðferðar á dreifðu stórfrumu B frumu eitlakkabameini