7 November 2016
EMA/623799/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

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

On 14 October 2016, orphan designation (EU/3/16/1745) was granted by the European Commission to Novartis Europharm Limited, United Kingdom, for autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 (also known as CTL019) 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 cell called B lymphocytes, or B cells. In patients with this cancer, the B cells multiply too 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 less than 4.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 231,000 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).

[*]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 513,700,000 (Eurostat 2016).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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). Autologous haematopoietic (blood) stem-cell transplantation was also used in patients at risk of the disease coming back after treatment. This is a procedure where the patient's bone marrow is replaced 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 an early clinical study showed that it may be effective in patients whose disease had come back after 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?

The B cells in patients with diffuse large B-cell lymphoma produce a protein on their surface called CD19. To make this medicine, T cells (a different type of white blood cells that are part of the body's natural defences) are taken from the patient. They are then modified in the laboratory by a virus that carries a gene into the cells which allows them to target CD19. The modified T cells are grown to increase their numbers before being given back to the patient. Once the modified T cells are returned to the patient, they are expected to recognise CD19 on the cancerous B cells, allowing the T cells to target and kill them.

The virus used in this medicine ('lentivirus') is modified in order not to 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 diffuse large B-cell lymphoma. Orphan designation of the medicine had been granted in EU for the treatment of B lymphoblastic leukaemia/lymphoma and in the United States for the treatment of acute lymphoblastic leukaemia, of chronic lymphocytic leukaemia and of diffuse large B-cell lymphoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 September 2016 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 EMA website, on the medicine's rare disease designations page.

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	Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19	Treatment of diffuse large B-cell lymphoma
Bulgarian	Автоложни Т клетки, трансдуцирани с лентивирусен вектор, съдържащ химерен антигенен рецептор, насочен срещу CD19	Лечение на дифузен В-едроклетъчен лимфом
Croatian	Autologne T-stanice transducirane lentivirusnim vektorom koji sadrži kimerični antigenski receptor usmjeren protiv CD19	Liječenje difuznog limfoma velikih B-stanica
Czech	Autologní T buňky transdukované lentivirálním vektorem obsahujícím chimerický antigenní receptor namířený proti CD 19	Léčba velkobuněčného difuzního B-lymfomu
Danish	Autologe T-celler transduceret med lentiviral vektor indholdende en kimerisk antigen-receptor rettet mod CD19	Behandling af diffust storcellet B-celle lymfom
Dutch	Autologe T-cellen getransduceerd met een lentivirale vector die een chimere antigenreceptor gericht tegen CD 19 bevat	Behandeling van diffuus grootcellig B-cel-lymfoom
Estonian	Autoloogsed T-rakud, mida on transdutseeritud lentiviraalse vektoriga, mis sisaldab kimäärset antigeeni retseptorit CD19 vastu	Diffuusse suure B-rakulise lümfoomi ravi
Finnish	Autologiset T-solut, joihin on siirretty lentivirusvektorilla CD19:n kimeerinen antigeenireseptori	Diffuusin suurisoluisen B-solulymfooman hoito
French	Lymphocytes T autologues transduits par un vecteur lentiviral contenant un récepteur chimérique dirigé contre l'antigène CD19	Traitement du lymphome diffus à grandes cellules B
German	Autologe T-Zellen, die mit einem lentiviralen Vektor, der einen gegen CD19 gerichteten chimären Antigen-Rezeptor enthält, transduziert sind	Behandlung des diffusen großzelligen B-Zell-Lymphoms
Greek	Αυτόλογα Τ- κύτταρα διαμολυσμένα με λεντι-ικό φορέα που περιέχει ένα χιμαιρικό υποδοχέα αντιγόνου έναντι του CD19	Θεραπεία του διάχυτου μεγαλοκυτταρικού λεμφώματος Β-κυττάρου (DLBCL)
Hungarian	CD19 ellenes, chimerikus antigén receptort tartalmazó, lentivírus vektorral transzdukált autológ T-sejtek	Diffúz nagy B-sejtes lymphoma kezelése
Italian	Cellule T autologhe trasdotte con un vettore lentivirale contente un recettore chimerico diretto contro l'antigene CD19	Terapia del Linfoma non-Hodgkin diffuso a grandi cellule di tipo B (DLBCL)
Latvian	Autologas T šūnas, kas transducētas ar lentivīrusa vektoru, kas satur pret CD19 vērstu himērisku antigēna receptoru	Difūzas lielo B šūnu limfomas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Autologinės T ląstelės, pakeistos lentivirusiniu vektoriumi, turinčiu chimerinį antigeno receptorių prieš CD19	Difuzinės stambiųjų B ląstelių limfomos gydymas
Maltese	Ċelluli T awtologużi trasformati permezz ta' vettur lentivirali li fih riċettur għal antiġen kimeriku dirett kontra CD19	Kura tal-limfoma taċ-ċelluli tat-tip B kbar mxerrda
Polish	Autologiczne komórki T transdukowane wektorem lentiwirusowym zawierające chimeryczny receptor antygenowy przeciw CD19	Leczenie rozlanego chłoniaka z dużych limfocytów B
Portuguese	Células T autólogas transduzidas com vetor lentiviral contendo um recetor antigénio quimérico anti CD19	Tratamento do linfoma difuso de grandes células B
Romanian	Celule T autologe transduse cu un vector lentiviral conţinând un receptor chimeric direcţionat împotriva antigenului CD19	Tratamentul limfomului difuz cu celule B mari
Slovak	Autológne T bunky transdukované lentivírusovým vektorom, ktorý obsahuje chimérický antigénový namierený proti CD19	Liečba difúzneho veľkobunkového lymfómu z buniek B
Slovenian	avtologne T celice, spremenjene s postopkom transdukcije z lentivirusnim vektorjem, ki vsebuje himerni antigenski receptor proti CD19	Zdravljenje razširjenega limfoma velikih B celic
Spanish	Células T autólogas transducidas con vector lentivirus que contienen un receptor antigénico quimérico contra CD19	Tratamiento del linfoma difuso de células B grandes
Swedish	Autologa T-celler transducerade med en lentivirusvektor innehållande en chimär antigenreceptor riktad mot CD19	Behandling av diffusa storcelliga B-cells lymfom
Norwegian	Autologe T-celler transdusert med en lentiviral vektor som inneholder en kimer antigenreseptor rettet mot CD19	Behandling av diffust storcellet B-celle lymfom
Icelandic	Genaflutningur í samgena T-frumur með lentiveirugenaferju sem inniheldur blendings (chimeric) mótefnavakaviðtaka sem beinist gegn CD19	Til meðferðar á dreifðu stórfrumu B frumu eitlakrabbameini