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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3 zeta chimeric antigen receptor for the treatment of diffuse large B-cell lymphoma

On 16 December 2014, orphan designation (EU/3/14/1393) was granted by the European Commission to Kite Pharma UK, Ltd, United Kingdom, for autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3 zeta chimeric antigen receptor for the treatment of diffuse large B-cell lymphoma.

What is diffuse large B-cell lymphoma?

Diffuse large B-cell lymphoma is the most common cancer of the lymphatic system, a network of vessels that transport fluid (lymph) from tissues through the lymph nodes and into the bloodstream. The cancer 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 initial treatment.

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

At the time of designation, diffuse large B-cell lymphoma affected approximately 2.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 123,000 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 511,100,000 (Eurostat 2014).

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), sometimes in combination with radiotherapy (treatment with radiation), and immunotherapy (medicines that stimulate the immune system to kill the cancer cells). Autologous haematopoietic (blood) stem cell transplantation was also used in patients at risk of the disease coming back after treatment. This is a complex procedure where patients receive their own stem cells to help restore the bone marrow.

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 early studies show a positive response in patients with progressive disease in whom other treatments did not work. 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 abnormal B cells in patients with diffuse large B-cell lymphoma produce a protein on their surface called CD19.

This medicine is made up of immune cells (called T cells) which are taken from the patient and modified in the laboratory with a virus that carries a gene into the T cells so that they can recognise and attach to CD19. The T cells are then given back to the patient, where they are expected to attach to CD19 on the cancer cells and kill them, and to activate other T cells.

The type of virus used in this medicine ('retrovirus') 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 the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 November 2014 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:

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3 zeta chimeric antigen receptor	Treatment of diffuse large B cell lymphoma
Bulgarian	Автоложни Т клетки, трансдуцирани с ретровирусен вектор, кодиращ химеричен анти-CD19 CD28/CD3-дзета антигенен рецептор	Лечение на дифузен В-едроклетъчен лимфом
Croatian	Autologne T-stanice transducirane retrovirusnim vektorom koji kodira za kimerični antigenski receptor CD28/CD3-zeta usmjeren protiv CD19	Liječenje difuznog limfoma velikih B-stanica
Czech	Autologní T buňky transdukované retrovirovým vektorem kódujícím anti-CD19 chimérický antigenní receptor odvozený z řetězce CD28/CD3 zeta	Léčba velkobuněčného difuzního B-lymfomu
Danish	Autologe T-celler transduceret med retroviral vektor, der koder en anti-CD19 kimær antigenreceptor udledt af CD28/zetakæde CD3	Behandling af diffust storcellet B-celle lymfom
Dutch	Autologe T-cellen getransduceerd met een retrovirale vector die voor een anti-CD19 chimere antigeenreceptor afgeleid van CD28/CD3-zeta codeert	Behandeling van diffuus grootcellig B-cel-lymfoom
Estonian	Autoloogsed T-rakud, mida on transdutseeritud retrovirusvektoriga, mis kodeerib CD19-vastast CD28 / tseetaahelaga CD3 kimäärse antigeeni retseptorit	Diffuusse suure β-rakulise lümfoomi ravi
Finnish	Autologiset T-solut, joihin on retrovirusvektoriin avulla istutettu anti-CD19 CD28/CD3 zeta-kimeerisen antigeenireseptorin koodi	Diffuusin suurisoluisen B-solulymfooman hoito
French	Lymphocytes T autologues transduits par un vecteur rétroviral codant pour un récepteur antigénique chimérique anti-CD19 dérivé de CD3/CD28 zêta	Traitement du lymphome diffus à grandes cellules B
German	Autologe T-Zellen, die mit einem retroviralen Vektor transduziert werden, der einen von CD28/CD3-zeta abgeleiteten chimären Anti-CD19-Antigenrezeptor kodiert	Behandlung des diffusen großzelligen B-Zell-Lymphoms
Greek	Αυτόλογα Τ-κύτταρα διαμολυσμένα με ρετροϊικό φορέα, ο οποίος κωδικοποιεί έναν αντι-CD19 χιμαϊρικό CD28/CD3-ζ αντιγονικό υποδοχέα	Θεραπεία του διάχυτου μεγαλοκυτταρικού λεμφώματος Β-κυττάρου (DLBCL)
Hungarian	Anti-CD19 CD28/CD3 zéta kiméra antigén receptort kódoló retrovírus vektorral transzdukált autológ T-sejtek	Diffúz nagy B-sejtes lymphoma kezelése

¹ At the time of designation

Language	Active ingredient	Indication
Italian	Cellule T autologhe trasdotte con vettore retrovirale che codifica per un recettore chimerico dell'antigene anti-CD19 derivato da CD28/CD3 zeta	Terapia del Linfoma non-Hodgkin diffuso a grandi cellule di tipo B (DLBCL)
Latvian	Autologas T šūnas, transducētas ar retrovirālu vektoru, kas kodē himērisku anti-CD19 CD28/CD3 zeta antigēna receptoru	Difūzas lielo B šūnu limfomas ārstēšana
Lithuanian	Autologinės T ląstelės, transdukuotos su retrovirusiniu vektoriumi, koduojančiu anti-CD19 CD28/CD3 zeta chimerinio antigeno receptorių	Difuzinės stambiųjų B ląstelių limfomos gydymas
Maltese	Ċelluli T awtologużi trasformati permezz ta' vettur retroviral li jikkodifika riċettur antigeniku kimeriku kontra CD19 assoċjat ma' CD28/CD3 zeta	Kura tal-linfoma taċ-ċelluli tat-tip B kbar mxerrda
Polish	Autologiczne limfocyty T transdukowane wektorem retrowirusowym kodującym chimeryczne receptory antygenowe przeciwiał anty-CD19 pochodzących z łańcucha CD28/CD3 zeta	Leczenie rozlanego chłoniaka z dużych limfocytów B
Portuguese	Células T autólogas transduzidas com um vetor retroviral codificando um recetor antigénico quimérico anti-CD19 CD28/CD3 zeta	Tratamento do linfoma difuso de grandes células B
Romanian	Celule T autologe transduse cu un vector retroviral ce codifică un receptor chimeric al antigenelor anti-CD19 si CD28/CD3 zeta	Tratamentul limfomului difuz cu celule B mari
Slovak	Autológne T bunky transdukované retrovírusovým vektorom kódujúcim chimérický antigénový receptor anti- CD19 a CD28/CD3 zeta	Liečba difúzneho veľkobunkového lymfómu z buniek B
Slovenian	Avtologne celice T, transducirane z retrovirusnim vektorjem, ki kodira himerni antigenski receptor anti-CD19 CD28/CD3	Zdravljenje razširjenega limfoma velikih B celic
Spanish	Células T autólogas transducidas con un vector retroviral que codifica un receptor quimérico de antígeno anti-CD19 derivado de CD28/CD3 zeta	Tratamiento del linfoma difuso de células B grandes
Swedish	Autologa T-celler transducerade med en retroviral vektor som kodar för en CD19-specifik chimär antigenreceptor från CD28/CD3-zetakedjan	Behandling av diffusa storcelliga B-cells lymfom
Norwegian	Autologe T-celler transdusert med retroviral vektor som koder for en anti-CD19 CD28/CD3 zeta kimær antigenreseptor	Behandling av diffust storcellet B-celle lymfom
Icelandic	Samgena T-frumur, umbreyttar með retróveirufurju, sem kóðar blendingsmótefnavakaviðtaka gegn CD19 úr CD28/CD3-zetakeðju	Til meðferðar á dreifðu stórfrumu B frumu eitlakrabbameini