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Public summary of opinion on orphan designation

Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti CD19 CD28/CD3-zeta chimeric antigen receptor and cultured for the treatment of mantle cell lymphoma

On 13 November 2019, orphan designation EU/3/19/2220 was granted by the European Commission to Kite Pharma EU B.V., Netherlands, for autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti CD19 CD28/CD3-zeta chimeric antigen receptor and cultured (also known as KTE-X19 CAR) for the treatment of mantle cell lymphoma.

What is mantle cell lymphoma?

Mantle cell lymphoma is an aggressive cancer of a type of white blood cell called B lymphocytes, or B cells. In mantle cell lymphoma, the B cells multiply quickly and live for too long, so they build up in the lymph nodes. The first sign of the disease is usually a lump in the neck, under the arm or in the groin, caused by an enlarged lymph node. Patients may also have fever, weight loss, tiredness and night sweats. Mantle cell lymphoma is usually diagnosed in people aged over 50 years. It is more common in men than in women.

Mantle cell lymphoma is a long-term debilitating and life-threatening disease associated with poor survival.

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

At the time of designation, mantle cell lymphoma affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 31,000 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 518,400,000 (Eurostat 2019).

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What treatments are available?

At the time of designation, the main treatments for mantle cell lymphoma included chemotherapy (medicines to treat cancer), immunotherapy (medicines that act on the body's immune system) and radiotherapy (treatment with radiation). Bortezomib, ibrutinib, lenalidomide and temsirolimus were specifically authorised in the EU for the treatment of mantle cell lymphoma that has come back after previous treatment or other treatments have not worked. Haematopoietic (blood) stem-cell transplantation was also used. This is a procedure where cells in the patient's bone marrow are replaced by stem cells to form new bone marrow that produces healthy blood cells.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with mantle cell lymphoma. Early studies showed improved survival in patients whose disease had come back after several treatments with other medicines. 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 the patient’s own T cells (a type of white blood cell) that have been modified genetically in the laboratory so that they make a protein called chimeric antigen receptor (CAR). CAR can attach to another protein on the surface of cancer cells called CD19.

When the medicine is given to the patient, the modified T cells are expected to attach to CD19 on the cancer cells and kill them, and to activate other T cells to attack the cancer.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with mantle cell lymphoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of mantle cell lymphoma. Orphan designation had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 10 October 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 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	Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti CD19 CD28/CD3-zeta chimeric antigen receptor and cultured	Treatment of mantle cell lymphoma
Bulgarian	Култивирани автоложни периферни кръвни селектирани CD4 и CD8 Т-клетки и активирани CD3 и CD28, трансдуцирани с ретровирусен вектор, експресиращ анти-CD19 CD28/CD3-зета химерен антигенен рецептор	Лечение на мантелно-клетъчна лимфом
Croatian	Autologne T stanice periferne krvi nakon selekcije CD4 i CD8 i aktivacije pomoću CD3 i CD28 transducirane retrovirusnim vektorom za ekspresiju kimeričnog antigenskog receptora CD28/CD3 zeta usmjerenog protiv CD19 i uzgojene u kulturi	Liječenje limfoma plaštenih stanica
Czech	Autologní T buňky z periferní krve, selektované CD4 a CD8 a aktivované CD3 a CD28, transdukované retrovirovým vektorem exprimujícím anti-CD19 CD28/CD3 zeta chimerický antigenní receptor a kultivované	Léčba lymfomu z plášťové zóny
Danish	Selekterede CD4- og CD8-T-celler samt aktiverede CD3- og CD28-T-celler fra autologt perifert blod, overført med en retroviral vektor, som udtrykker en CD28/CD3-zeta kimærisk antigen-receptor mod CD19, og dyrkes frem	Behandling af mantelcellelymfom
Dutch	Autologe CD4- en CD8-T-cellen geselecteerd uit perifeer bloed en geactiveerd door CD3 en CD28, getransduceerd met retrovirale vector die CD28/CD3zeta chimere antigeenreceptor tegen CD19 tot expressie brengt en gekweekt	Behandeling van mantelcellymfoom

[1] At the time of designation

Language	Active ingredient	Indication
Estonian	CD4- ja CD8-selekteeritud ning CD3- ja CD28-aktiveeritud autoloogsed perifeerse vere T-rakud, mis on transdutseeritud anti-CD19 ning CD28/CD3-dzeeta kimäärse antigeeni retseptoriga ning seejärel kultiveeritud	Mantelrakulise lümfoomi ravi
Finnish	Viljellyt, autologiset, perifeerisen veren selektoidut CD4- ja CD8-T-solut ja aktivoidut CD3- ja CD28-T-solut, jotka on transduktoitu retrovirusvektorilla ilmentämään CD28/CD3-zeetaa sisältävää kimeeristä anti-CD19-antigeenireseptoria	Manttelisolu-lymfooman hoito
French	Lymphocytes T de sang périphérique autologue CD4 et CD8 sélectionnés et CD3 et CD28 activés, transduits par un vecteur rétroviral, exprimant un récepteur antigénique chimérique anti-CD19 CD28/CD3-zêta et cultivés	Traitement des lymphomes du manteau
German	Kultivierte autologe T-Zellen aus dem peripheren Blut, CD4- und CD8-selektiert, CD3- und CD28- aktiviert, die mit retroviralem Vektor transduziert wurden und einen chimären anti-CD19 CD28/CD3-zeta Antigenrezeptor expremieren	Behandlung von Mantelzelllymphom
Greek	Αυτόλογα Τ κύτταρα περιφερικού αίματος, επιλεγμένα ως προς CD4 και CD8 και ενεργοποιημένα ως προς CD3 CD28, διαμολυσμένα με ρετροϊικό φορέα που εκφράζει έναν αντι-CD19 χιμαιρικό CD28/CD3-ζ αντιγονικό υποδοχέα και έχουν υποβληθεί σε καλλιέργεια	Θεραπεία του λεμφώματος μανδυκών κυττάρων
Hungarian	CD19 elleni CD28/CD3 zéta kiméra antigénreceptort expresszáló retrovírus vektorral transzdukált és tenyésztett, CD3- és CD28-aktivált, kiválasztott CD4 és CD8 autológ perifériásvér-T-sejtek	Köpenysejtes lymphoma kezelése
Italian	Linfociti T CD4 e CD8 selezionati e linfociti CD3 e CD28 attivati, ottenuti da sangue periferico autologo, trasdotti con vettore retrovirale che codifica per un recettore chimerico dell'antigene anti-CD19 CD28/CD3 zeta, e messi in coltura	Trattamento del linfoma con cellule a mantello

Language	Active ingredient	Indication
Latvian	Autologas perifēro asiņu CD4 un CD8 selektētas T šūnas, kas ir CD3 un CD28 aktivētas, transducētas ar retrovīrusa vektoru,kas ekspresē anti CD19 CD28/CD3-zēta himērisko antigēna receptoru, un kultivētas	Mantijšūnu limfomas ārstēšana
Lithuanian	Iš periferinio kraujoCD4 ir CD8 atrinktos ir CD3 ir CD28 aktyvintos kultivuotos autologinės T ląstelės, transdukuotos retrovirusiniu vektoriumi, išreiškiančiu anti CD19 CD28/CD3-zeta chimerinio antigeno receptorius	Mantijos ląstelių limfomos gydymas
Maltese	Ċelluli T awtologi u kkulturati tad-demm periferali CD4 u CD8 magħżula u CD3 u CD28 attivati trasdotti permezz ta' vettur retrovirali li jesprimu riċettur ta' antiġen kimeriku anti CD19 CD28/CD3-żeta	Kura tal-limfoma taċ-ċelloli tal-mantell
Polish	Autologiczne komórki T wyselekcjonowane z krwi obwodowej na podstawie ekspresji cząsteczek CD4 i CD8, aktywowane cząsteczkami CD3 i CD28 oraz transdukowane retrowirusowym wektorem, wykazującym ekspresję chimerycznego receptora antygenowego anty-CD19 CD28/CD3-zeta, a następnie poddane hodowli	Leczenie chłoniaków z komórek płaszczowych
Portuguese	Células T CD4 e CD8 selecionadas e CD3 e CD28 ativadas de sangue periférico autólogas, transduzidas com vetor retroviral, expressando um recetor antigénico quimérico anti-CD19 contendo CD28/CD3 zeta e cultivadas	Tratamento de linfoma de células do manto
Romanian	Limfocite T autologe din sângele periferic selectate CD4 și CD8 și activate CD3 și CD28, transduse cu vector retroviral ce exprimă un receptor chimeric CD28/CD3-zeta al antigenului anti-CD19 și cultivate	Tratamentul limfomului cu celule în manta
Slovak	Kultivované autológne T lymfocyty periférnej krvi vybrané podľa expresie CD4 a CD8 s aktivovaným receptorom CD3 a CD28 transdukované retrovírusovým vektorom exprimujúcim chimérický antigénový receptor anti-CD19, CD28/CD3-zeta	Liečba lymfómu plášťovej zóny

Language	Active ingredient	Indication
Slovenian	Avtologne T celice periferne krvi, po selekciji CD4 in CD8 ter aktivaciji CD3 in CD28, transducirane z retrovirusnim vektorjem, ki izraža himerni antigenski receptor, vsebujoč CD28/CD3-zeta in je usmerjen proti CD19, ter so bile gojene v kulturi	Zdravljenje limfoma plaščnih celic
Spanish	Células T autólogas de sangre periférica CD4 y CD8 seleccionadas y CD3 y CD28 activadas, transducidas con un vector retroviral, que expresan el receptor de antígeno quimérico anti-CD19 CD28/CD3-zeta y cultivadas	Tratamiento del linfoma de células del manto
Swedish	Selekterade CD4- och CD8-T-celler samt aktiverade CD3- och CD28-T-celler från autologt perifert blod, som överförts med en retroviral vektor, uttrycker en CD28/CD3-zeta-innehållande chimär antigenreceptor mot CD19, och har odlats fram	Behandling av mantelcellslymfom
Norwegian	Selekterte CD4 og CD8 T-celler fra autologt perifert blod som er aktivert via CD3 og CD28, transdusert med retroviral vektor og uttrykker anti-CD19 CD28/CD3-zeta kimær antigenreseptor, og som deretter er dyrket	Behandling av mantelcelle-lymfom
Icelandic	Samgena T-frumur í útlægu blóði, valdar af CD4 og CD8 frumum og virkjaðar af CD3 og CD28 frumum, ferjaðar með retróveiruferju sem tjáir and-CD19 CD28/CD3-zeta blendingsmótefnaviðtaka og ræktaðar	Meðferð möttulfrumu eitlakrabbameins