13 November 2015
EMA/COMP/596693/2015
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 mantle cell lymphoma

On 9 October 2015, orphan designation (EU/3/15/1552) 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 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 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, 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 women. Mantle cell lymphoma is a long-term debilitating and life-threatening disease that is associated with poor overall survival.

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

At the time of designation, mantle cell lymphoma affected less than 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 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).

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 stimulate the body's own immune system

*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 512,900,000 (Eurostat 2015).

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to kill the cancer cells) and radiotherapy (treatment with radiation). Temsirolimus, bortezomib and ibrutinib were specifically authorised in the EU for the treatment of mantle cell lymphoma that has come back after previous treatment or has not responded to other treatments. Haematopoietic (blood) stem-cell transplantation was also used. This is a complex procedure where patients receive stem cells to help restore the bone marrow.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with mantle cell lymphoma because early studies show that it might improve the outcome of patients whose disease has 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 abnormal B cells in patients with mantle 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. These modified T cells are then given back to the patient, where they are expected to attach to CD19 on the cancer cells and kill them. These T cells are also expected to activate other T cells from the patient to act against the cancer 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 mantle cell lymphoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for mantle cell lymphoma 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 3 September 2015 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

For details of the current sponsor of the orphan designation please refer to the information on the main web page of this Public Summary of Opinion.

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 retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor	Treatment of mantle cell lymphoma
Bulgarian	Автоложни Т клетки, трансдуцирани с ретровирусен вектор, кодиращ химеричен анти-CD19 CD28/CD3-дзета антигенен рецептор	Лечение на мантелно-клетъчна лимфома
Croatian	Autologne T-stanice transducirane retrovirusnim vektorom koji kodira za kimerični antigenski receptor CD28/CD3-zeta usmjeren protiv CD19	Liječenje limfoma plaštenih stanica
Czech	Autologní T buňky transdukované retrovirovým vektorem kódujícím anti-CD19 chimérický antigenní receptor odvozený z řetězce CD28/CD3 zeta	Léčba lymfomu z plášťové zóny
Danish	Autologe T-celler transduceret med retroviral vektor, der koder en anti-CD19 kimær antigenreceptor udledt af CD28/zetakæde CD3	Behandling af mantelcellelymfom
Dutch	Autologe T-cellen getransduceerd met een retrovirale vector die voor een anti-CD19 chimere antigeenreceptor afgeleid van CD28/CD3-zeta codeert	Behandeling van mantelcellymfoom
Estonian	Autoloogsed T-rakud, mida on transdutseeritud retrovirusvektoriga, mis kodeerib CD19-vastast CD28 / tseetaahelaga CD3 kimäärse antigeeni retseptorit	Mantelrakulise lümfoomi ravi
Finnish	Autologiset T-solut, joihin on retrovirusvektorin avulla istutettu anti-CD19 CD28/CD3 zeta-kimeerisen antigeenireseptorin koodi	Manttelisolu-lymfooman hoito
French	Lymphocytes T autologues transduits par un vecteur rétroviral codant pour un récepteur antigénique chimérique anti-CD19 dérivé de CD3/CD28 zêta	Traitement des lymphomes du manteau
German	Autologe T-Zellen, die mit einem retroviralen Vektor transduziert werden, der einen von CD28/CD3-zeta abgeleiteten chimären Anti-CD19-Antigenrezeptor kodiert	Behandlung von Mantelzelllymphom
Greek	Αυτόλογα Τ-κύτταρα διαμολυσμένα με ρετροϊικό φορέα, ο οποίος κωδικοποιεί έναν αντι-CD19 χιμαιρικό CD28/CD3-ζ αντιγονικό υποδοχέα	Θεραπεία του λεμφώματος μανδυκών κυττάρων
Hungarian	Anti-CD19 CD28/CD3 zéta kiméra antigén receptort kódoló retrovírus vektorral transzdukált autológ T-sejtek	Köpenysejtes lymphoma kezelése
Italian	Cellule T autologhe trasdotte con vettore retrovirale che codifica per un recettore chimerico dell'antigene anti-CD19 derivato da CD28/CD3 zeta	Trattamento del linfoma con cellule a mantello
Latvian	Autologas T šūnas, transducētas ar retrovirālu vektoru, kas kodē himērisku anti-CD19 CD28/CD3 zeta antigēna receptoru	Mantijšūnu limfomas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Autologinės T ląstelės, transdukuotos su retrovirusiniu vektoriumi, koduojančiu anti-CD19 CD28/CD3 zeta chimerinio antigeno receptorių	Mantijos ląstelių limfomos gydymas
Maltese	Ċelluli T awtologużi trasformati permezz ta' vettur retrotivirali li jikkodifika riċettur antiġeniku kimeriku kontra CD19 assoċjat ma' CD28/CD3 żeta	Kura tal-limfoma taċ-ċelloli tal-mantell
Polish	Autologiczne limfocyty T transdukowane wektorem retrowirusowym kodującym chimeryczne receptory antygenowe przeciwciał anty-CD19 pochodzących z łańcucha CD28/CD3 zeta	Leczenie chłoniaków z komórek płaszczowych
Portuguese	Células T autólogas transduzidas com um vetor retroviral codificando um recetor antigénico quimérico anti-CD19 CD28/CD3 zeta	Tratamento de linfoma de células do manto
Romanian	Celule T autologe transduse cu un vector retroviral ce codifică un receptor chimeric al antigenelor anti-CD19 si CD28/CD3 zeta	Tratamentul limfomului cu celule în manta
Slovak	Autológne T bunky transdukované retrovírusovým vektorom kódujúcim chimérický antigénový receptor anti-CD19 a CD28/CD3 zeta	Liečba lymfómu plášťovej zóny
Slovenian	Avtologne celice T, transducirane z retrovirusnim vektorjem, ki kodira himerni antigenski receptor anti-CD19 CD28/CD3	Zdravljenje limfoma plaščnih 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 de células del manto
Swedish	Autologa T-celler transducerade med en retroviral vektor som kodar för en CD19-specifik chimär antigenreceptor från CD28/CD3-zetakedjan	Behandling av mantelcellslymfom
Norwegian	Autologe T-celler transdusert med retroviral vektor som koder for en anti-CD19 CD28/CD3 zeta kimær antigenreseptor	Behandling av mantelcelle-lymfom
Icelandic	Samgena T-frumur, umbreyttar með retróveiruferju, sem kóðar blendingsmótefnavakaviðtaka gegn CD19 úr CD28/CD3-zetakeðju	Meðferð möttulfrumu eitlakrabbameins