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Public summary of opinion on orphan designation

Autologous CD4$^+$ and CD8$^+$ T cells expressing a CD19-specific chimeric antigen receptor for the treatment of follicular lymphoma

On 25 May 2018, orphan designation (EU/3/18/2018) was granted by the European Commission to Celgene Europe Limited, United Kingdom, for autologous CD4$^+$ and CD8$^+$ T cells expressing a CD19-specific chimeric antigen receptor (also known as JCAR017) for the treatment of follicular lymphoma.

What is follicular lymphoma?

Follicular lymphoma is a cancer of a type of white blood cell called B lymphocytes or B cells. In follicular lymphoma, 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, caused by an enlarged lymph node. Patients may also have fever, weight loss, tiredness and night sweats.

Follicular lymphoma is usually diagnosed in people aged over 50 years. It is a long-term debilitating and life-threatening disease due to organ damage and the cancer coming back.

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

At the time of designation, follicular lymphoma affected approximately 3.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 197,000 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 follicular lymphoma available in the EU included chemotherapy (medicines to treat cancer) combined with immunotherapy (medicines that stimulate the body's own immune system to kill the cancer cells). The medicines ibritumomab tiuxetan, idelalisib, interferon alfa-2b, obinutuzumab, pixantrone and rituximab were authorised for the treatment of follicular lymphoma.

*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 517,400,000 (Eurostat 2018).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with follicular lymphoma because early results had shown prolonged responses in patients whose disease had come back after, or not responded to, other treatments. 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 follicular lymphoma produce a protein on their surface called CD19.

This medicine is made up of two types of immune cells (called $CD4^+$ and $CD8^+$ T cells) which are taken from the patient. The T cells are modified in the laboratory with a virus that carries a gene into the T cells that allows them to target CD19. The modified T cells are then grown to increase their numbers. When given back to the patient, the T cells 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 virus used to carry the gene into the cells has been modified so that it cannot reproduce and cause disease in humans.

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 with the medicine in patients with follicular lymphoma were ongoing.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 April 2018 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 CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor	Treatment of follicular lymphoma
Bulgarian	Автоложни CD4+ и CD8+ Т-клетки, експресиращи CD19-специфичен химерен антигенен рецептор	Лечение на фоликуларен лимфом
Croatian	Autologne T stanice tipa CD4+ i CD8+ koje izražavaju CD19 specifični kimerični antigenski receptor	Liječenje folikularnog limfoma
Czech	Autologní CD4+ a CD8+ pozitivní T-lymfocyty exprimující specifický chimérický antigenní receptor CD19	Léčba folikulárního lymfomu
Danish	Autologe CD4+ og CD8+ T-celler, udtrykkende CD19-specifik kimær antigenreceptor	Behandling af follikulært lymfom
Dutch	Autologe CD4+ en CD8+ T-cellen die een CD19-specifieke chimere antigeenreceptor tot expressie brengen	Behandeling van folliculair lymfoom
Estonian	Autoloogsed CD4+ja CD8+ T-rakud, millel avaldub CD19-spetsiifiline kimäärne antigeeni retseptor	Follikulaarse lümfoomi ravi
Finnish	Autologiset CD4+ ja CD8+-T-solut, jotka ilmentävät CD19:lle spesifistä kimeeristä antigeenireseptoria	Follikulaarisen lymfooman hoito
French	Lymphocytes T CD4+ CD8+ autologues exprimant le récepteur antigénique chimérique (CAR) anti-CD19	Traitement des lymphomes folliculaires
German	Autologe CD4+ und CD8+ T-Zellen, die einen CD19-spezifischen, chimären Antigen-Rezeptor exprimieren	Behandlung des follikulären Lymphoms
Greek	Αυτόλογα CD4+ και CD8+ Τ-κύτταρα που εκφράζουν έναν χιμαιρικό αντιγονικό υποδοχέα έναντι του CD19	θεραπεία του θηλακιώδους λεμφώματος
Hungarian	CD19-specifikus kiméra antigén receptort expresszáló autológ CD4+ és CD8+ T-sejtek.	Follicularis lymphoma kezelése
Italian	Cellule autologhe T CD4+ e CD8+ che esprimono il recettore chimerico specifico per l'antigene CD19	Trattamento del linfoma follicolare
Latvian	Autologas CD4+ un CD8+ T šūnas, kas ekspresē pret CD19 specificsku himērisku antigēna receptoru	Folikulārās limfomas ārstēšana
Lithuanian	Autologinės CD4+ CD8+ T ląstelės su CD19 specifinio chimerinio antigeno receptoriaus raiška	Folikulinės limfomos gydymas
Maltese	Celluli T CD4+ u CD8+ awtologi li jesprimu riċettatur ta' antiġene kimeriku speċifiku għal CD19.	Kura tal-limfoma follikulari
Polish	Autologiczne komórki T CD4+ i CD8+ z ekspresją CD19-specyficznych chimerycznych receptorów antygenowych	Leczenie chłoniaków grudkowych
Portuguese	Células T CD4+ e CD8+ autólogas que exprimem o recetor quimérico do antigénio específico para CD19	Tratamento do linfoma folicular
Romanian	Celule T CD4+ și CD8+ autologe care exprimă receptorul de antigen chimeric CD19 specific	Tratamentul limfomului folicular

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Autológne CD4+ a CD8+ T-lymfocyty exprimujúce CD19-špecifický chimérický antigénny receptor	Liečba folikulárneho lymfómu
Slovenian	avtologne celice T tipa CD4+ in CD8+, ki izražajo CD19 specifičen himerni antigenski receptor	Zdravljenje folikularnega limfoma
Spanish	Células T autólogas CD4+ y CD8+ que expresan un receptor del antígeno quimérico específico de CD19	Tratamiento del linfoma folicular
Swedish	Autologa CD4+ och CD8+ T-celler som uttrycker CD19-specifik chimär antigenreceptor	Behandling av follikulärt lymfom
Norwegian	Autologe CD4+ og CD8+ T celler som uttrykker en CD19-spesifikk kimær antigenreseptor	Behandling av follikulært lymfom
Icelandic	Samgena CD4+ og CD8+ T-frumur sem tjá CD19-sértækan blendingsmótefnavakaviðtaka	Meðferð á follicular eitilfrumukrabbameini