5 August 2020
EMADOC-628903358-2369

Public summary of opinion on orphan designation

Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains for the treatment of multiple myeloma

On 4 June 2020, orphan designation EU/3/20/2277 was granted by the European Commission to FGK Representative Service GmbH, Germany, for autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (also known as CT053) for the treatment of multiple myeloma.

What is multiple myeloma?

Multiple myeloma (also called plasma cell myeloma) is a cancer of a type of white blood cell called plasma cells. Plasma cells are produced in the bone marrow, the spongy tissue inside the large bones in the body. In multiple myeloma, the division of plasma cells becomes uncontrolled, resulting in abnormal, immature plasma cells multiplying and filling up the bone marrow. This interferes with production of normal white blood cells, red blood cells and platelets (components that help the blood to clot), leading to complications such as anaemia (low red blood cell counts), bone pain and fractures, raised blood calcium levels and kidney disease.

Multiple myeloma is a debilitating and life-threatening disease particularly because it disrupts the normal functioning of the bone marrow, damages the bones and causes kidney failure.

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

At the time of designation, multiple myeloma affected approximately 4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 208,000 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).

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

What treatments are available?

At the time of designation, several medicines were authorised for multiple myeloma in the EU. The main treatment for multiple myeloma was chemotherapy (medicines to treat cancer) usually combined with corticosteroids to reduce the activity of the body's immune (defence) system. After chemotherapy patients received a stem-cell transplant if they were considered suitable for it. Stem-cell transplantation is a procedure where the patient's bone marrow is replaced with 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 multiple myeloma. This is because early results have shown that the medicine was beneficial in patients whose cancer had come back or not responded after extensive treatment; this compares favourably to other therapies used in this group of patients.

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 medicine is made up of 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). This protein is designed to attach to a target called BCMA, which is found on plasma cells. When the modified cells, called CAR-T cells, are given to the patient, they are expected to attach to BCMA on the plasma cells, thereby killing the abnormal plasma cells and helping to clear the cancer from the body.

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 multiple myeloma were ongoing.

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

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 23 April 2020, 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 T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains	Treatment of multiple myeloma
Bulgarian	Автоложна, обогатена с Т лимфоцити популация от клетки, трансдуцирани с лентивирусен вектор, кодиращ химерен антигенен рецептор, насочен към човешкия антиген на матурация на В клетки с 4-1BB и CD3-зета вътреклетъчни сигнални домейни	Лечение на мултиплен миелом
Croatian	Populacija stanica obogaćena autolognim T limfocitima transducirana lentivirusnim vektorom koji kodira kimerični antigenski receptor usmjeren na antigen sazrijevanja humanih B stanica sa 4-1BB i CD3-zeta intracelularnim domenama signalizacije	Liječenje multiplog mijeloma
Czech	Autologními T lymfocyty obohacená populace buněk transdukovaná s lentivirovým vektorem kódujícím chimerický antigenní receptor zacílený na lidský antigen maturace B-buněk s 4-1BB a CD3-zeta intracelulárními signálními doménami	Léčba mnohočetného myelomu
Danish	Autolog T lymfocyt-beriget cellepopulation, transduceret med en lentiviral vektor, kodende for en kimær antigenreceptor rettet mod humant B-celle modningsantigen med 4-1BB og CD3-zeta intracellulære signaleringsdomæner	Behandling af myelomatose
Dutch	Autologe T-lymfocyt-verrijkte populatie van cellen die getransduceerd zijn met een lentivirale vector welke een chimere antigeenreceptor codeert die zich richt op humaan B-cel maturatie-antigeen met 4-1BB en CD3-zeta intracellulaire signaleringsdomeinen	Behandeling van multipel myeloom
Estonian	Autoloogne T-lümfotsüütidega rikastatud rakupopulatsioon, mida on transdutseeritud lentiviraalse vektoriga, mis kodeerib rakusiseseid 4-1BB ja CD3-dzeeta signaaldomeene sisaldavat kimäärset antikeha retseptorit ja mis on suunatud inimese B-rakkude küpsemise antigeeni vastu	Multiibelse müeloomi ravi

[1] At the time of designation

Language	Active ingredient	Indication
Finnish	Autologiset T-lymfosyyttirikastetut solut, joihin on siirretty ihmisen B-solun maturaatioantigeeniin kohdistuvaa kimeeristä antigeenireseptoria koodaava lentivirusvektori, jossa on 4-1BB:n ja CD3-zetan solunsisäiset signaalinvälitysdomeenit	Multippeli myelooman hoito
French	Population de lymphocytes T autologues enrichie en cellules transduites avec un vecteur lentiviral codant un récepteur d'antigène chimérique qui cible l'antigène de maturation des lymphocytes B humains avec les domaines de signalement intracellulaire 4-1BB et CD3-zeta	Traitement du myélome multiple
German	Autologe Zellpopulation angereichert mit T-Lymphozyten, mit einem lentiviralen Vektor transduziert der für einen chimären Antigen-Rezeptor kodiert, der gegen das humane B-Zellen-Maturationsantigen mit den intrazellulären Signaldomänen 4-1BB und CD3-zeta gerichtet ist	Behandlung des multiplen Myeloms
Greek	Πληθυσμός αυτόλογων κυττάρων εμπλουτισμένος με Τ λεμφοκύτταρα και διαμολυσμένος με λεντι-ιικό φορέα που κωδικοποιεί ένα χιμαιρικό υποδοχέα αντιγόνου κατά του ανθρώπινου αντιγόνου ωρίμανσης Β κυττάτων με ενδοκυτταρικές περιοχές σήμανσης 4-1ΒΒ και CD3-ζ	Θεραπεία πολλαπλού μυελώματος
Hungarian	Humán B-sejt maturációs antigént célzó kimér antigén receptort kódoló lentivirális vektorral transzdukált, autológ T-limfocitával gazdagított sejtpopuláció, 4-1BB és CD3-zeta intracelluláris jeladó doménekkel	Myeloma multiplex kezelése
Italian	Popolazione arricchita con linfociti T autologhi trasdotti con un vettore lentivirale che codifica per un recettore antigenico chimerico diretto contro l'antigene di maturazione delle cellule B umano con domini di segnalazione intracellulare 4-1BB e CD3-zeta	Trattamento del mieloma multiplo
Latvian	Ar autologiem T limfocītiem bagātināta šūnu populācija, kas transducēta ar lentivīrusa vektoru, kurš kodē himērisku antigēna receptoru, kas vērsts pret cilvēka B šūnu nobriešanas antigēnu, ar 4-1BB un CD3-zeta intracelulārajiem signālceļu domēniem	Multiplās mielomas ārstēšana
Lithuanian	Autologiniais T limfocitais praturtintas ląstelių klonas, transdukuotas lentivirusiniu vektoriumi, koduojančiu chimerinį antigeno receptorių, nukreiptą į žmogaus B ląstelių brendimo antigeną su 4-1BB ir CD3-zeta tarpląsteliniais signaliniais domenais	Dauginės mielomos gydymas

Language	Active ingredient	Indication
Maltese	Popolazzjoni awtologa arrikita b'limfoċiti-T ta' ċelluli transdotti b'vettur lentivirali b'ikkowdjar ta' riċettur ta' antiġen kimeriku li fil-mira tiegħu għandu l-antiġen ta' maturazzjoni taċ-ċellola B umana b'dominji ta' senjalazzjoni intraċellulari 4-1BB u CD3-żeta	Kura tal-mjeloma multipla
Polish	Populacja krwinek autologicznych wzbogacona w limfocyty T, obejmująca komórki transdukowane wektorem lentiwirusowym zawierającym sekwencję kodującą chimeryczną formę receptora antygenowego skierowanego przeciwko antygenowi dojrzewania limfocytów B, zawierającą wewnątrzkomórkowe domeny sygnałowe 4-1BB i CD3-zeta	Leczenie szpiczaka mnogiego
Portuguese	População de células autólogas enriquecida em linfócitos T transduzida com um vetor lentiviral, que codifica um recetor antigénico quimérico, dirigido ao antigénio de maturação de células B humanas com domínios de sinalização intracelular 4-1BB e CD3-zeta	Tratamento do mieloma múltiplo
Romanian	Populație îmbogăţită de limfocite T autologe transduse cu un vector lentiviral care codifică receptorul antigenului chimeric care vizează antigenul de maturizare a limfocitelor B umane cu domenii de semnalizare intracelulare 4-1BB și CD3-zeta	Tratamentul mielomului multiplu
Slovak	Populácia buniek obohatená autológnymi T-lymfocytmi transdukovanými lentivirálnym vektorom kódujúcim antigénový receptor zacielený na ľudský antigén dozrievania B bunky s intracelulárnymi signálnymi doménami 4-1BB a CD3-zeta	Liečba mnohopočetného myelómu
Slovenian	Obogatena populacija avtolognih T-limfocitnih celic, transduciranih z lentivirusnim vektorjem, ki kodirajo himerni antigenski receptor dozorevanja humanih celic Bz intracelularnimi domenami signalizacije 4-1BB in CD3-zeta	Zdravljenje multiplega mieloma
Spanish	Población enriquecida con linfocitos T autólogos que contiene células transducidas con un vector lentivírico que codifica un receptor de antígenos quimérico selectivo para el antígeno de maduración de los linfocitos B humanos con dominios de señalización intracelular 4-1BB y CD3-zeta	Tratamiento del mieloma múltiple

Language	Active ingredient	Indication
Swedish	Autologa T-lymfocytberikade cellerinnehållande en lentiviral vektor som kodar för en chimär antigenreceptor riktad mot human-B-cellsmognadsantigen med 4-1BB och CD3-zeta intracellulära signaleringsdomäner	Behandling av multipelt myelom
Norwegian	Autolog T-lymfocyttberiket populasjon av celler transdusert med en lentiviral vektor som koder for en kimær antigenreseptor rettet mot humant B-cellemodningsantigen med 4-1BB og CD3-zeta intracellulære signaleringsdomener	Behandling av myelomatose
Icelandic	Hópur auðgaður samgena T-eitilfrumna sem er veiruleiddur með lentiveiruferju sem kóðar fyrir blendingsmótefnavakaviðtaka sem tengist sérstökum mótefnavaka þroskaðrar B-frumu (BCMA) úr mönnum og er með 4-1BB og CD3-zeta hneppi fyrir innanfrumu boðleiðaflutning.	Meðferð við mergæxli