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Public summary of opinion on orphan designation

Autologous human T cells genetically modified ex-vivo with a lentiviral vector encoding a chimeric antigen receptor for B-cell maturation antigen for the treatment of multiple myeloma

On 28 February 2020, orphan designation EU/3/20/2252 was granted by the European Commission to Janssen-Cilag International N.V., Belgium, for autologous human T cells genetically modified ex-vivo with a lentiviral vector encoding a chimeric antigen receptor for B-cell maturation antigen (also known as JNJ-68284528 or LCAR-B38M CAR-T cells) 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).

*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 519, 200,000 (Eurostat 2020).

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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 immune system, the body's natural defences. 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 clinical data in patients who had previously received other types of treatment showed that the medicine was effective in many patients and a high number of them had no signs of the disease after treatment (complete response). 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). With this receptor on their surface, the modified cells, called CAR-T cells, can attach to a target on the surface of plasma cells called B-cell maturation antigen (BCMA). When the medicine is given to the patient, the modified T cells are expected to attach to and kill the abnormal plasma cells, thereby 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, this medicine was not authorised anywhere in the EU for the treatment of multiple myeloma. Orphan designation had been granted in the United States for the treatment of this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 22 January 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 human T cells genetically modified ex-vivo with a lentiviral vector encoding a chimeric antigen receptor for B-cell maturation antigen	Treatment of multiple myeloma
Bulgarian	Автоложни човешки Т клетки, генетично модифицирани ex vivo с лентивирусен вектор, кодиращ химерен антигенен рецептор срещу В клетъчен матурационен антиген	Лечение на мултиплен миелом
Croatian	Autologne ljudske T stanice genetički modificirane ex vivo koristeći lentivirusni vektor koji kodira kimerični antigenski receptor za antigen sazrijevanja B stanica.	Liječenje multiplog mijeloma
Czech	Autologní humánní T-buňky geneticky modifikované ex-vivo s lentivirovým vektorem kódující chimérický antigenní receptor pro antigen maturace B-buněk	Léčba mnohočetného myelomu
Danish	Autologe humane T-celler, genetisk modificerede ex vivo ved brug af en lentiviral vektor, der koder en kimær antigenreceptor rettet mod B celle modningsantigen	Behandling af multipelt myelom
Dutch	Autologe humane T-cellen die ex vivo genetisch zijn gemodificeerd met een lentivirale vector die codeert voor een chimere antigeenreceptor voor het B cel maturatie antigen	Behandeling van multipel myeloom
Estonian	B-raku küpsemisvalgu kimäärset antigeeniretseptorit kodeeriva lentiviirusvektoriga geneetiliselt *ex vivo* muundatud inimese autoloogsed T-rakud	Multiibelse müeloomi ravi
Finnish	Autologiset ihmisen T-solut, joita on geenimuokattu ex-vivo B-solujen maturaatioantigeenin (BCMA) tunnistavaa kimeeristä antigeenireseptoria koodaavan lentivirusvektorin avulla	Multippeli myelooman hoito
French	Lymphocytes T humains autologues génétiquement modifiés *ex-vivo* au moyen d'un vecteur lentiviral codant pour un récepteur antigénique chimérique de maturation des cellules B	Traitement du myélome multiple

[1] At the time of designation

Language	Active ingredient	Indication
German	Autologe humane T Zellen, die ex vivo genetisch mit einem lentiviralen Vektor modifiziert wurden, der einen chimären Antigenrezeptor für das B Zell Reifungsantigen kodiert	Behandlung des multiplen Myeloms
Greek	Αυτόλογα ανθρώπινα Τ λεμφοκύτταρα γενετικά τροποποιημένα ex vivo με φορέα λεντοϊού που κωδικοποιεί ένα χειμερικό αντιγονικό υποδοχέα για το αντιγόνο ωρίμανσης Β κυττάρων	Θεραπεία πολλαπλού μυελώματος
Hungarian	B-sejt maturációs antigént célzó, kiméra antigén receptort kódoló, lentivirális vektor felhasználásával, ex vivo, genetikailag módosított autológ humán T sejtek	Myeloma multiplex kezelése
Italian	Cellule T umane autologhe modificate geneticamente ex vivo mediante un vettore lentivirale che codifica per un recettore chimerico di antigene diretto verso l'antigene di maturazione delle cellule B	Trattamento del mieloma multiplo
Latvian	Ar B šūnu nobriešanas antigēna himērisku antigēnu receptoru kodējošu lentivīrusa vektoru *ex vivo* ģenētiski modificētas autologas cilvēka T šūnas	Multiplās mielomas ārstēšana
Lithuanian	Autologinės žmogaus T ląstelės, genetiškai modifikuotos *ex vivo* su lentiviruso vektoriumi, koduojančiu chimerinį antigeno receptorių B ląstelių brendimo antigenui	Dauginės mielomos gydymas
Maltese	Ċelloli T awtologi tal-bniedem modifikati b'mod ġenetiku ex-vivo b'vettur lentivirali li jipproduċi riċettur kimeriku ta' antiġene għall-antiġene ta' maturazzjoni taċ-ċellula B	Kura tal-mjeloma multipla
Polish	Autologiczne ludzkie limfocyty T genetycznie zmodyfikowane w warunkach ex vivo za pomocą wektora lentiwirusowego kodującego chimeryczny receptor antygenowy dla antygenu dojrzewania komórek B (ang. BCMA, B cell maturation antigen)	Leczenie szpiczaka mnogiego
Portuguese	Células T autólogas humanas geneticamente modificadas ex vivo com um vetor lentiviral que codifica um receptor antigénico quimérico para o antigénio de maturação das células B	Tratamento do mieloma múltiplo
Romanian	Celule T autologe umane, modificate genetic ex vivo, utilizând un vector lentiviral care codifică un receptor antigenic chimeric pentru antigenul de maturare a celulelor B	Tratamentul mielomului multiplu

Language	Active ingredient	Indication
Slovak	Autológne ľudské T-bunky geneticky modifikované ex vivo prostredníctvom lentivírusového vektora kódujúceho chimerický antigénový receptor pre antigén maturácie B-buniek	Liečba mnohopočetného myelómu
Slovenian	Avtologne humane celice T, ki so ex vivo gensko spremenjene s pomočjo lentivirusnega vektorja, tako da kodirajo himerni antigenski receptor	Zdravljenje multiplega mieloma
Spanish	Células T autólogas humanas geneticamente modificadas ex vivo con un vetcor lentiviral que codifica un receptor antigénico quimérico para o antigénio de maturacion de las células	Tratamiento del mieloma múltiple
Swedish	Autologa humana T-celler som genmodifierats ex vivo med en lentivirusvektor som kodar för en chimär antigenreceptor riktad mot BCMA (B cell maturation antigen)	Behandling av multipelt myelom
Norwegian	Autologe humane T celler genetisk modifisert ex vivo med en lentiviral vektor som koder for en kimær antigenreseptor for B-celle modningsantigen	Behandling av myelomatose
Icelandic	Samgena manna T-frumur, erfðabreyttar utan líkamans, með lentiveirugenaferju sem táknar fyrir blendings-vakaviðtaka fyrir BCMA (B-cell maturation antigen)	Meðferð við mergfrumuæxli