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Public summary of opinion on orphan designation

Autologous T-cells transduced with lentiviral vector encoding an anti-SLAMF7 CD28/CD3-zeta chimeric antigen receptor for the treatment of plasma cell myeloma

On 27 February 2017, orphan designation (EU/3/17/1833) was granted by the European Commission to Dr. Michael Hudecek, Germany, for autologous T-cells transduced with lentiviral vector encoding an anti-SLAMF7 CD28/CD3-zeta chimeric antigen receptor for the treatment of plasma cell myeloma.

What is plasma cell myeloma?

Plasma cell myeloma (also called multiple myeloma) is a cancer of a type of white blood cell called plasma cells. Plasma cells originate from the bone marrow, the spongy tissue inside the large bones in the body. In plasma cell myeloma the division of plasma cells becomes out of control, resulting in abnormal, immature plasma cells multiplying and filling up the bone marrow. This interferes with the 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.

Plasma cell 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, plasma cell myeloma affected less than 4 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 206,000 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, several medicines were already authorised for plasma cell myeloma in the EU. The main treatment for plasma cell myeloma was chemotherapy (medicines to treat cancer)

*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 515,700,000 (Eurostat 2017).

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usually combined with corticosteroids to reduce the activity of the immune system, the body's natural defences. Where chemotherapy did not work, some patients received an allogeneic stem-cell transplant (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow). Radiotherapy (using radiation to kill cancer cells) was used to treat pain due to bone damage and prevent further damage. Interferon alfa was sometimes used in combination with chemotherapy.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with plasma cell myeloma. Laboratory studies showed that the medicine helped eliminate myeloma cells from the blood, spleen and bone marrow and improved survival, and its effects compared well with those of other authorised 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 plasma cells in patients with the condition produce a protein on their surface called SLAMF7. To make this medicine, T cells (a type of white blood cell that is part of the body's natural defences) are taken from the patient. They are then modified in the laboratory by a virus that carries a gene into the cells which allows them to target SLAMF7. The modified T cells are grown to increase their numbers before being given back to the patient. Once the modified T cells are returned to the patient, they are expected to recognise SLAMF7 on the cancerous plasma cells, allowing the T cells to target and kill them.

The virus used in this medicine ('lentivirus') 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, no clinical trials with the medicine in patients with plasma cell myeloma had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for plasma cell myeloma 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 19 January 2017 recommending the granting of this designation.

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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 T cells transduced with lentiviral vector encoding an anti-SLAMF7 CD28/CD3-zeta chimeric antigen receptor	Treatment of plasma cell myeloma
Bulgarian	Автоложни Т клетки, трансдуцирани с лентивирусен вектор, кодиращ химеричен анти-SLAMF7 CD28/CD3-дзета антигенен рецептор	Лечение на плазмоцитен миелом
Croatian	Autologne T-stanice transducirane lentivirusnim vektorom koji kodira za kimerični antigenski receptor CD28/CD3-zeta usmjeren protiv SLAMF7	Liječenje multiplog mijeloma
Czech	Autologní T buňky transdukované lentivirovým vektorem kódujícím anti-SLAMF7 chimérický antigenní receptor odvozený z řetězce CD28/CD3 zeta	Léčba myelomu
Danish	Autologe T-celler transduceret med lentiviral vektor, der koder en anti-SLAMF7 kimær antigenreceptor udledt af CD28/zetakæde CD3	Behandling af plasmacellemyelom
Dutch	Autologe T-cellen getransduceerd met een lentivirale vector die voor een anti-SLAMF7 chimere antigeenreceptor afgeleid van CD28/CD3-zeta codeert	Behandeling van plasmacel myeloom
Estonian	Autoloogsed T-rakud, mida on transdutseeritud lentiviirusvektoriga, mis kodeerib SLAMF7-vastast CD28/CD3 tseetaahelaga kimäärse antigeeni retseptorit	Plasmarakulise müeloomi ravi
Finnish	Autologiset T-solut, joihin on lentivirusvektorin avulla istutettu anti-SLAMF7 CD28/CD3 zeta- kimeerisen antigeenireseptorin koodi	Plasmasolumyelooman hoito
French	Lymphocytes T autologues transduits par un vecteur lentiviral codant pour un récepteur antigénique chimérique anti-SLAMF7 dérivé de CD3/CD28 zêta	Traitement du myélome des cellules plasmatiques
German	Autologe T-Zellen, mit einem lentiviralen Vektor transduziert, der einen von CD28/CD3-zeta abgeleiteten chimären Anti- SLAMF7-Antigenrezeptor kodiert	Behandlung des Plasmazell Myeloms
Greek	Αυτόλογα Τ-κύτταρα διαμολυσμένα με φορέα λεντιϊού, ο οποίος κωδικοποιεί έναν αντι-SLAMF7 χιμαιρικό CD28/CD3-ζ αντιγονικό υποδοχέα	Θεραπεία του πλασματοκυτταρικού μυελώματος
Hungarian	Anti-SLAMF7 CD28/CD3 zéta kiméra antigén receptort kódoló lentivírus vektorral transzdukált autológ T-sejtek	Plasma sejtes myeloma kezelése
Italian	Cellule T autologhe trasdotte con vettore lentivirale che codifica per un recettore chimerico dell'antigene anti-SLAMF7 derivato da CD28/CD3 zeta	Trattamento del Mieloma Plasmacellulare
Latvian	Autologas T šūnas, kas transducētas ar lentivīrusa vektoru, kas kodē himērisku anti-SLAMF7 CD28/CD3 zeta antigēna receptoru	Plazmas šūnu mielomas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Autologinės T ląstelės, transdukuotos su lentivirusiniu vektoriumi, koduojančiu anti-SLAMF7 CD28/CD3 zeta chimerinio antigeno receptorių	Plazminių ląstelių mielomos gydymas
Maltese	Ċelluli T awtologużi trasformati permezz ta' vettur lentivirali li jikkodifika riċettur antiġeniku kimeriku kontra SLAMF7 assoċjat ma' CD28/CD3 żeta	Kura tal-mjeloma taċ-ċelluli tal-plasma
Polish	Autologiczne limfocyty T transdukowane wektorem lentiwirusowym kodującym chimeryczne receptory antygenowe przeciwciał anty-SLAMF7 pochodzących z łańcucha CD28/CD3 zeta	Leczenie szpiczaka mnogiego
Portuguese	Células T autólogas transduzidas com um vetor lentiviral codificando um recetor antigénico quimérico anti-SLAMF7 CD28/CD3 zeta	Tratamento do mieloma de células plasmáticas
Romanian	Celule T autologe transduse cu un vector lentiviral ce codifică un receptor chimeric al antigenului anti-SLAMF7 derivat din CD28/CD3 zeta	Tratamentul mielomului plasmocitar
Slovak	Autológne T bunky transdukované lentivírusovým vektorom kódujúcim chimérický antigénový receptor anti-SLAMF7 a CD28/CD3 zeta	Liečba myelómu z plazmatických buniek
Slovenian	Avtologne celice T, transducirane z lentivirusnim vektorjem, ki kodira himerni antigenski receptor anti-SLAMF7 CD28/CD3 zeta	Zdravljenje plazmocitoma
Spanish	Células T autólogas transducidas con un vector lentiviral que codifica un receptor quimérico de antígeno anti-SLAMF7 derivado de CD28/CD3 zeta	Tratamiento del mieloma de células plasmáticas
Swedish	Autologa T-celler transducerade med en lentiviral vektor som kodar för en SLAMF7-specifik chimär antigenreceptor från CD28/CD3-zetakedjan	Behandling av plasmacellsmyelom
Norwegian	Autologe T-celler transdusert med en lentiviral vektor som koder for en kimær SLAMF7-spesifikk CD28/CD3-zeta antigenreseptor	Behandling av plasmacellemyelom
Icelandic	Samgena T-frumur, umbreyttar með lentiveiruferju, sem kóðar fyrir blendingsmótefnavakaviðtaka gegn SLAMF7 úr CD28/CD3-zetakeðju	Meðferð á plasmafrumumýelómi