



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

6 August 2020  
EMADOC-628903358-2380

## Public summary of opinion on orphan designation

Autologous CD4+ and CD8+ T cells transduced with a lentiviral vector encoding an affinity enhanced T cell receptor specific to MAGE-A4 for the treatment of soft tissue sarcoma

On 4 June 2020, orphan designation EU/3/20/2286 was granted by the European Commission to Adaptimmune Limited, United Kingdom, for autologous CD4+ and CD8+ T cells transduced with a lentiviral vector encoding an affinity enhanced T cell receptor specific to MAGE-A4 (also known as ADP-A2M4) for the treatment of soft tissue sarcoma.

### What is soft tissue sarcoma?

Soft tissue sarcoma is a cancer that affects the soft, supportive tissues of the body. It can occur in muscles, blood vessels, fat tissue or in other tissues that support, surround and protect organs. Patients with soft tissue sarcoma do not usually have symptoms in the early stages of the disease. First symptoms appear when the tumour grows large enough to cause swelling and pain.

Soft tissue sarcoma is a long-term debilitating and life-threatening disease, particularly when the cancer has spread to other parts of the body.

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

At the time of designation, soft tissue sarcoma affected approximately 4.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 239,000 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 soft tissue sarcoma were surgery and chemotherapy (medicines to treat cancer). Radiotherapy (treatment with radiation) was also used. Several medicines were authorised in the EU for the treatment of soft tissue sarcoma.

---

\*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).



The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with soft tissue sarcoma because evidence from studies in patients suggest a positive response in patients for whom existing treatments have not worked.

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?**

This medicine contains the patient's own T cells (a type of white blood cell and part of the body's natural defences) that have been modified genetically in the laboratory so that they can attach to cancer cells that produce a protein called MAGE-A4.

When the medicine is given to the patient, the modified T cells are expected to attach to a part of MAGE-A4 which is present on the cancer cells and kill them, and to encourage other immune cells to attack the cancer.

### **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 soft tissue sarcoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of soft tissue sarcoma. Orphan designation of the medicine had been granted in the United States for soft tissue sarcoma.

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Autologous CD4+ and CD8+ T cells transduced with a lentiviral vector encoding an affinity enhanced T cell receptor specific to MAGE-A4	Treatment of soft tissue sarcoma
Bulgarian	Автоложни CD4+ и CD8+ Т клетки, трансдуцирани с лентивирусен вектор, кодиращ Т-клетъчен рецептор с повишен афинитет специфичен за MAGE-A4	Лечение на сарком на меките тъкани
Croatian	Autologne CD4+ i CD8+ T stanice transducirane lentivirusnim vektorom koji kodira T stanični receptor s poboljšanim afinitetom specifičnim za MAGE-A4	Liječenje sarkoma mekih tkiva
Czech	Autologní CD4+ a CD8+ T buňkytransdukované s lentivirovým vektorem kódujícím T buněčný receptor se zvýšenou afinitou specifickou pro MAGE-A4	Léčba sarkomu měkkých tkání
Danish	Autolog CD4+ og CD8+ T celler transduceret med en lentiviralvektor indeholdende en affinitetsforbedret T celle receptor specifikt målrettet MAGE-A4 tumorantigenet	Behandling af bløddelsarkom
Dutch	Autologe CD4+ en CD8+ T-cellen getransduceerd met lentivirale vector welke een affiniteit versterkte T-cel receptor heeft specifiek gericht op het MAGE-A4	Behandeling weke delen sarcoom
Estonian	Autoloogsed CD4+ ja CD8+ T-rakud, mida on transdutseeritud lentiviirusvektoriga, mis kodeerib suurenenud afiinsusega MAGE-A4 spetsiifilist T-raku retseptorit	Pehmete kudede sarkoomi ravi
Finnish	Autologiset CD4+ ja CD8+ T-solut, joihin on lentivirusvektorin avulla siiretty affiniteetiltaan parannettu, MAGE-A4 kasvaimen antigeenille spesifinen T-solureseptori	Pehmytkudossarkooman hoito

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
French	Cellules T CD4+ et CD8+ autologues transduites avec un vecteur lentiviral codant un récepteur des cellules T d'affinité accrue pour cibler l'antigène MAGE-A4	Traitement des sarcomes des tissus mous
German	Autologe CD4+ und CD8+ T-Zellen transduziert mit einem lentiviralen vektor, der einen T-Zell-Rezeptor mit erhöhter affinität gegen das MAGE-A4 tumorantigen enthält	Behandlung des Weichteilsarkoms
Greek	Αυτόλογα Τ κύτταρα CD4+ και CD8+ μετασχηματίζονται με φορέα λεντοϊού που φέρει Τ κυτταρικό υποδοχέα ενισχυμένης συγγένειας έναντι του MAGE-A4	Θεραπεία του σαρκώματος των μαλακών ιστών
Hungarian	MAGE-A4 antigént célzó, fokozott affinitású T-sejt receptort tartalmazó, lentivirális vektorral transzdukált autológ CD4+ és CD8+ T-sejtek	Lágy szöveti sarcoma kezelése
Italian	Cellule T CD4+ e CD8+ autologhe trasdotte con un vettore lentivirale contenente un recettore delle cellule T ad affinità potenziata diretto verso l'antigene tumorale MAGE-A4	Trattamento dei sarcomi dei tessuti molli
Latvian	Autologas CD4+ un CD8+ T šūnas, kas transducētas ar lentivīrusa vektoru, kas kodē paaugstinātas afinitātes pret MAGE-A4 vērstu T šūnu receptoru	Mīksto audu sarkomas ārstēšana
Lithuanian	Autologinės CD4+ ir CD8+ T ląstelės, transdukuotos su lentivirusiniu vektoriumi, turinčiu padidinto jautrumo T ląstelių receptorių, specifiską MAGE-A4	Minkštųjų audinių sarkomos gydymas
Maltese	Ċelloli T awtologi CD4+ u CD8+ transdotti b'vettur lentivirali b'ikkowdjar ta' ricettur taċ-ċellola T imsaħħaħ b'affinità speċifiku għall-MAGE-A4	Kura tas-sarkoma tat-tessuti rotob
Polish	Autologiczne komórki T CD4+ i CD8+ transdukowane wektorem lentiwirusowym zawierającym receptor komórek T o zwiększonym powinowactwie, skierowany przeciw antygenowi nowotworowemu MAGE-A4	Leczenie mięsaków tkanek miękkich
Portuguese	Células T CD4+ e CD8+ autólogas transduzidas com um vetor lentiviral que codifica um receptor de células T com afinidade aumentada para o antígeno tumoral MAGE-A4	Tratamento do sarcoma dos tecidos moles

Language	Active ingredient	Indication
Romanian	Celule T autologe CD4+ și CD8+ transduse cu un vector lentiviral ce codează un receptor pentru celule T cu afinitate crescută specific pentru MAGE-A4	Tratamentul sarcomului țesuturilor moi
Slovak	Autológne CD4+ a CD8+ T bunky transdukované s lentivirálnym vektorom kódujúcim T-bunkový receptor s vylepšenou afinitou zameriavajúci sa na nádorový antigén MAGE-A4	Liečba sarkómu mäkkých tkanív
Slovenian	Autologne CD4+ and CD8+ T-celice, transducirane z lentivirusnim vektorjem, ki kodirajo zvečano afiniteto za T-celični receptor , specifičen za MAGE-A4	Zdravljenje sarkoma mehkih tkiv
Spanish	Células T autólogas CD4+ y CD8+transducidas con un vector lentiviral que contiene un receptor de células T de afinidad aumentada dirigido al antígeno tumoral MAGE-A4	Tratamiento del sarcoma de tejidos blandos
Swedish	Autologa CD4+ och CD8+ T-celler konstruerade med en affinitetförbättrade T-cell-receptor riktad mot tumörantigen MAGE-A4	Behandling av mjukdelssarkom
Norwegian	Autologe CD4+ og CD8+ T celler transdusert med en lentiviral vektor som koder for en affinitetsforsterket T-cellereseptor spesifikk mot MAGE-A4	Behandling av bløtvevssarkom
Icelandic	Samgena CD4+ og CD8+ T-frumur með innleidda lentiveirufurju sem kóðar fyrir T-frumuviðtaka með aukna sækni sem er sértækur fyrir MAGE-A4	Meðferð við mjúkvefjasarkmeini