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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Live-attenuated non-replicative *Pseudomonas aeruginosa* strain expressing large T antigen of Merkel cell polyomavirus for the treatment of Merkel cell carcinoma

On 18 November 2016, orphan designation (EU/3/16/1781) was granted by the European Commission to APCure SAS, France, for live-attenuated non-replicative *Pseudomonas aeruginosa* strain expressing large T antigen of Merkel cell polyomavirus for the treatment of Merkel cell carcinoma.

What is Merkel cell carcinoma?

Merkel cell carcinoma (also known as cutaneous neuro-endocrine carcinoma) is a skin cancer that starts in 'neuro-endocrine' cells called Merkel cells. Neuro-endocrine cells release hormones into the blood when stimulated by the nervous system. Merkel cell carcinoma usually appears as a painless red-blue lump on the head and neck, but it can also be found on the arms and legs, and sometimes on the trunk.

Merkel cell carcinoma is a debilitating and life-threatening condition because it grows rapidly and spreads quickly to other parts of the body. Once this cancer has spread, it is associated with very poor survival.

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

At the time of designation, Merkel cell carcinoma affected less than 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 21,000 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 513,700,000 (Eurostat 2016).



What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU to treat Merkel cell carcinoma. Patients were treated with surgery and radiotherapy (treatment with radiation). Chemotherapy (medicines to treat cancer) was used for cancer that had spread.

How is this medicine expected to work?

The medicine works by stimulating the patient's immune system, the body's natural defences, so that it targets and destroys cancer cells. It is made of *Pseudomonas aeruginosa* bacteria, which have been attenuated (weakened) so that they do not cause disease and cannot multiply in the body. The bacteria have also been modified to produce the protein Large T (LT) which is found in a majority of Merkel cell carcinomas.

When the medicine is injected into the body, the patient's immune system is activated by the *Pseudomonas aeruginosa* and learns to treat LT as 'foreign'. This encourages the immune system to attack the cancer cells in Merkel cell carcinoma because they have the LT protein, so reducing the growth of the cancer.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

No clinical trials had been started in patients with Merkel cell carcinoma.

At the time of submission, the medicine was not authorised anywhere in the EU for Merkel cell carcinoma 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 6 October 2016 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Live-attenuated non-replicative <i>Pseudomonas aeruginosa</i> strain expressing large T antigen of Merkel cell polyomavirus	Treatment of Merkel cell carcinoma
Bulgarian	Жив атенюиран не репликиращ се щам на <i>Pseudomonas aeruginosa</i> , експресиращ голям Т антиген на Меркел-клетъчен полиомавирус	Лечение на Меркел-клетъчен карцином
Croatian	Živ oslabljen ne replicirajući soj <i>Pseudomonas aeruginosa</i> koji izražava veliki T antigen poliooma virusa Merkelovih stanica	Liječenje karcinoma Merkelovih stanica
Czech	Živý oslabený non replikující <i>Pseudomonas aeruginosa</i> kmen exprimující velký T antigen polyomaviru Merkelových buněk	Léčba karcinomu z Merkelových buněk
Danish	Levende, svækkede ikke-replikativ <i>Pseudomonas aeruginosa</i> stamme, der udtrykker stort T-antigen af Merkel celle polyomavirus	Behandling af Merkelcellekarcinom
Dutch	Levend verzwakt non replicatieve <i>Pseudomonas aeruginosa</i> stam welke groot T-antigeen van Merkel cel polyomavirus uitdrukt	Behandeling van Merkelcelcarcinoom
Estonian	Merkelirakulise poliõoviiruse suurt T-antigeeni ekspresseeriv <i>Pseudomonas aeruginosa</i> elus nõrgestatud mitte-replitseeruv tüvi	Merkelirakulise vähi ravi
Finnish	Levande försvagat icke replica <i>Pseudomonas aeruginosa</i> stam som uttrycker stort T-antigen av Merkel Cell polyomavirus	Merkelinsolukarsinooman hoito
French	Souche vivante atténuée non répliquative de <i>Pseudomonas aeruginosa</i> exprimant l'antigène Large T du polyomavirus de Merkel	Traitement du carcinome à cellules de Merkel
German	Abgeschwächten Lebend nicht replikativen <i>Pseudomonas aeruginosa</i> Stamm exprimieren große T-Antigen von Merkel Polyomavirus	Behandlung von Merkelzellkarzinomen
Greek	Ζωντανό εξασθενημένο μη πολλαπλασιαζόμενο στέλεχος <i>Pseudomonas aeruginosa</i> που εκφράζει το μεγάλο Τ αντιγόνο του ιού του καρκινώματος Μέρκελ.	Θεραπεία Καρκινώματος Κυττάρων Merkel
Hungarian	Merkel sejt poliómavirus nagy T-antigénjét expresszáló élő, gyengített nem replikáló <i>Pseudomonas aeruginosa</i> törzs	Merkel sejtes carcinoma kezelése
Italian	<i>Ceppo di Pseudomonas aeruginosa</i> vivo attenuato non replicante, esprime il large T antigen of Merkel cell polyomavirus	Trattamento del carcinoma delle cellule di Merkel
Latvian	Dzīvu, novājinātu, reproducēties nespējīgu <i>Pseudomonas aeruginosa</i> celms, kas ekspresē Merkela šūnu poliomas vīrusa lielo T antigēnu	Merkela šūnu karcinomas ārstēšana

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	Gyva susilpninta nereplikacinė <i>Pseudomonas aeruginosa</i> padermė, ekspresuojanti didžiulį Merkelio ląstelių poliomaviruso T antigeną	Merkelio ląstelių karcinomos gydymas
Maltese	Razza <i>Pseudomonas aeruginosa</i> mhux replikattiva u ħajja attenwata li tesprimi antiġen T kbir taċ-ċellola polimavirus Merkel	Kura tal-karcinoma taċ-ċelloli ta' Merkel
Polish	Żywy atenuowany niereplikujący szczep <i>Pseudomonas aeruginosa</i> eskprymujący duży antygen T poliomawirusa komórki Merkel	Leczenie raka z komórek Merkla
Portuguese	Estirpe viva atenuada não-replicativa de <i>Pseudomonas aeruginosa</i> expressando o antígeno T grande do poliomávirus de Merkel	Tratamento de carcinoma de células de Merkel
Romanian	Tulpină vie atenuată, nonreplicativă de <i>Pseudomonas aeruginosa</i> care exprimă antigenul large T al poliomavirusului Merkel	Tratamentul carcinomului cu celule Merkel
Slovak	Živý oslabený nereplikujúci sa kmeň <i>Pseudomonas aeruginosa</i> vyjadrujúci veľký T antigén polyomavírusu Merkelových buniek	Liečba rakoviny z Merkelových buniek
Slovenian	Živ, oslabljen ne-replikativen sev <i>Pseudomonas aeruginosa</i> , ki izraža veliki T antigen Merkel poliomavirusa	Zdravljenje karcinoma Merklovih celic
Spanish	Cepa de <i>Pseudomonas aeruginosa</i> vivo atenuado no replicativo que expresa el antígeno T grande del poliomavirus de Merkel	Tratamiento del carcinoma de células de Merkel
Swedish	Levande försvagad icke-replikativ <i>Pseudomonas aeruginosa</i> stam som uttrycker stort T-antigen av Merkel polyomavirus	Behandling av merkelcellskarcinom
Norwegian	Levende, svekket ikke-replikerbar stamme av <i>Pseudomonas aeruginosa</i> som uttrykker stort T-antigen fra Merkelcelle polyomavirus	Begandling av Merkelcellekarsinom
Icelandic	Lifandi, veikluðum nonreplicative <i>Pseudomonas aeruginosa</i> útsetning sem tjáir stór T mótefnisvaka Merkel pólyómaveiru	Meðferð við Merkel frumu krabbameini