



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

29 January 2016
EMA/COMP/778956/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human monoclonal IgG1 antibody against programmed death ligand-1 for the treatment of Merkel cell carcinoma

On 14 December 2015, orphan designation (EU/3/15/1590) was granted by the European Commission to Merck KGaA, Germany, for recombinant human monoclonal IgG1 antibody against programmed death ligand-1 for the treatment of Merkel cell carcinoma.

What is Merkel cell carcinoma?

Merkel cell carcinoma (also known as cutaneous neuro-endocrine carcinoma) is a type of 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 long-term 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).

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 chemotherapy (medicines to treat cancer), surgery and

*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 512,900,000 (Eurostat 2015).



radiotherapy (treatment with radiation). However, in most patients whose disease had spread, the disease usually came back after treatment.

How is this medicine expected to work?

This medicine is a 'monoclonal antibody', a type of protein designed to recognise and attach to a protein called 'programme death ligand-1' (PD-L1). This protein is expressed in many cancer cells and it is thought to help to suppress the body's defences (immune cells) thereby protecting cancer cells from being attacked by the immune cells.

By attaching to the PD-L1 protein, the medicine is expected to remove this suppressive effect, allowing the immune cells to recognise and kill the cancer cells. In addition, by attaching to the cancer cells it is thought that the antibody helps to kill them directly. This is expected to slow down the growth of 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 Merkel cell carcinoma were ongoing.

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 12 November 2015 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	Recombinant human monoclonal IgG1 antibody against programmed death ligand-1	Treatment of Merkel cell carcinoma
Bulgarian	Рекомбинантно човешко моноклонално антитяло от клас IgG1 срещу лиганд-1 на програмираната смърт	Лечение на Меркел-клетъчен карцином
Croatian	Rekombinantno ljudsko monoklonsko IgG1 protutijelo protiv liganda-1 apoptoze stanice	Liječenje karcinoma Merkelovih stanica
Czech	Rekombinát lidské monoklonální IgG1 protilátky ki ligandu-1 programované buněčné smrti	Léčba karcinomu z Merkelových buňek
Danish	Rekombinant humant monoklonalt IgG1-antistof mod programmeret Death Ligand-1	Behandling af Merkelcellekarcinom
Dutch	Recombinant humaan monoklonaal IgG1-antilichaam tegen geprogrammeerde celdood ligand-1	Behandeling van Merkelcelcarcinoom
Estonian	<i>Programmed Death Ligand-1</i> vastane rekombinantne inimese monoklonaalne IgG1 antikeha	Merkelirakulise vähi ravi
Finnish	Rekombinantti ihmisen monoklonaalinen IgG1-vastaine ohjelmoitunutta solukuoleman ligandi-1: tä vastaan	Merkelinsolukarsinooman hoito
French	Anticorps IgG1 monoclonal humain recombinant contre le ligand de la protéine de mort programmée 1	Traitement du carcinome à cellules de Merkel
German	Rekombinanter humaner monoklonaler IgG1-Antikörper gegen programmed death ligand-1	Behandlung von Merkelzellkarzinomen
Greek	Ανασυνδυασμένο ανθρώπινο μονοκλωνικό αντισωμα IgG1 έναντι του συνδέτη-1 προγραμματισμένου κυτταρικού θανάτου	Θεραπεία Καρκινώματος Κυττάρων Merkel
Hungarian	Programozott sejthalál ligandum-1 elleni rekombináns humán monoklonális IgG1 antitest	Merkel sejtes carcinoma kezelése
Italian	Anticorpo monoclonale ricombinante IgG1 umano diretto contro il ligando 1 di morte programmata	Trattamento del carcinoma delle cellule di Merkel
Latvian	Cilvēka rekombinanta IgG1 monoklonāla antivielā pret programmētās nāves ligandu 1	Merkela šūnu karcinomas ārstēšana
Lithuanian	Rekombinantinis žmogaus monokloninis IgG1 antikūnas prieš programuotos ląstelių žūties ligandą-1	Merkelio ląstelių karcinomos gydymas
Maltese	Antikorp IgG1 monoklonali uman rikombinanti kontra l-ligand-1 ta' mewt iprogrammata	Kura tal-karcinoma taċ-ċelloli ta' Merkel
Polish	Rekombinowane ludzkie przeciwciało monoklonalne IgG1 przeciwko ligandowi receptora programowanej śmierci 1	Leczenie raka z komórek Merkla
Portuguese	Anticorpo monoclonal humano recombinante de tipo IgG1 contra o ligante de morte celular programada 1	Tratamento de carcinoma de células de Merkel
Romanian	Anticorp monoclonal uman recombinant de tip IgG1 împotriva ligandului-1 implicat în moartea celulară programată	Tratamentul carcinomului cu celule Merkel

¹ At the time of designation

Language	Active ingredient	Indication
Slovak	Rekombinantná ľudská monoklonálna IgG1 protilátka proti ligandu-1 programovanej apoptózy	Liečba rakoviny z Merkelových buniek
Slovenian	Rekombinantno humano monoklonsko IgG1-protitelo proti ligandu-1 programirane celične smrti	Zdravljenje karcinoma Merklvih celic
Spanish	Anticuerpo monoclonal IgG1 humano recombinante contra el ligando 1 de muerte programada	Tratamiento del carcinoma de células de Merkel
Swedish	Rekombinant human monoklonal IgG1-antikropp mot programmerad död ligand 1	Behandling av merkelcellskarcinom
Norwegian	Rekombinant humant monoklonalt IgG1-antistoff mot programmert dødsligand-1	Begandling av Merkelcellekarsinom
Icelandic	Raðbrigða manna einstofna IgG1 mótefni gegn forrituðu einstofna frumudauðapróteini-1	Meðferð við Merkel frumu krabbameini