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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Live attenuated *Listeria monocytogenes* delta *actA*/delta *inlB* strain expressing human mesothelin for the treatment of pancreatic cancer

On 11 January 2016, orphan designation (EU/3/15/1603) was granted by the European Commission to Medpace Germany GmbH, Germany, for live attenuated *Listeria monocytogenes* delta *actA*/delta *inlB* strain expressing human mesothelin (also known as CRS-207) for the treatment of pancreatic cancer.

What is pancreatic cancer?

Pancreatic cancer is cancer of the pancreas, a small organ that lies behind the stomach. The pancreas has two functions: to produce a fluid that helps with the digestion of food, and to produce hormones such as insulin. Due to the absence of symptoms in the early stages of pancreatic cancer, the majority of patients are diagnosed when the cancer has spread nearby or to other parts of the body.

Pancreatic cancer is a very severe and life-threatening disease that is associated with shortened life expectancy.

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

At the time of designation, pancreatic cancer affected less than 2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 103,000 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 authorised in the EU for treating pancreatic cancer. The choice of treatment depended on several factors, including how far the disease had advanced. Treatments included surgery, radiotherapy (treatment with radiation) and 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 512,900,000 (Eurostat 2015).



The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with pancreatic cancer because early results suggest that it may improve survival of patients whose disease had not responded to previous therapy, when given as part of a combination treatment. 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 works by stimulating the patient's immune system, the body's natural defences, so that it targets and destroys the cancer cells. It is made of *Listeria monocytogenes* bacteria, which have been attenuated (weakened) so that they do not cause disease in humans. The bacteria have also been modified to produce mesothelin. Mesothelin is found at high levels on many types of cancer cells, including pancreatic cancer cells.

When the medicine is injected into the body, the patient's immune system learns to treat mesothelin as 'foreign' and is expected to destroy pancreatic cancer cells carrying mesothelin on their surface.

The medicine is given as part of a combination treatment including another medicine (called 'two allogeneic irradiated pancreatic tumour cell lines' or GVAX) which is also expected to stimulate the immune system to recognise pancreatic cancer cells as foreign and so causes the body to attack the cancer.

What is the stage of development of this medicine?

The effects of this 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 pancreatic cancer were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for pancreatic cancer. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 December 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	Live attenuated <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> strain expressing human mesothelin	Treatment of pancreatic cancer
Bulgarian	Жив атенюиран щам delta <i>actA</i> /delta <i>inlB</i> на <i>Listeria monocytogenes</i> , експресиращ човешки мезотелин	Лечение на рак на панкреаса
Croatian	Živi atenuirani soj bakterije <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> koji ekspirira ljudski mezotelin	Liječenje raka gušterače
Czech	Živý atenuovaný <i>Listeria monocytogenes</i> kmen delta <i>actA</i> /delta <i>inlB</i> exprimující lidský mezotelin	Léčba karcinomu pankreatu
Danish	Levende, attenueret <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> -stamme, der udtrykker humant mesothelin	Behandling af pancreascancer
Dutch	Levend geattenueerde <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> stam met expressie van humaan mesotheel	Behandeling van pancreaskanker
Estonian	<i>Listeria monocytogenes</i> 'e delta- <i>actA</i> / delta- <i>inlB</i> nõrgestatud elustüvi, mis ekspresseerib inimese mesoteliini	Pankreasevähi ravi
Finnish	Elävä heikennetty <i>Listeria monocytogenes</i> delta <i>actA</i> -/delta <i>inlB</i> -kanta, jossa ekspressoituu ihmisen mesoteliini	Haimasyövän hoito
French	Souche vivante atténuée de <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> exprimant la mésothéline humaine	Traitement du cancer pancréatique
German	Humanes Mesothelin exprimierender, attenuierter Delta- <i>actA</i> /Delta- <i>inlB</i> -Lebendstamm von <i>Listeria monocytogenes</i>	Behandlung des Pankreaskarzinoms
Greek	Ζωντανό εξασθενημένο στέλεχος <i>Listeria monocytogenes</i> δέλτα <i>actA</i> /δέλτα <i>inlB</i> που εκφράζει ανθρώπινη μεσοθηλίνη	Θεραπεία καρκίνου του παγκρέατος
Hungarian	Humán mezotelint expresszáló élő, attenuált <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> törzs	Hasnyálmirigyrák kezelése
Italian	Ceppo vivo attenuato delta <i>actA</i> /delta <i>inlB</i> di <i>Listeria monocytogenes</i> che esprime la mesotelina umana	Trattamento del cancro pancreatico
Latvian	Dzīvu, novājinātu <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> celms, kas ekspresē cilvēka mezotelīnu	Aizkuģa dziedzera vēža ārstēšana
Lithuanian	Gyva, susilpninta <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> padermė, turinti žmogaus mezoteliną	Kasos vėžio gydymas
Maltese	Razza ta' <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> ħajja attenwata li tesprimi mesothelin uman	Kura tal-kanċer tal-frixa
Polish	Żywy atenuowany szczep delta <i>actA</i> /delta <i>inlB</i> <i>Listeria monocytogenes</i> ekspresujący ludzką mezotelinę	Leczenie raka trzustki

¹ At the time of designation

Language	Active ingredient	Indication
Portuguese	Estirpe delta <i>actA</i> /delta <i>inlB</i> de <i>Listeria monocytogenes</i> viva atenuada que expressa a mesotelina humana	Tratamento do carcinoma do pâncreas
Romanian	Tulpină vie atenuată de <i>Listeria monocytogenes</i> delta <i>actA</i> / delta <i>inlB</i> care exprimă mezotelina umană	Tratamentul cancerului pancreatic
Slovak	Živý oslabený kmeň <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> exprimujúci ľudský mezotelín	Liečba rakoviny pankreasu
Slovenian	Živ oslavljeni sev <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> , ki izraža humani mezotelin	Zdravljenje raka trebušne slinavke
Spanish	<i>Listeria monocytogenes</i> viva atenuada cepa delta <i>actA</i> /delta <i>inlB</i> que expresa la mesotelina humana	Tratamiento del cáncer de páncreas
Swedish	Levande attenuerad <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> som uttrycker humant mesotelin	Behandling av pankreascancer
Norwegian	Levende svekket <i>Listeria monocytogenes</i> delta <i>actA</i> - /delta <i>inlB</i> -stamme som utskiller humant mesotelin	Behandling av pankreascancer
Icelandic	Lifandi veiklaður <i>Listeria monocytogenes</i> delta <i>actA</i> /delta <i>inlB</i> stofn sem tjáir manna mesótélín	Meðferð briskrabbameins