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EMA/COMP/778963/2015
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 treatment of malignant mesothelioma



On 14 December 2015, orphan designation (EU/3/15/1594) was granted by the European Commission to Medpace Germany GmbH, Germany, for live attenuated *Listeria monocytogenes* delta actA/delta inlB strain expressing human mesothelin for treatment of malignant mesothelioma.

## What is malignant mesothelioma?

Malignant mesothelioma is a cancer that affects the mesothelial cells (found on the inner linings of the organs), mainly in the pleura (the lining of the lungs) and in the peritoneum (the lining of the abdominal cavity). It is usually caused by exposure to asbestos. Mesothelioma of the pleura causes difficulty breathing and chest pain, and mesothelioma of the peritoneum causes ascites (a build-up of fluid in the abdomen) and abdominal pain.

Malignant mesothelioma is life-threatening because it may lead to heart or breathing problems, lung infections and bowel obstruction. Patients have very poor survival, only living for a year, on average, after diagnosis.

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

At the time of designation, malignant mesothelioma affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 26,000 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 treatment for malignant mesothelioma was surgery followed by chemotherapy (medicines to treat cancer) or radiotherapy (treatment with radiation). If the disease

*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).

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was too advanced for surgery, chemotherapy alone was used. Only one medicine, pemetrexed, was specifically authorised in the EU for the treatment of malignant pleural mesothelioma.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with malignant mesothelioma because early clinical studies showed that it might improve the outcome of patients with this condition when added to standard treatment for malignant mesothelioma. 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 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 large amounts of the mesothelin protein. Mesothelin is found at high levels on many types of cancer cells, including mesothelioma cells.

When the medicine is given, the patient's immune system is expected to learn to treat mesothelin as 'foreign'. This is expected to stimulate an immune response against the mesothelioma cells carrying mesothelin on their surface, resulting in the immune system attacking and destroying the cancer cells.

## 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 malignant mesothelioma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for malignant mesothelioma. Orphan designation of the medicine had been granted in the United States for mesothelioma.

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.

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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 | Live attenuated *Listeria monocytogenes* delta *actA*/delta *inlB* strain expressing human mesothelin | Treatment of malignant mesothelioma |
| Bulgarian | Жив атенюиран щам delta *actA*/delta *inlB* на *Listeria monocytogenes,* експресиращ човешки мезотелин | Лечение на малигнен мезотелиом |
| Croatian | Živi atenuirani soj bakterije *Listeria monocytogenes* delta *actA*/delta *inlB* koji eksprimira ljudski mezotelin | Liječenje malignog mezotelioma |
| Czech | Živý atenuovaný *Listeria monocytogenes* kmen delta *actA*/delta *inlB* exprimující lidský mezotelin | Léčba maligního mezoteliomu |
| Danish | Levende, attenueret *Listeria monocytogenes* delta *actA*/delta *inlB*-stamme, der udtrykker humant mesothelin | Behandling af malignt mesotheliom |
| Dutch | Levend geattenueerde *Listeria monocytogenes* delta *actA*/delta *inlB* stam met expressie van humaan mesotheel | Behandeling van maligne mesothelioom |
| Estonian | *Listeria monocytogenes*'e delta-*actA* / delta-*inlB* nõrgestatud elustüvi, mis ekspresseerib inimese mesoteliini | Pahaloomulise mesotelioomi ravi |
| Finnish | Elävä heikennetty *Listeria monocytogenes* delta *actA*-/delta *inlB*-kanta, jossa ekspressoituu ihmisen mesoteliini | Malignin mesotelioman hoito |
| French | Souche vivante atténuée de *Listeria monocytogenes* delta *actA*/delta *inlB* exprimant la mésothéline humaine | Traitement du mésothéliome malin |
| German | Humanes Mesothelin exprimierender, attenuierter Delta-*actA*/Delta-*inlB*-Lebendstamm von *Listeria monocytogenes* | Behandlung des malignen Mesothelioms |
| Greek | Ζωντανό εξασθενημένο στέλεχος *Listeria monocytogenes* δέλτα *actA*/δέλτα *inlB* που εκφράζει ανθρώπινη μεσοθηλίνη | Θεραπεία κακοήθους μεσοθηλιώματος |
| Hungarian | Humán mezotelint expresszáló élő, attenuált *Listeria monocytogenes* delta *actA*/delta *inlB* törzs | Rosszindulatú mesothelioma kezelése |
| Italian | Ceppo vivo attenuato delta *actA*/delta *inlB* di *Listeria monocytogenes* che esprime la mesotelina umana | Trattamento del mesotelioma maligno |
| Latvian | Dzīvu, novājinātu *Listeria monocytogenes* delta *actA*/delta *inlB* celms, kas ekspresē cilvēka mezotelīnu | Ļaundabīgas mezoteliomas ārstēšana |
| Lithuanian | Gyva, susilpninta *Listeria monocytogenes* delta *actA*/delta *inlB* padermė, turinti žmogaus mezoteliną | Piktybinės mezoteliomos gydymas |
| Maltese | Razza ta' *Listeria monocytogenes* delta *actA*/delta *inlB* ħajja attenwata li tesprimi mesothelin uman | Kura tal-mesoteljoma malinna |
| Polish | Żywy atenuowany szczep delta *actA*/delta *inlB Listeria monocytogenes* eksprymujący ludzką mezotelinę | Leczenie złośliwego międzybłoniaka |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Portuguese | Estirpe delta *actA*/delta *inlB* de *Listeria monocytogenes* viva atenuada que expressa a mesotelina humana | Tratamento do Mesotelioma maligno |
| Romanian | Tulpină vie atenuată de *Listeria monocytogenes* delta *actA*/ delta *inlB* care exprimă mezotelina umană | Tratamentul mezoteliomului malign |
| Slovak | Živý oslabený kmeň *Listeria monocytogenes* delta *actA*/delta *inlB* exprimujúci ľudský mezotelín | Liečba malígneho mezoteliómu |
| Slovenian | Živ oslabljeni sev *Listeria monocytogenes* delta *actA*/delta *inlB*, ki izraža humani mezotelin | Zdravljenje malignega mezotelioma |
| Spanish | *Listeria monocytogenes* viva atenuada cepa delta *actA*/delta *inlB* que expresa la mesotelina humana | Tratamiento del mesotelioma maligno |
| Swedish | Levande attenuerad *Listeria monocytogenes* delta *actA*/delta *inlB* som uttrycker humant mesotelin | Behandling av malignt mesoteliom |
| Norwegian | Levende svekket *Listeria monocytogenes* delta *actA*-/delta *inlB*-stamme som utskiller humant mesotelin | Behandling av malignt mesoteliom |
| Icelandic | Lifandi veiklaður *Listeria monocytogenes* delta *actA*/delta *inlB* stofn sem tjáir manna mesótelín | Meðferð við illkynja miðþekjuæxli |