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EMA/COMP/793173/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pegylated recombinant arginine deiminase for the treatment of malignant mesothelioma

On 15 January 2015, orphan designation (EU/3/14/1409) was granted by the European Commission to Designerx Europe Limited, United Kingdom, for pegylated recombinant arginine deiminase for the 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 bowel obstruction, heart or breathing problems and lung infections. 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 approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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 511,100,000 (Eurostat 2014).

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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 pegylated recombinant arginine deiminase 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 used with 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?

The medicine is made of an enzyme, arginine deiminase, which breaks down an aminoacid called arginine, a substance that is needed by cancer cells to grow. Cancer cells are unable to produce their own arginine and therefore they take it directly from the blood. When administered to patients with malignant mesothelioma, arginine deiminase breaks down the arginine present in the blood, and the cancer cells are thus deprived of their supply. As a consequence they cannot grow and eventually die.

The medicine is produced by a method known as 'recombinant DNA technology': the enzyme is made by bacteria into which a gene (DNA) has been introduced that makes them able to produce it. The enzyme has also been modified by a process called 'pegylation', meaning that it has been attached to a chemical called polyethylene glycol, which is expected to prolong the time needed to remove the medicine from the body.

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 11 December 2014 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:

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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	Pegylated recombinant arginine deiminase	Treatment of malignant mesothelioma
Bulgarian	Пегилирана рекомбинантна аргинин деиминаза	Лечение на малигнен мезотелиом
Croatian	Pegilirana rekombinantna arginindeiminaza	Liječenje malignog mezotelioma
Czech	Pegylovaná rekombinantní deimináza argininu	Léčba maligního mezoteliomu
Danish	Pegyleret rekombinant arginindeiminase	Behandling af malignt mesotheliom
Dutch	Gepegyleerd recombinant arginine deïminase	Behandeling van maligne mesothelioom
Estonian	Pegüleeritud rekombinantne arginiindeiminaas	Pahaloomulise mesotelioomi ravi
Finnish	Pegyloitu rekombinantti arginiinideiminaasi	Malignin mesotelioman hoito
French	Arginine désiminase recombinante pégylée	Traitement du mésothéliome malin
German	Pegylierte rekombinante Arginindeiminase	Behandlung des malignen Mesothelioms
Greek	Πεγκυλιωμένη ανασυνδυασμένη αποϊμινάση αργινίνης	Θεραπεία κακοήθους μεσοθηλιώματος
Hungarian	Pegilált rekombináns arginin deimináz	Rosszindulatú mesothelioma kezelése
Italian	Arginina deiminasi ricombinante pegilata	Trattamento del mesotelioma maligno
Latvian	Pegilēta rekombinantā arginīndeiminmāze	Ļaundabīgas mezoteliomas ārstēšana
Lithuanian	Pegiliuota rekombinantinė arginino deiminazė	Piktybinės mezoteliomos gydymas
Maltese	Arginine deiminase rikombinanti peġilat	Kura tal-mesoteljoma malinna
Polish	Pegylowana rekombinowana deiminaza argininowa	Leczenie złośliwego międzybłoniaka
Portuguese	Arginina desiminase recombinante peguilada	Tratamento do Mesotelioma maligno
Romanian	Arginin deiminază recombinantă pegilată	Tratamentul mezoteliomului malign
Slovak	Pegylovaná rekombinantná arginindeimináza	Liečba malígneho mezoteliómu
Slovenian	Pegilirana rekombinantna deiminaza arginina	Zdravljenje malignega mezotelioma
Spanish	Arginina deiminasa recombinante pegilado	Tratamiento del mesotelioma maligno
Swedish	Pegylerat rekombinant arginindeiminas	Behandling av malignt mesoteliom
Norwegian	Pegylert rekombinant arginindeiminase	Behandling av malignt mesoteliom
Icelandic	PEG-tengt raðbrigða arginíndeímínasi	Meðferð við illkynja miðþekjuæxli

[1] At the time of designation