8 March 2017
EMA/19916/2017
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Doxorubicin hydrochloride in a lipid-based pegylated nanoparticle modified with a 31-aminoacid peptide targeting nucleolin for the treatment of malignant mesothelioma

On 12 January 2017, orphan designation (EU/3/16/1814) was granted by the European Commission to TREAT U, S.A., Portugal, for doxorubicin hydrochloride in a lipid-based pegylated nanoparticle modified with a 31-aminoacid peptide targeting nucleolin 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 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 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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 treatments for malignant mesothelioma were surgery and chemotherapy (medicines to treat cancer) with or without radiotherapy (treatment with radiation). If

*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).

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the disease was too advanced for surgery, chemotherapy alone was used. One medicine, pemetrexed, was authorised throughout the EU for the treatment of malignant pleural mesothelioma. A second medicine, raltitrexed, was authorised for the treatment of malignant pleural mesothelioma in some European countries.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with malignant mesothelioma because laboratory studies indicate it may reduce growth of tumours resistant to existing treatments. 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?

Doxorubicin hydrochloride is a cancer medicine that has been used for many years. It is thought to work by interfering with the DNA within cells, preventing them from making more copies of DNA and making proteins. This means that cancer cells cannot divide and they eventually die.

In this medicine, doxorubicin hydrochloride is encapsulated within tiny fat-based particles (nanoparticles) which are attached to a peptide (a short chain of amino acids). This peptide targets a protein (nucleolin) found in high amounts in cancer cells, allowing the medicine to be delivered directly to 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, no clinical trials with the medicine in patients with malignant mesothelioma had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for malignant mesothelioma 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 8 December 2016 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	Doxorubicin hydrochloride in a lipid-based pegylated nanoparticle modified with a 31-aminoacid peptide targeting nucleolin	Treatment of malignant mesothelioma
Bulgarian	Доксорубицинов хидрохлорид в пегилирани наночастици с липидна основа, модифицирани с 31-аминокиселинен пептид насочен срещу нуклеолин	Лечение на малигнен мезотелиом
Croatian	Doksirubicin hidroklorid u pegiliranim nanočesticama na bazi lipida modificiran peptidom od 31 aminokiseline koji cilja nucleolin	Liječenje malignog mezotelioma
Czech	Doxorubicin hydrochlorid v pegylovaných nanočásticích lipidové báze modifikovaný 31-aminoacid peptidu cíleně se vázající na nukleolin	Léčba maligního mezoteliomu
Danish	Doxorubicinhydrochlorid i en lipid-baseret pegyleret nanopartikel modificeret med et 31-aminosyre peptid målrettet mod nucleolin	Behandling af malignt mesotheliom
Dutch	Doxorubicinehydrochloride in een lipide gebaseerd gepegyleerd nanodeeltje gemodificeerd met een 31-aminozuur peptide “targeting” nucleoline	Behandeling van maligne mesothelioom
Estonian	Doksorubitsiinvesinikkloriid, mis paikneb lipiidil baseeruval pegüleeritud nanoosakesel, mida on modifitseeritud nukleoliinile suunatud 31-aminohappe peptiidiga	Pahaloomulise mesotelioomi ravi
Finnish	Doksorubisiinihydrokloridia lipidipohjaisessa pegyloidussa nanopartikkelissa, jota on muokattu 31-aminohappo peptidillä, jonka kohteena on nucleolin	Malignin mesoteliooman hoito
French	Chlorhydrate de doxorubicine dans une nanoparticlue pégylée avec une base de lipides modifiée par un peptide de 31 acides aminés dirigée vers la nucléoline	Traitement du mésothéliome malin
German	Doxorubicin-Hydrochlorid in einem lipidbasierten pegylierten Nanopartikel, modifiziert mit einem Peptid von 31-Aminosäure gegen Nucleolin gerichtet	Behandlung des malignen Mesothelioms
Greek	Υδροχλωρική δοξορουβικίνη σε ένα πεγκυλιωμένο νανοσωματίδιο με βάση λιπιδίων, τροποποιημένο με ένα πεπτίδιο 31 αμινοξέων που στοχεύει τη νουκλεολίνη	Θεραπεία κακοήθους μεσοθηλιώματος
Hungarian	Nukleolint célzó 31 aminosavas peptiddel módosított lipid-bázisú pegilált nanorészecskébe zárt doxorubicin hidroklorid	Rosszindulatú mesothelioma kezelése
Italian	Doxorubicina cloridrato in una nanoparticella pegilata a base lipidica modificata con un peptide di 31 aminoacidi rivolto verso nucleolina	Trattamento del mesotelioma maligno

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Doksorubicīna hidrohlorīds lipīdu bāzes pegilētā nanodaļiņā, kas modificēta ar pret nukleolīnu vērstu 31-aminoskābes peptīdu	Ļaundabīgas mezoteliomas ārstēšana
Lithuanian	Doksorubicino hidrochloridas lipidų pagrindu pegiliuotose nanodalelėse, kurios modifikuotos su 31-os aminorūgšties peptidu, nukreiptu į nukleoliną	Piktybinės mezoteliomos gydymas
Maltese	Doxorubicin kloridrat f'nanopartikula pegilat bbażata fuq il-lipidi immodifikat b'peptide 31-amminoaċidu li jimmira nucleolin	Kura tal-mesoteljoma malinna
Polish	Chlorowodorek doksorubicyny w złożonej z lipidów pegylownej nanocząsteczce zmodyfikowanej 31-aminokwasowym peptydem ukierunkowanym na nukleolinę	Leczenie złośliwego międzybłoniaka
Portuguese	Cloridrato de doxorrubicina numa nanopartícula peguilada de base lipídica modificada com um peptídeo de 31 aminoácidos direcionada à nucleolina	Tratamento do Mesotelioma maligno
Romanian	Clorhidrat de doxorubicină într-o nanoparticulă pegilată pebază de lipide, modificată cu o peptidă de 31 de aminoacizi ce ţinteşte nucleolinul	Tratamentul mezoteliomului malign
Slovak	Doxorubicíniumchlorid v pegylovanej nanočastici na báze lipidu modifikovanej s 31-aminokyselinovým peptidom cieleným na nukleolín	Liečba malígneho mezoteliómu
Slovenian	Doksorubicinijev klorid, pegiliran v lipidnih nanodelcih in modificiran z 31-aminokislinskim peptidom za tarčni nukleolin	Zdravljenje malignega mezotelioma
Spanish	Hidrocloruro de doxorubicina en una nanopartícula pegilada lipídica modificada con un péptido de 31 aminoácidos dirigida a la nucleolina	Tratamiento del mesotelioma maligno
Swedish	Doxorubicinhydroklorid i en lipid-baserad pegylerat nanopartikel modifierad med en 31-aminosyra-peptid riktad mot nukleolin	Behandling av malignt mesoteliom
Norwegian	Doksorubicinhydroklorid i en lipidbasert pegylert nanopartikkel modifisert med etpeptid med 31 aminosyrer rettet mot nukleolin	Behandling av malignt mesoteliom
Icelandic	Doxórúbicín hýdróklóríðií fitubyggðu pegýleruðu nanóagnaþyrpingum breytt með 31amínósýru peptíði sem beinist gegnnúkleólíni	Meðferð við illkynja miðþekjuæxli