12 August 2015
EMA/COMP/272314/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Modified adenovirus serotype 5/35 containing a CMV promoter-driven transgene cassette with the human transgenes for a membrane-bound CD40 ligand and full length 4-1BBL for the treatment of pancreatic cancer

On 28 July 2015, orphan designation (EU/3/15/1516) was granted by the European Commission to Lokon Pharma AB, Sweden, for modified adenovirus serotype 5/35 containing a CMV promoter-driven transgene cassette with the human transgenes for a membrane-bound CD40 ligand and full length 4-1BBL for the treatment of pancreatic cancer.

What is pancreatic cancer?

Pancreatic cancer is cancer of the pancreas, an organ that lies behind the stomach. The pancreas has two functions: to produce a fluid that helps to digest 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.

*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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Treatments included surgery, radiotherapy (treatment with radiation) and chemotherapy (medicines to treat cancer).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with pancreatic cancer because experimental studies suggest that its use in combination with available treatments may lead to improved effects on cancer. 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 up of an 'oncolytic' virus, a virus that has been modified so that it can target, infect and destroy cancer cells, but not normal cells. When inside a cancer cell, the virus is expected to take over the cell's replication apparatus and use it to make more copies of itself. This is expected to kill the cell, leaving the virus to spread to neighbouring cancer cells. In addition, the modifications to the virus prepare the cell for self-destruction and cause infected cells to produce substances that stimulate the immune system (the body's natural defences), which will also help to destroy 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, no clinical trials with the medicine in patients with pancreatic cancer had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 June 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:

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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	Modified adenovirus serotype 5/35 containing a CMV promoter-driven transgene cassette with the human transgenes for a membrane-bound CD40 ligand and full length 4-1BBL	Treatment of pancreatic cancer
Bulgarian	Модифициран аденовирус серотип 5/35, съдържащ трансгенна касета с човешки трансгени за мембранно-свързан CD40 лиганд и пълноверижен 4-1BBL, активирана от CMV промотор	Лечение на рак на панкреаса
Croatian	Modificirani adenovirus serotipa 5/35 koji sadrži transgensku kazetu koja se sastoji od CMV promotora i ljudskih transgena koji kodiraju za membranski CD40 ligand i za 4-1BBL u punoj duljini	Liječenje raka gušterače
Czech	Modifikovaný adenovirový sérotyp 5/35 obsahující promotor CMV-řízený transgenovou kazetu s lidskými transgeny pro membránově vázaný CD40 ligand a plné délce 4-1BBL	Léčba karcinomu pankreatu
Danish	Modificeret adenovirus serotype 5/35 indeholdende en CMV-promotor-drevet transgen kassette med de humane transgener for en membranbundet CD40 ligand og fuld længde 4-1BBL	Behandling af pancreascancer
Dutch	Gemodificeerd adenovirus, serotype 5/35, welke een CMV-promotor gedreven transgene cassette bevat met de humane transgenen voor een membraangebonden CD40-ligand en de volledige lengte 4-1BBL	Behandeling van pancreaskanker
Estonian	Modifitseeritud adenoviiruse serotüüp 5/35, mis sisaldab CMV-promootorjuhitava transgeeni kassetti membraaniga seonduva CD40 ligandi inimese transgeenidest ja täispikkusest 4-1BBL	Pankreasevähi ravi
Finnish	Modifioitu serotyypin 5/35 adenovirus, joka sisältää CMV-promoottoriin perustuvan siirtogeenikasetin, jossa ovat ihmisen siirtogeenit solukalvoon sitoutuvalle CD40-ligandille ja täyspitkälle 4-1BBL:lle	Haimasyövän hoito
French	Adénovirus modifié de sérotype 5/35 contenant une cassette de transgène déterminée par un promoteur CMV, avec les transgènes humains pour un ligand de CD40 lié à la membrane et pleine longueur 4-1BBL	Traitement du cancer pancréatique

[1] At the time of designation

Language	Active ingredient	Indication
German	Modifiziertes Adenovirus-Serotyp 5/35, welches eine CMV-Promotor kontrollierte Transgen-Kassette enthält, bestehend aus menschlichen Transgenen für den membrangebundenen CD40-Liganden und für 4-1BBL in voller Länge	Behandlung des Pankreaskarzinoms
Greek	Τροποποιημένος αδενοϊος οροτύπου 5/35 που περιέχει μία γονιδιακή κασέτα υπό τον έλεγχο ενός προαγωγέα CMV, με τα ανθρώπινα διαγονιδια για έναν CD40 συνδέτη που προσδένεται στη μεμβράνη, και για την πλήρους μήκους πρωτεϊνη 4-1BB1	Θεραπεία καρκίνου του παγκρέατος
Hungarian	Módosított adenovírus szerotípus 5/35 amely egy CMV-promóter által irányított transzgén kazettát tartalmaz az emberi transzgénekkel egy membránhoz kötött CD40-ligandumhoz és teljes hosszúságú 4-1BBLhez	Hasnyálmirigyrák kezelése
Italian	Adenovirus modificato di serotipo 5/35, con un promotore CMV che regola una cassetta umana transgenica contenente un ligando CD40 legato alla membrana e la sequenza intera di 4-1BBL	Trattamento del cancro pancreatico
Latvian	Modificēts adenovīrusa 5/35 serotips, kas satur CMV promotera kontrolētu transgēnu kaseti ar cilvēka transgēniem membrānu saistam CD40 ligandam un pilna garuma 4-1BBL	Aizkuņģa dziedzera vēža ārstēšana
Lithuanian	Modifikuotas adenoviruso 5/35 serotipas, turintis CMV promotoriaus valdomą transgeninę kasetę su žmogaus prie membranos prijungto CD40 ligando ir viso ilgio 4-1BBL transgenais	Kasos vėžio gydymas
Maltese	Serotip 5/35 tal-adenovirus modifikat li fih cassette b'transġene ta' CMV mmexxi minn promotur ma' transġeni umani għal ligand CD40 marbut mal-membrana u 4-1BBL komplut	Kura tal-kanċer tal-frixa
Polish	Zmodyfikowany adenowirus serotypu 5/35 zawierający kasetę ekspresyjną, gdzie promotor CMV kontroluje dwa trangeny, związany z błoną komórkową ligand CD40 oraz pełnej długości 4-1BBL	Leczenie raka trzustki
Portuguese	Adenovírus serótipo 5/35 modificado contendo uma cassete de transgene conduzido pelo promotor de CMV com os transgenes humanos de um ligando de CD40 ligada à membrana e comprimento total 4-1BBL	Tratamento do carcinoma do pâncreas
Romanian	Adenovirus modificat de serotip 5/35 cu ce conţine o casetă transgenică controlată de un promotor CMV, alcătuită din transgenele umane pentru ligandul CD40 legat de membrană și pentru 4-1BBL de lungime completă	Tratamentul cancerului pancreatic

Language	Active ingredient	Indication
Slovak	Modifikovaný adenovirový sérotyp 5/35 obsahujúci transgénu kazetu, kde promótor CMV kontroluje ľudské transgénes membránovo viazané CD40 ligandy v plnej dĺžke 4-1BBL	Liečba rakoviny pankreasu
Slovenian	Modificiran adenovirus serotipa 5/35, ki vsebuje s CMV-promotorjem kontrolirano kaseto s človeškimi transgeni za membransko vezan ligand CD40 in 4-1BBL v celotnoj dolžini	Zdravljenje raka trebušne slinavke
Spanish	Adenovirus modificado del serotipo 5/35, con un promotor CMV que regula un cassette transgénico con los transgenes humanos de un ligando de CD40 unido a membrana y del 4-1BBL completo	Tratamiento del cáncer de páncreas
Swedish	Modifierat adenovirus serotyp 5/35 innehållande en CMV promotor-driven transgenkassett med de humana transgenerna för en membranbunden CD40-ligand och full längd 4-1BBL	Behandling av pankreascancer
Norwegian	Modifisert adenovirus serotype 5/35 som inneholder en CMV promotor-drevet transgenkassett med de humane transgenene for et membranbundet CD40 ligand og full lengde 4-1BBL	Behandling av pankreascancer
Icelandic	Breytt adenóveira sermisgerð 5/35 sem inniheldur CMV stýrisvæðaþætti víxlgena snældu með mennskum erfðabreytum fyrir himnu-bundið CD40 tengil og fulla lengd 4-1BBL	Meðferð briskrabbameins