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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector containing human alpha-1 antitripsin gene for the treatment of congenital alpha-1 antitrypsin deficiency

On 20 March 2007, orphan designation (EU/3/07/440) was granted by the European Commission to The Matthews Consultancy Ltd, United Kingdom, for recombinant adeno-associated viral vector containing human alpha-1 antitrypsin gene for the treatment of congenital alpha-1 antitrypsin deficiency.

The Matthews Consultancy Ltd changed its name to TMC Pharma Services Ltd in October 2009.

What is congenital alpha-1 antitrypsin deficiency?

Congenital alpha-1 antitrypsin deficiency is an inherited disease characterised by reduced levels in the blood of the substance alpha-1 antitrypsin (AAT). This substance is a protein that is normally made by the liver and reaches other organs (such as the lungs) after being released into the blood circulation. AAT inactivates some substances, such as elastase, normally produced by the body. The action of elastase is to destroy certain molecules that form the lung tissue. If AAT is missing then the action of elastase is no longer opposed. In the long term, this may damage the lungs and cause a lung disease where air is abnormally accumulated in the lungs. Lung disease due to AAT deficiency is often called "hereditary emphysema" or emphysema secondary to congenital AAT deficiency. The condition is chronically debilitating and life-threatening.

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

At the time of designation, congenital AAT deficiency affected approximately 2.5 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 115,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

*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 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

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What treatments are available?

Therapy for lung disease due to AAT deficiency includes the use of medicines to help breathing, or to help to clear mucus (phlegm) from the lungs. The frequent lung infections seen in this disorder require treatment with antibiotics. Oxygen may also be given in the more advanced stages; lung transplantation may be used in the most severe cases. Human alpha-1 antitrypsin, to be administered intravenously, is authorised for replacement therapy of this condition.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that "recombinant adeno-associated viral vector containing human alpha-1 antitripsin gene" might be of potential significant benefit for the treatment of emphysema secondary to congenital AAT deficiency, because it might represent a significant contribution to patient care. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

"Recombinant adeno-associated viral vector containing human alpha-1 antitripsin gene" is a medicinal product which uses a virus to carry the gene necessary for the production of the AAT protein. A virus is a small organism capable of introducing genetic material in cells. The type of virus (adeno-associated virus) used in this medicinal product is modified in order to avoid causing any disease in humans. The administration of the virus containing the human AAT gene is expected to increase the concentration of AAT. In this way AAT would be able to oppose the effects of elastase. This action is expected to slow down or stop the worsening of the lung disease.

What is the stage of development of this medicine?

The effects of recombinant adeno-associated viral vector containing human alpha-1 antitripsin gene were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with in patients with congenital AAT deficiency were ongoing.

Recombinant adeno-associated viral vector containing human alpha-1 antitripsin gene was not authorised anywhere in the world for emphysema secondary to congenital AAT deficiency or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 February 2007 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

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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	Recombinant adeno-associated viral vector containing human acid alpha-glucosidase-gene	Treatment of glycogen storage disease type II (Pompe's disease)
Bulgarian	Рекомбинантен аденоасоцииран вирусен вектор, съдържащ ген на човешка киселинна алфа – глюкозидаза	Лечение на гликогеноза тип II (Болест на Помпе)
Czech	Rekombinantní adeno-asociovaný virový vektor obsahující lidský gen pro kyselou alfa-glukosidázu	Léčba glykogen střádavé choroby typu II (Pompeho choroba)
Danish	Rekombinant adeno-associeret virusvektor indeholdende humant, sur alpha-glucosidase gen	Behandling af glycogenoplagringslidelse type II (Pompe's sygdom)
Dutch	Recombinant adeno- geassocieerde virale vector welke het humaan zure alfa-glucosidase-gen bevat	Behandeling van de glycogeenstapelingsziekte type II (Pompe-ziekte)
Estonian	Inimese happelise alfa-glükosidaasi geeni sisaldav rekombinantne adeno-assotsieerunud viirusvektor	Glükogenoos II (Pompe tõve) ravi
Finnish	Rekombinantti adenoassosioitu virusvektori, joka sisältää alfa-glukosidaasi-geenin	Tyyppi II glykogenoosin (Pompen tauti)hoito
French	Vecteur viral recombinant associé à l'adénovirus contenant le gène humainde la glucosidase alpha acide	Traitement de la glycogénose de type II (maladie de Pompe)
German	Rekombinant hergestellter, adeno-assoziierter Virenvektor, der das humane saure Alpha-Glucosidase-Gen enthält	Behandlung der Glykogenspeicherkrankheit Typ II (Pompe-Krankheit)
Greek	Ανασυνδυασμένο αδενικό ιογενές άνυσμα περιέχον ανθρώπινο οξύ άλφα-γλουκολιτικό γονίδιο	Θεραπεία της Γλυκογόνωσης τύπου II (Νόσος του Pompe)
Hungarian	Humán savas alfa-glukozidáz gént tartalmazó rekombináns adeno-vírus vektor	II.-es típusú glycogentárolási betegség kezelése (Pompe-kór)
Italian	Vettore virale ricombinante adeno-associato, contenente il gene dell'alfa-glucosidasi acida umana	Trattamento della glicogenosi, tipo II (malattia di Pompe)
Latvian	Rekombinants adeno saistīts vīrusa vectors, kas satur cilvēka skābās alfa-glikozidāzes gēnu	2 tipa glikogēna uzkrāšanās slimības (Pompes slimība) ārstēšana

[1] At the time of designation

Language	Active Ingredient	Indication
Lithuanian	Rekombinantinis adeno – asocijuotas virusinis vektorius, pernešantis žmogaus rūgščiosios alfa gliukozidazės geną	II tipo glikogenozės (Pompe ligos) gydymas
Maltese	Vektor virali rikombinanti adeno-assoċjat li għandu l-ġene ta' l-aċidu alpha-glucosidase uman	Kura tal-glikoġenożi tat-tip II (marda ta' Pompe)
Polish	Rekombinowanywektor adenowirusowy zawierający ludzki enzym zwany kwasem alfa – glukoidalnym	Leczenie choroby spichrzeniowej glukogenu typu II (choroby Pompego)
Portuguese	Vector de adenovirus recombinante que contem o gene humano da alfa-glicosidase ácida	Tratamento da glicogenose de tipo II (Doença de Pompe)
Romanian	Vector viral adeno-asociat recombinant care conţine gena umană a acid alfa glucozidazei	Tratamentul glicogenozei de tip II (Boala lui Pompe)
Slovak	Rekombinantný adeno-asociovaný vírusový vektor obsahujúci ľudský gén pre kyslú alfa-glukozidázu	Liečba glykogenózy typu II (Pompeho choroba)
Slovenian	Rekombinantni adenovirusni vektor ki vsebuje gen humane kisle alfa-glikozidaze	Zdravljenje bolezni kopičenja glikogena tip II (Pompejeva bolezen)
Spanish	Vector vírico adenoasociado recombinante que contiene el gen humano de la alfa-glucosidasa ácida	Tratamiento de la enfermedad de almacenamiento del glucógeno tipo II (enfermedad de Pompe)
Swedish	Rekombinant adenassocierad virusvektor som innehåller humana-alfa-glukosidas-genen	Behandling av glykogen upplagringssjukdom typ II (Pompes sjukdom)
Norwegian	Rekombinant adenoassosiert virusvektor som inneholder humant alfaglukosidase-gen	Behandling av glykogenose type II (Pompes sykdom)
Icelandic	Raðbrigða adenó-tengd veiruferja sem inniheldur manna súrt alfa-glúkósídasa gen	Meðferð við glýkógen upphleðslusjúkdómi af gerð II (Pompe sjúkdómur)