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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 8 containing the human *MD1* gene for treatment of Duchenne muscular dystrophy

On 19 November 2014, orphan designation (EU/3/14/1381) was granted by the European Commission to Généthon, France, for adeno-associated viral vector serotype 8 containing the human *MD1* gene for treatment of Duchenne muscular dystrophy.

What is Duchenne muscular dystrophy?

Duchenne muscular dystrophy (DMD) is a genetic disease that gradually causes weakness and atrophy (wasting) of the muscles. It mainly affects boys, and usually starts before the age of six years. The muscle weakness usually starts in the hips and legs, before affecting the arms, chest and the heart. Patients with DMD lack normal dystrophin, a protein found in muscles. Because this protein helps to protect muscles from injury as muscles contract and relax, in patients with DMD the muscles become weaker and eventually stop working.

DMD causes long-term disability and is life threatening because of its effects on the heart and the respiratory muscles (muscles that are used to breathe). The disease usually leads to death in adolescence or early adulthood.

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

At the time of designation, DMD affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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, one medicine, Translarna, had been authorised in the EU for treating DMD in patients with a specific genetic defect (called a 'nonsense mutation') in the dystrophin gene. The

[*]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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

sponsor has provided sufficient information to show that adeno-associated viral vector serotype 8 containing the human *MD1* gene might be of significant benefit for patients with DMD because it works in a different way to Translarna and has the potential to treat patients irrespective of the type of mutation they have in their dystrophin gene.

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?

In DMD, the lack of dystrophin is caused by an abnormality in the gene responsible for the protein's production. This medicine is made of a virus that contains a gene called human *MD1*, a shortened version of the normal dystrophin gene designed to replace the defective one, and is specifically intended to work in tissues lacking dystrophin. When given to the patient, the virus is expected to carry the gene into the cells of the relevant tissues, where it will allow a working version of dystrophin to be produced.

This type of treatment is known as gene replacement therapy and the type of virus used in this medicine ('adeno-associated virus') does not cause disease in humans.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of adeno-associated viral vector serotype 8 containing the human MD1 gene in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with DMD had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for DMD 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 9 October 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:

Généthon
1 bis rue de l'Internationale
91000 Evry
France
Tel. +33 1 69 47 29 17
Fax +33 1 69 47 19 46
E-mail: clinical_development@genethon.fr

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	Adeno-associated viral vector serotype 8 containing the human *MD1* gene	Treatment of Duchenne muscular dystrophy
Bulgarian	аденосвързан вирусен вектор серотип 8, съдържащ човешки *MD1* ген	Лечение на мускулна дистрофия на Duchenne
Croatian	Adeno-povezani virusni vektor serotipa 8 koji sadrži ljudski gen *MD1*	Liječenje Duchenneove mišićne distrofije
Czech	Sérotyp 8 adeno asociovaný virový vektor, obsahující lidský gen *MD1*	Léčba pacientů s Duchennovou muskulární dystrofií
Danish	Adenoassocieret viral vektor serotype 8 indeholdende det humane *MD1* gen	Behandling af Duchenne muskeldystrofi
Dutch	Adenogeassocieerde virale vector, serotype 8, welke het humane gen *MD1* bevat	Behandeling van Duchenne spierdystrofie
Estonian	Adenoga assotsieeruv viirusvektori serotüüp 8, mis sisaldab inimese *MD1* geeni	Duchenne'i lihasdüstroofia ravi
Finnish	Adenoassosioitu virusvektori, serotyyppiä 8, joka sisältää ihmisen *MD1* geenin	Duchennen lihasdystrofian hoito
French	Vecteur viral adéno-associé de sérotype 8 contenant le gène humain *MD1*	Traitement de la dystrophie musculaire de Duchenne
German	Das humane *MD1* Gen beinhaltender, adeno-assoziierter viraler Vektor Serotyp 8	Behandlung der Duchenne-Muskeldystrophie
Greek	Αδενο-σχετιζόμενος ιικός φορέας ορότυπου 8 που περιέχει το ανθρώπινο γονίδιο *MD1*	Θεραπεία της μυϊκής δυστροφίας Duchenne
Hungarian	Humán *MD1* gént tartalmazó 8-as szerotípusú adeno-asszociált vírus vector	Duchenne dystrophia kezelése
Italian	Vettore virale adeno-associato del serotipo 8 contenente il gene umano *MD1*	Trattamento della distrofia muscolare di tipo Duchenne
Latvian	Adeno-saistītā vīrālā vektora 8. serotips, kas satur cilvēka *MD1* gēnu	Dišēna muskuļu distrofijas ārstēšana
Lithuanian	Adeno-asocijuotas viruso vektoriaus 8 serotipas, pernešantis žmogaus *MD1* geną	Duchenne (Diušeno) raumenų distrofijos gydymas
Maltese	Vettur imnissel mill-adenovirus tas-serotip 8 li fih il-ġene uman *MD1*	Kura tad-distrofija muskolari tat-tip Duchenne
Polish	Wektor adenowirusowy serotypu 8 zawierający ludzki gen *MD1*	Leczenie zaniku mięśni typu Duchenne'a
Portuguese	Vector viral adeno-associado de serotipo 8 contendo o gene humano *MD1*	Tratamento da distrofia muscular de Duchenne
Romanian	Vector viral adeno-asociat de serotip 8 conţinând gena umană *MD1*	Tratamentul distrofiei musculare Duchenne
Slovak	Adeno-asociovaný vírusový vektor sérotypu 8 obsahujúci l'udský gén *MD1*	Liečba Duchennovej muskulárnej dystrofie

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Adeno-pridruženi virusni vektor serotipa 8, ki vsebuje človeški gen *MD1*	Zdravljenje Duchennove mišične distrofije
Spanish	Vector viral adenoasociado del serotipo 8 que conteniene el gene humano *MD1*	Tratamiento de la distrofia muscular de Duchenne
Swedish	Adenoassocierad virusvektor serotyp 8, innehållande den mänskliga genen *MD1*	Behandling av Duchennes muskeldystrofi
Norwegian	Adenoassosiert virusvektor serotype 8 som inneholder det humane genet *MD1*	Behandling av Duchennes muskeldystrofi
Icelandic	Adenótengd veiruferja af sermisgerð 8 sem inniheldur manna *MD1* gen	Meðferð á Duchenne vöðvarýrnun