30 September 2015
EMA/COMP/500586/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 8 containing the human *MTM1* gene for the treatment of X-linked myotubular myopathy

On 10 August 2015, orphan designation (EU/3/15/1539) was granted by the European Commission to Audentes Therapeutics UK Limited, United Kingdom, for adeno-associated viral vector serotype 8 containing the human *MTM1* gene for the treatment of X-linked myotubular myopathy.

What is X-linked myotubular myopathy?

X-linked myotubular myopathy is an inherited condition in which there are abnormalities in the structure and function of muscle cells due to mutations (changes) in the gene responsible for producing the protein myotubularin. This gene, *MTM1*, is located on the X chromosome and the condition affects boys almost exclusively, since girls have a second X chromosome and a second copy of the gene. Patients are generally born with severe muscle weakness, including weakness of the muscles needed to breathe, and they are unable to breathe normally without mechanical assistance.

The condition is severely debilitating and life threatening due to the muscle weakness and impaired breathing, and most patients die within two years of birth.

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

At the time of designation, X-linked myotubular myopathy affected approximately 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of around 1,000 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?

No satisfactory methods of treatment were authorised in the EU at the time of application. Patients received supportive treatment, including mechanical assistance with breathing.

[*]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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How is this medicine expected to work?

The medicine is made of a virus that contains normal copies of the *MTM1* gene which is responsible for producing the myotubularin protein. When injected into the patient it is expected that the virus will carry the gene into muscle cells, enabling the cells to produce the missing protein. This is expected to allow the muscles to develop and function normally, relieving the symptoms of the condition.

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?

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 this medicine in patients with X-linked myotubular myopathy had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for X-linked myotubular myopathy. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 July 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	Adeno-associated viral vector serotype 8 containing the human *MTM1* gene	Treatment of X-linked myotubular myopathy
Bulgarian	Аденосвързан вирусен вектор серотип 8, съдържащ човешкия *MTM1* ген	Лечение на Х-свързана миотубуларна миопатия
Croatian	Adeno-povezani virusni vektor serotipa 8 koji sadrži ljudski gen *MTM1*	Liječenje X-vezane miotubularne miopatije
Czech	Sérotyp 8 adeno asociovaný virový vektor, obsahující lidský gen *MTM1*	Léčba X-vázané myotubulární myopatie
Danish	Adenoassocieret viral vektor serotype 8 indeholdende det humane *MTM1* gen	Behandling af X-bundet myotubulær myopati
Dutch	Adenogeassocieerde virale vector, serotype 8, welke het humane gen *MTM1* bevat	Behandeling van X-gebonden myotubulaire myopathie
Estonian	Adenoga assotsieeruv viirusvektori serotüüp 8, mis sisaldab inimese *MTM1* geeni	X-liitelise müotubulaarse müopaatia ravi
Finnish	Adenoassosioitu virusvektori, serotyyppiä 8, joka sisältää ihmisen *MTM1* geenin	X-kromosomiin liittyvän synnynnäisen myotubulaarisen lihassairauden hoito
French	Vecteur viral adéno-associé de sérotype 8 contenant le gène humain *MTM1*	Traitement de la myopathie myotubulaire liée à l'X
German	Das humane *MTM1* Gen beinhaltender, adeno-assoziierter viraler Vektor Serotyp 8	Behandlung der X-chromosomalen myotubulären Myopathie
Greek	Αδενο-σχετιζόμενος ιικός φορέας ορότυπου 8 που περιέχει το ανθρώπινο γονίδιο *MTM1*	Θεραπεία της φυλοσύνδετης μυοσωληναριακής μυοπάθειας
Hungarian	Humán *MTM1* gént tartalmazó 8-as szerotípusú adeno-asszociált vírus vector	Az X-hez kötött myotubularis myopathia kezelése
Italian	Vettore virale adeno-associato del serotipo 8 contenente il gene umano *MTM1*	Trattamento della miopatia miotubulare legata al cromosoma X
Latvian	Adeno-saistītā virālā vektora 8. serotips, kas satur cilvēka *MTM1* gēnu	Ar X hromosomu saistītās miotubulārās miopātijas ārstēšana
Lithuanian	Adeno-asocijuotas viruso vektoriaus 8 serotipas, pernešantis žmogaus *MTM1* geną	Su X chromosoma susijusios miotubulinės miopatijos gydymas
Maltese	Vettur imnissel mill-adenovirus tas-serotip 8 li fih il-ġene uman *MTM1*	Kura tal-mijopatija mijotubulari marbuta mal-kromosoma X
Polish	Wektor adenowirusowy serotypu 8 zawierający ludzki gen *MTM1*	Leczenie miopatii miotubularnej związanej z chromosomem X
Portuguese	Vector viral adeno-associado de serotipo 8 contendo o gene humano *MTM1*	Tratamento da miopatia miotubular ligada ao cromossoma X
Romanian	Vector viral adeno-asociat de serotip 8 conţinând gena umană *MTM1*	Tratamentul miopatiei miotubulare X-linkate
Slovak	Adeno-asociovaný vírusový vektor sérotypu 8 obsahujúci l'udský gén *MTM1*	Liečba X-viazanej myotubulárnej myopatie

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Adeno-pridruženi virusni vektor serotipa 8, ki vsebuje človeški gen *MTM1*	Zdravljenje na kromosom X vezane miotubularne miopatije
Spanish	Vector viral adenoasociado del serotipo 8 que conteniene el gene humano *MTM1*	Tratamiento de la miopatía miotubular ligada al cromosoma X
Swedish	Adenoassocierad virusvektor serotyp 8, innehållande den mänskliga genen *MTM1*	Behandling av X-bunden myotubulär myopati
Norwegian	Adenoassosiert virusvektor serotype 8 som inneholder det humane genet *MTM1*	Behandling av X-bundet myotubulær myopati
Icelandic	Adenótengd veiruferja af sermisgerð 8 sem inniheldur manna *MTM1* gen	Meðferð við X-tengdum vöðvakvilla í vöðvapíplum