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Public summary of opinion on orphan designation

Synthetic antisense oligonucleotide directed against human dystrophin pre-mRNA for treatment of Duchenne muscular dystrophy

On 31 July 2018, orphan designation (EU/3/18/2051) was granted by the European Commission to Wave life Sciences Ireland Limited, Ireland, for synthetic antisense oligonucleotide directed against human dystrophin pre-mRNA (also known as WVE 210201) for the 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 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 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, the medicine Translarna (ataluren) was authorised in the EU for the treatment of a small group of patients with DMD caused by a particular type of mutation (change),

*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 517,400,000 (Eurostat 2018).

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called a nonsense mutation, in the dystrophin gene. Patients also received supportive treatment such as physiotherapy.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with DMD because early laboratory data indicate that it could maintain the levels of dystrophin and function in certain patients whose disease is not caused by the nonsense mutation and for whom there are currently no authorised 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?

DMD can be caused by a number of genetic mutations (changes) affecting the dystrophin gene which stop the production of a normal dystrophin protein, leading to a shortened protein that does not function properly.

The medicine is an 'antisense oligonucleotide', a small strand of synthetic genetic material that has been designed to attach to the mutated genetic material of muscle cells. This enables the protein-making apparatus in the cells to move past the mutation, so that the cells are able to produce a functional dystrophin protein. This is expected to improve the symptoms of the condition.

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, a clinical trial with the medicine in patients with DMD was ongoing.

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 21 June 2018 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	Activeingredient	Indication
English	Synthetic antisense oligonucleotide directed against human dystrophin pre-mRNA	Treatment of Duchenne muscular dystrophy
Bulgarian	Синтетичен антисенс олигонуклеотид, насочен срещу пре-иРНК за човешки дистрофин	Лечение на мускулна дистрофия на Duchenne
Croatian	Sintetski protusmjerni oligonukleotid usmjeren protiv pre-mRNA ljudskog distrofina	Liječenje Duchenneove mišićne distrofije
Czech	Syntetický antisense oligonukleotid namířený proti lidské dystrofinové pre-mRNA	Léčba pacientů s Duchennovou muskulární dystrofií
Danish	Syntetisk antisensoligonukleotid rettet mod human dystrofin pre-mRNA	Behandling af Duchenne muskeldystrofi
Dutch	Synthetische antisense-oligonucleotide gericht tegen menselijk dystrofine pre-mRNA	Behandeling van Duchenne spierdystrofie
Estonian	Inimese düstrofiini eellas-mRNA vastu suunatud sünteetiline *antisense* oligonukleotiid	Duchenne'i lihasdüstroofia ravi
Finnish	Synteettinen antisense-oligonukleotidi, jonka kohteena on ihmisen dystropiinin esivälittäjäaineen pre-mRNA	Duchennen lihasdystrofian hoito
French	Oligonucléotide antisens synthétique dirigé contre l'acide ribonucléique pré-ARNm	Traitement de la dystrophie musculaire de Duchenne
German	Gegen menschliche Dystrophin-Prä-mRNA gerichtetes synthetisches Antisense-Oligonukleotid	Behandlung der Duchenne-Muskeldystrophie
Greek	Συνθετικό συμπληρωματικό ολιγονουκλεοτίδιο κατευθυνόμενο ενάντια στο προ-mRNA της ανθρώπινης δυστροφίνης	Θεραπεία της μυϊκής δυστροφίας Duchenne
Hungarian	A humán disztrofin pre-mRNS ellen irányuló szintetikus antisense oligonukleotid	Duchenne dystrophia kezelése
Italian	Oligonucleotide sintetico antisenso diretto contro il pre-mRNA della distrofina umana	Trattamento della distrofia muscolare di tipo Duchenne
Latvian	Sintētisks antisensa oligonukleotīds, kas vērsts pret cilvēka distrofīna pre-mRNS	Dišēna muskuļu distrofijas ārstēšana
Lithuanian	Sintetinis priešprasmis oligonukleotidas, nukreiptas prieš žmogaus distrofino pre-iRNR	Duchenne (Diušeno) raumenų distrofijos gydymas
Maltese	Oligonukleotid antisens sintetiku dirett kontra d-distrofin uman ta' qabel l-mRNA	Kura tad-distrofija muskolari tat-tip Duchenne
Polish	Syntetyczny antysensowy oligonukleotyd skierowany przeciwko pre-mRNA dystrofiny ludzkiej	Leczenie zaniku mięśni typu Duchenne'a
Portuguese	Oligonucleótido anti-senso sintético direcionado contra o pré-ARNm da distrofina humana	Tratamento da distrofia muscular de Duchenne
Romanian	Oligonucleotid sintetic antisens ce ţinteşte pre-ARNm-ul distrofinei umane	Tratamentul distrofiei musculare Duchenne

[1] At the time of designation

Language	Activeingredient	Indication
Slovak	Syntetický antisense oligonukleotid smerovaný proti mRNA ľudského dystrofínu	Liečba Duchennovej muskulárnej dystrofie
Slovenian	Sintetični protismerni oligonukleotid usmerjen proti mRNA humanega distrofina	Zdravljenje Duchennove mišične distrofije
Spanish	Oligonucleótido antisentido sintético dirigido contra el pre-ARNm de la distrofina humana	Tratamiento de la distrofia muscular de Duchenne
Swedish	Syntetisk antisensoligonukleotid riktad mot pre-mRNA för humant dystrofin	Behandling av Duchennes muskeldystrofi
Norwegian	Syntetisk antisense-oligonukleotid rettet mot humant dystrofin pre-mRNA	Behandling av Duchennes muskeldystrofi
Icelandic	Samtengdur tjáningarhindri beint gegn pre-mRNA dystrópíni manna	Meðferð á Duchenne vöðvarýrnun