European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5') (C-m^{5}U-C-C-A-A-C-A-m^{5}U-C-A-A-G-G-A-A-G-A-m^{5}U-G-G-C-A-m^{5}U-m^{5}U-m^{5}U-C-m^{5}U-A-G), P-[4[[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]carbonyl]-1-piperazinyl] N,N-dimethylaminophosphonamidate for the treatment of Duchenne muscular dystrophy

On 3 December 2008, orphan designation (EU/3/08/586) was granted by the European Commission to AVI Biopharma International, United Kingdom, for RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5') (C-m5U-C-C-A-A-C-A-m5U-C-A-A-G-G-A-A-G-A-m5U-G-G-C-A-m5U-m5U-m5U-C-m5U-A-G), P-[4[[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]carbonyl]-1-piperazinyl] N,N-dimethylaminophosphonamidate for the treatment of Duchenne muscular dystrophy.

What is Duchenne muscular dystrophy?
Duchenne muscular dystrophy (DMD) is an inherited genetic disease characterised by progressive weakening of the muscles. It mainly affects boys, usually before the age of six years. The muscle weakness starts in the hips and legs, before reaching the chest, arms, and possible heart, later on. Patients with DMD do not produce enough of a protein called dystrophin. As dystrophin is an important component of muscle fibres, the muscles of patients with DMD cannot grow, so they become weak and eventually stop working.
DMD causes long-term disability and is life-threatening because of its effects on the heart and on respiratory muscles (muscles that are used to breathe).

What is the estimated number of patients affected by the condition?
At the time of designation, DMD affected approximately 0.3 in 10,000 people in the European Union (EU)[*]. This is below the threshold for orphan designation which is 5 in 10,000, and is equivalent to a total of around 15,000 people. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?
At the time of submission of the application for orphan drug designation, there were no treatments available in the EU that could cure DMD. The main treatments for the disease were corticosteroids to slow down the progression of the disease, and physiotherapy, which was used to relieve symptoms and improve the patient's general condition.
The sponsor has provided sufficient information to show that RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5')(C-m^{5}U-C-C-A-A-C-A-m^{5}U-C-A-A-G-G-A-A-G-A-m^{5}U-G-G-C-A-m^{5}U-m^{5}U-m^{5}U-C-m^{5}U-A-G),P-[4-[[2-[2-(2hydroxyethoxy)ethoxy]ethoxy]carbonyl]-

[*] Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).

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1-piperazinyl]-N,N-dimethylaminophosphonamidate might be of potential significant benefit for patients because of the way the medicine is expected to work. This could improve the overall outcome of patients with DMD. 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 thought to promote the production of a truncated (shortened) form of the dystrophin protein. This truncated protein is expected to act in a similar way to the full dystrophin protein, helping the body to make up for the loss of dystrophin, and relieving the symptoms of DMD.

What is the stage of development of this medicine?
The effects of RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G),P-[4-[[2-[2-(2hydroxyethoxy)ethoxy]ethoxy]carbonyl]-1-piperazinyl] N,N-dimethylaminophosphonamidate have been evaluated in experimental models.
At the time of submission of the application for orphan designation, clinical trials in patients with DMD were ongoing.
Orphan designation of this product had been granted in the United States for DMD.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 October 2008 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 Community) 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 marketing authorisation.

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Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-hydroxyethoxy)ethoxy] ethoxy]carbonyl]-1-piperazinyl]-N,N-dimethylaminophosphonamidate	Treatment of Duchenne muscular dystrophy
Bulgarian	РНК, [P-деокси-P-(диметиламино)] (2',3'-дидеокси-2',3'-имино-2',3'-секо) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-хидроксиетокси)етокси] етокси]карбонил]-1-пиперазинил]-N,N-диметиламинофосфонамидат	Лечение на мускулна дистрофия на Duchenne
Czech	RNA, [P-deoxy-P-(dimetylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-hydroxyetoxy)etoxy]etoxy] karbonyl]-1-piperazinyl]-N,N-dimetylaminofosfonamidát	Léčba pacientů s Duchennovou muskulární dystrofií
Danish	RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G),P-[4-[[2-[2-(2-hydroxyethoxy)ethoxy] ethoxy]carbonyl]-1-piperazinyl]-N,N-dimethylaminofosfonamidat	Behandling af Duchenne muskeldystrofi
Dutch	RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy] carbonyl]-1-piperazinyl]-N,N-dimethylaminofosfonamidaat	Behandeling van Duchenne spierdystrofie
Estonian	RNA, [*P*-desoksü-*P*-(dimetüülamino)](2',3'-didesoksü-2',3'-imino-2',3'-*seco*)(2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), *P*-[4-[[2-[2-(2-hüdroksüetoksü)etoksü]etoksü] karbonüül]-1-piperasinüül]-*N*,*N*-dimetüülaminofosfoonamidaat	Duchenne'i lihasdüstroofia ravi
Finnish	RNA, [P-deoksi-P-(dimetyyliamino)] (2',3'-dideoksi-2',3'-imino-2',3'-seko) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-hydroksietoksi)etoksi]etoksi] karbonyyli]-1-piperatsinyyli]-N,N-dimetyyliaminofosfonamidaatti	Duchennen lihasdystrofian hoito

French	ARN, [P-désoxy-P-(diméthylamino)] (2',3'-didésoxy-2',3'-imino-2',3'-séco) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-hydroxyéthoxy)éthoxy]éthoxy] carbonyl]-1-pipérazinyl]-N,N-diméthylaminophosphonamidate	Traitement de la dystrophie musculaire de Duchenne
German	RNA, [P-Deoxy-P-(Dimethylamino)] (2',3'-Dideoxy-2',3'-Imino-2',3'-Seco) (2'a→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-m^5U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-Hydroxy-Ethoxy)Ethoxy] Ethoxy]Carbonyl]-1-Piperazinyl]-N,N-Dimethylaminophosphonamidat	Behandlung der Duchenne-Muskeldystrophie
Greek	RNA, [P-δεοξυ-P-(διμεθυλαμινο)] (2',3'-διδεοξυ-2',3'-ιμινο-2',3'-seco) (2'α→5')(C-m^5U-C-C-A-A-C-A-m^5U-C-A-A-G-G-A-A-G-A-^{5}U-G-G-C-A-m^5U-m^5U-m^5U-C-m^5U-A-G), P-[4-[[2-[2-(2-υδροξυαιθοξυ)αιθοξυ]αιθοξυ] καρβονυλο]-1-πιπεραζινυλο]-N,N-φωσφονικοαμιδικοδιμεθυλαμινο	Θεραπεία της μυϊκής δυστροφίας Duchenne
Slovak	RNA, [P-deoxy-P-(dimetylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seko) (2'a→5')(C-m5U-C-C-A-A-C-A-m5U-C-A-A-G-G-A-A-G-A-m5U-G-G-C-A-m5U-m5U-m5U-C-m5U-A-G), P-[4-[[2-[2-(2-hydroxyetoxy)etoxy]etoxy] karbonyl]-1-piperazinyl]-N,N-dimetylaminofosfonamidát	Liečba Duchennovej muskulárnej dystrofie
Slovenian	RNA, [P-deoksi-P-(dimetilamino)] (2',3'-dideoksi-2',3'-imino-2',3'-seko) (2'a→5')(C-m5U-C-C-A-A-C-A-m5U-C-A-A-G-G-A-A-G-A-m5U-G-G-C-A-m5U-m5U-m5U-C-m5U-A-G), P-[4-[[2-[2-(2-hidroksietoksi)etoksi]ethoksi] carbonil]-1-piperazinil]-N,N-dimetilaminofosfonamidat	Zdravljenje Duchennove mišične distrofije
Spanish	ARN, [P-deoxy-P-(dimetilamina)] (2',3'-dideoxi -2',3'-imino-2',3'-seco) (2'a→5')(C-m5U-C-C-A-A-C-A-m5U-C-A-A-G-G-A-A-G-A-m5U-G-G-C-A-m5U-m5U-m5U-C-m5U-A-G), P-[4-[[2-[2-(2- hidroxietoxi)etoxi]etoxi] carbonilo]-1-piperazinilo]-N,N-dimetilaminofosfonamida	Tratamiento de la distrofia muscular de Duchenne
Swedish	RNA, [P-deoxi-P-(dimetylamino)] (2',3'-dideoxi-2',3'-imino-2',3'-seko) (2'a→5')(C-m5U-C-C-A-A-C-A-m5U-C-A-A-G-G-A-A-G-A-m5U-G-G-C-A-m5U-m5U-m5U-C-m5U-A-G), P-[4-[[2-[2-(2-hydroxietoxi)etoxi]etoxi] karbonyl]-1-piperazinyl]-N,N-dimetylaminofosfonamidat	Behandling av Duchennes muskeldystrofi

Norwegian	RNA, [P-deoksy-P-(dimetylamino)] (2',3'-dideoksy-2',3'-imino-2',3'-seco) (2'a→5')(C-m5U-C-C-A-A-C-A-m5U-C-A-A-G-G-A-A-G-A-m5U-G-G-C-A-m5U-m5U-m5U-C-m5U-A-G), P-[4-[[2-[2-(2-hydroksyetoksy)etoksy]etoksy] karbonyl]-1-piperazinyl]-N,N-dimetylaminofosfonamidat	Behandling av Duchennes muskeldystrofi
Icelandic	RKS (RNA), [P-deoxý-P-(tvímetýlamínó)] (2',3'-tvídeoxý-2',3'-ímínó-2',3'-secó) (2'a→5')(C-m5U-C-C-A-A-C-A-m5U-C-A-A-G-G-A-A-G-A-m5U-G-G-C-A-m5U-m5U-m5U-C-m5U-A-G), P-[4-[[2-[2-(2-hýdroxýetoxý) etoxý]etoxý]karbónýl]-1-piperasínýl]-N,N-tvímetýlamínófosfónamídat	Meðferð á Duchenne vöðvarýrnun