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

Document Date: London, 18 September 2009
Doc.Ref.: EMEA/COMP/1250/2006 Rev.1

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in March 2009 on request of the Sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of 2'-O-methyl-phosphorothioate oligonucleotide for the treatment of Duchenne muscular dystrophy

On 16 February 2006, orphan designation (EU/3/06/357) was granted by the European Commission to Prosensa B.V., The Netherlands, for 2'-O-methyl-phosphorothioate oligonucleotide for the treatment of Duchenne muscular dystrophy.

What is Duchenne muscular dystrophy?
Duchenne muscular dystrophy is an inherited genetic disease with onset usually before the age of 6. It is characterised by symmetrical progressive diminishing and weakness of the muscles, first at the height of the pelvis and legs, later on also the muscles of the chest and arms are involved. Genes located on structures present in each cell of the body (the chromosomes), carry the genetic information that determines the characteristics of each individual. In humans, the so-called X and Y-chromosomes determine the sex, but carry also other genetic information. Duchenne muscular dystrophy is caused by an abnormality of a gene located on the X chromosome. This gene is responsible for the production of a protein, dystrophin, in the muscle cells. This means that patients suffering from this condition do not produce the dystrophin protein or produce a non-functional dystrophin. As boys, contrary to girls, only have one single copy of chromosome X, thus one single copy of dystrophin gene, they have much higher probabilities of suffering from Duchenne muscular dystrophy. Duchenne muscular dystrophy is chronically debilitating and life-threatening.

What is the estimated number of patients affected by the condition?
At the time of designation, Duchenne muscular dystrophy affected approximately 0.5 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 23,000 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).

What treatments are available?
At the time of submission of the application for orphan designation, no satisfactory method had been authorised in the European Union for treatment of the condition. Treatment of patients with Duchenne muscular dystrophy primarily involves physiotherapy as supportive treatments.

[*]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).

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: orphandrugs@emea.europa.eu http://www.emea.europa.eu

How is this medicine expected to work?
2'-O-methyl-phosphorothioate oligonucleotide is a medicinal product, which might overcome the abnormality in the production of dystrophin. The product would allow skipping the abnormal parts of the gene responsible for the lack of functional dystrophin production. Thus it could enable the production of shorter versions of the dystrophin protein, but still capable of ensuring the same functions as the normal full-length dystrophin.

What is the stage of development of this medicine?
The evaluation of the effects of 2'-O-methyl-phosphorothioate oligonucleotide in experimental models is ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with Duchenne muscular dystrophy were initiated.

2'-O-methyl-phosphorothioate oligonucleotide was not authorised anywhere worldwide for Duchenne muscular dystrophy or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 11 January 2006 a positive opinion recommending the grant of the above-mentioned 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 a marketing authorisation.

For more information:
Sponsor's contact details:
Prosensa B.V.
Einsteinweg 55
2333 CC Leiden
The Netherlands
Telephone: +31 71 527 42 02
E-mail: contact@prosensa.nl

Patients' associations contact points:

Duchenne Parent Project UK (PPUK)
Epicentre
41 West Street
London
E11 4LJ
United Kingdom
Telephone: +44 20 85 56 99 55
E-mail: info@ppuk.org

AFM : Association Française contre les Myopathies
BP 59
1 Rue de l'Internationale
91002 Evry Cedex
France
Telephone: +33 1 69 47 28 28 / +33 81 08 11 088
Telefax: +33 1 60 77 12 16
E-mail: afm@afm.genethon.fr

DGM : Deutsche Gesellschaft für Muskelkranke e.V.
Im Moos 4
79112 Freiburg
Germany
Telephone: +49 76 65 94 470
Telefax: +49 76 65 94 47 20
E-mail: info@dgm.org

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

Language	Active Ingredient	Indication
English	2'-O-methyl-phosphorothioate oligonucleotide	Treatment of Duchenne muscular dystrophy
Czech	2'-O-methyl-phosphorothioate oligonucleotide	Léčba pacientů s Duchennovou muskulární dystrofií
Danish	2'-O-methyl-phosphorothioatOligonucleotid	Behandling af Duchenne muskeldystrofi
Dutch	2'-O-methyl-phosphorothioate oligonucleotide	Behandeling van Duchenne spierdystrofie
Estonian	2'-O-methyl-phosphorothioate oligonukleotiid	Duchenne'i lihasdüstroofia ravi
Finnish	2'-O-metyyli-fosforotioaatti Oligonukleotidi	Duchennen lihasdystrofian hoito
French	2'-O-methyl-phosphorothioate oligonucléotide	Traitement de la dystrophie musculaire de Duchenne
German	2'-O-methyl-phosphorothioate Oligonucleotid	Behandlung der Duchenne-Muskeldystrophie
Greek	2'-O-μεθυλοφωσφοροθειοϊκό ολιγονουκλεοτίδιο	Θεραπεία της μυϊκής δυστροφίας Duchenne
Hungarian	2'-O- metil-foszforotionát-oligonukleotid	Duchenne dystrophia kezelése
Italian	2'-O-metil-fosforotioato oligonucleotide	Trattamento di distrofia muscolare di tipo Duchenne
Latvian	2'-O-metil-fosfortioāta oligonucleotīds	Dišēna muskuļu distrofijas ārstēšana
Lithuanian	2'-O-metil-fosforotioato oligonukleotidas	Duchenne (Diušeno) raumenų distrofijos gydymas
Polish	2'-O-metylo-fosforotoanu Oligonukleotyd	Leczenie zaniku mięśni typu Duchenne'a
Portuguese	2'-O-methyl-phosphorothioate oligonucleótido	Tratamento da distrofia muscular de Duchenne
Slovak	2'-O-metyl-fosforotioát oligonukleotid	Liečba Duchennovej muskulárnej dystrofie
Slovenian	2'-O-metil-fosforotioat oligonukleotid	Zdravljenje Duchennove mišične distrofije
Spanish	2'-O-metil-fosforotioato oligonucleótido	Tratamiento de la distrofia muscular de Duchenne
Swedish	2'-O-metyl-fosforotioat oligonukletid	Behandling av Duchennes muskeldystrofi
Norwegian	2'-O-metyl-fosforotioate oligonukleotid	Behandling av Duchennes muskeldystrofi
Icelandic	2'-O-methýl-phosphóróthíóat ólígónókleótíð	Meðferð á Duchenne vöðvarýrnun