5 May 2014
EMA/COMP/95948/2014 Corr.[1]
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Phosphorothioate oligonucleotide targeted to transthyretin for the treatment of ATTR amyloidosis

On 26 March 2014, orphan designation (EU/3/14/1250) was granted by the European Commission to Isis USA Ltd, United Kingdom, for phosphorothioate oligonucleotide targeted to transthyretin for the treatment of ATTR amyloidosis.

What is ATTR amyloidosis?

ATTR amyloidosis belongs to a group of diseases called systemic amyloidosis in which deposits of proteins (called amyloids) accumulate and cause damage in body organs. In ATTR amyloidosis the amyloids consist of transthyretin, a protein produced in the liver that transports various substances in the blood.

In patients with ATTR amyloidosis, transthyretin deposits accumulate mainly in the heart and the nervous system causing symptoms such as muscle weakness in the limbs and, at later stages, inability to walk, problems affecting the stomach and the gut (leading to malnutrition), and bladder dysfunction.

ATTR amyloidosis is a long-term debilitating disease due to the progressive worsening of nervous system symptoms. It is also life threatening because the amyloid deposits may accumulate in the heart and cause fatal heart conditions.

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

At the time of designation, ATTR amyloidosis affected less than 3 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 153,000 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).

[1] Correction of the paragraph "How is this medicine expected to work?", 7 June 2018.
[*]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).

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What treatments are available?

At the time of designation, the only medicine authorised in the EU to treat ATTR amyloidosis was Vyndaqel (tafamidis). The only other treatment option was liver transplantation.

The sponsor has provided sufficient information to show that the medicine 'phosphorothioate oligonucleotide targeted to transthyretin' might be of significant benefit for patients with ATTR amyloidosis because it works in a different way to existing treatment and early studies in experimental models show that it might improve the outcome of patients at different stages of the disease. 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?

This medicine is an 'antisense oligonucleotide', a very short piece of synthetic genetic material which has been designed to attach to the genetic material of cell responsible for producing the transthyretin protein. This is expected to reduce transthyretin production, thereby reducing the formation of amyloids and relieving the symptoms of ATTR amyloidosis.

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, clinical trials with the medicine in patients with ATTR amyloidosis were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for ATTR amyloidosis. 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 6 February 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:

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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[3], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Phosphorothioate oligonucleotide targeted to transthyretin	Treatment of ATTR amyloidosis
Bulgarian	Форсфоротиоат олигонуклеотид насочен към транстиретин	Лечение на транстиретинова амилоидоза
Czech	Fosforothioaát oligonukleotid cílený k transthyretinu	Liječenje obiteljske amiloidne polineuropatije
Croatian	Fosforotioatni oligonukleotid usmjeren na transtiretin	Liječenje ATTR amiloidoze
Danish	Fosforothioat oligonukleotid rettet mod transthyretin	Behandling af familiær ATTR amyloidose i
Dutch	Fosforothioaat oligonucleotide gericht tegen transthyretine	Behandeling van ATTR- amyloïdose
Estonian	Transtüretiinile suunatud fosforotioaat oliginukleotiid	Transtüretiiniga seotud amülodoosi (ATTR) ravi
Finnish	Transtyretiiniin kohdennettu fosforotioaattioligonukleotidi	Suvuittain esiintyvän amyloidipolyneuropatian hoito
French	Oligonucléotide phosphorothioate dirigé contre la transthyrétine	Traitement de l'amyloïdose ATTR
German	Transthyretin-spezifisches Phosphorothioat-Oligonukleotid	Behandlung der ATTR-Amyloidose
Greek	Φωσφορο-θειοϊκό ολιγονουκλεοτίδιο έναντι της τρανσθυρετίνης	Θεραπεία της ATTR-αμυλοείδωσης
Hungarian	Transztiretin célpontú foszfor-tioát oligonukleotid	ATTR típusú amyloidosis kezelése
Italian	Oligonucleotide fosforotioato contro la transtiretina	Trattamento della amiloidosi da transtiretina
Latvian	Pret transtiretīnu vērsts fosfortioāta oligonukleotīds	ATTR amiloidozes ārstēšana
Lithuanian	Fosforotioato oligonukleotidas nukreiptas į transtiretiną	ATTR amiloidozės gydymas
Maltese	Oligonukleotide *phosphothioate* immirat għat-*transthyretin*	Kura tal-amilojdosi assoċjata mat-*transthyretin* (ATTR)
Polish	Oligonulkeotyd tiofosforanowy hamujący wytwarzanie trnstyretyny	Leczenie amyloidozy wrodzonej typu ATTR
Portuguese	Oligonucleótido fosforotioato específico da transtirretina	Tratamento da amiloidose associada à transtirretina
Romanian	Oligonucleotidă fosforotioat care vizează transtiretina	Tratamentul polineuropatiei amiloide familiale
Slovak	Fosforotioát oligonucleotid zacielený na transtyretín	Liečba ATTR amyloidózy

[3] At the time of designation

Language	Active ingredient	Indication
Slovenian	Fosorotioatni oligonukleotid usmerjen za transtiretrin	Zdravljenje ATTR amiloidoze
Spanish	Oligonucleótido fosforotioato específico de la transtirretina	Tratamiento de polineuropatía amiloide familiar
Swedish	Fosfortioatoligonukleotider riktade mot transtyretin	Behandling av ATTR amyloidos
Norwegian	Fosfortioat oligonukleotid rettet mot transtyretin	Behandling av ATTR amyloidose
Icelandic	Fosfórótíóat ólígónúkleótíð sem beinist að transtýretíni	Meðferð við ATTR mýlildisfjöltaugakvilla