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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Synthetic double-stranded siRNA oligonucleotide directed against transthyretin mRNA for the treatment of transthyretin-mediated amyloidosis

On 6 April 2017, orphan designation (EU/3/11/857) was granted by the European Commission to Alnylam UK Limited, United Kingdom, for synthetic double-stranded siRNA oligonucleotide directed against transthyretin mRNA (also known as patisiran) for the treatment of transthyretin-mediated amyloidosis.

What is transthyretin-mediated amyloidosis?

Transthyretin-mediated 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 are made up 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. Patient with this condition usually have heart problems and 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 amyloid deposits in the heart can 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 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 10,000 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).

*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 515,700,000 (Eurostat 2017).

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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). Vyndaqel was authorised to delay nerve damage caused by ATTR amyloidosis in patients with the early stage of nerve disease. The only other treatment option was liver transplantation.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with all forms of ATTR amyloidosis because early studies in patients showed that the medicine may stabilise the heart symptoms of the condition. 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 made of a small strand of synthetic genetic material, called 'small interfering RNA' (siRNA), that stops the gene for transthyretin from working and thereby blocks the production of transthyretin in the liver. This reduces the accumulation of transthyretin deposits in the tissues and slows down the progression of the disease.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of orphan designation, clinical trials with the medicine in patients with ATTR amyloidosis were ongoing.

At the time of orphan designation, this medicine was not authorised anywhere in the EU for ATTR amyloidosis.

This medicine had been designated orphan on 15 April 2011 for the treatment of familial amyloid polyneuropathy (FAP). At the request of the sponsor and having assessed the additional data submitted, the COMP adopted a positive opinion on 19 January 2017 recommending the designation be changed to treatment of transthyretin-mediated amyloidosis, a class of diseases to which FAP belongs.

Orphan designation of the medicine has been granted in the United States for familial amyloidotic polyneuropathy.

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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	Active ingredient	Indication
English	Synthetic double-stranded siRNA oligonucleotide directed against transthyretin mRNA	Treatment of transthyretin-mediated amyloidosis
Bulgarian	Синтетичен, двойно-спирален siRNA олигонуклеотид, насочен срещу транстиретинова mRNA	Лечение на транстиретин-медиирана амилоидоза
Croatian	Sintetski dvolančani oligonukleotid siRNA usmjeren protiv mRNA transtiretina	Liječenje transtiretinske amiloidoze
Czech	Syntetický dvouvláknový oligonukleotid siRNA proti mRNA transtyretinu	Léčba transthyretinové amyloidózy
Danish	Syntetisk dobbeltstrenget siRNA-oligonukleotid rettet mod mRNA transthyretin	Behandling af transthyretin medieret amyloidose
Dutch	Synthetisch dubbelstrengig siRNA oligonucleotide gericht tegen transthyretine mRNA	Behandeling van transthyretine-gemedieerde amyloïdose
Estonian	Sünteetiline kahe ahelaga siRNA oligonukleotiid, mis on suunatud transtüretiini mRNA vastu	Transtüretiiniga seotud amüloidoosi ravi
Finnish	Transtyretiini mRNA:han kohdistuva synteettinen kaksijuosteinen siRNA oligonukleotidi	Transtyretiinivälitteisen amyloidoosin hoito
French	Oligonucléotide ARNsi bicaténaire synthétique dirigé contre l'ARNm transthyrétine	Traitement de l'amylose à transthyrétine
German	Gegen Transthyretin-mRNA gerichtetes, synthetisches doppelsträngiges siRNA Oligonucleotid	Behandlung der Transthyretin-vermittelten Amyloidose
Greek	Συνθετικό διπλής έλικας ολιγονουκλεΐδιο siRNA κατευθυνόμενο κατά του mRNA τρανσθυρετίνης	Θεραπεία της σχετιζόμενης με την τρανσθυρετίνη αμυλοείδωσης
Hungarian	Transthyretin mRNS elleni szintetikus, kétszálú siRNS oligonukleotid	Transztiretin-mediált amyloidosis kezelése
Italian	Oligonucleotide siRNA sintetico a doppio filamento diretto contro il mRNA della transtiretina	Trattamento dell'amiloidosi da accumulo di transtiretina
Latvian	Sintētisks dubultspirāles siRNS oligonukleotīds, kas vērsts pret transtiretīna mRNS	Transtiretīna mediētas amiloidozes ārstēšana
Lithuanian	Sintetinis, dvigrandės siRNR oligonukleotidas, nukreiptas prieš transtiretino Mrnr	Transtiretino medijuotos amiloidozės gydymas
Maltese	Oligonukleotide sintetiku tas-siRNA b'katina doppja immirat kontra transthyretin mRNA	Kura ta' amilojdożi medjata minn transthyretin
Polish	Syntetyczny dwuniciowy oligonukleotyd siRNA skierowany przeciwko mRNA transtyretyny	Leczenie amyloidozy transtyretynowej
Portuguese	Oligonucleótido sintético siRNA de cadeia dupla dirigido contra mRNA de transtiretina	Tratamento da amiloidose associada à transtirretina

[1] At the time of designation

Language	Active ingredient	Indication
Romanian	Oligonucleotid sintetic ARNsi dublu catenar direcţionat împotriva transtiretinei ARNm	Tratamentul amiloidozei cu transtiretină
Slovak	Syntetický oligonukleotid dvojvláknovej siRNA nasmerovaný proti transtyretínovej mRNA	Liečba transtyretínovej amyloidózy
Slovenian	Sintetični oligonukleotid dvoverižne siRNK, usmerjen proti mRNK transtiretina	Zdravljenje transtiretinske amiloidoze
Spanish	Oligonucleótido sintético de ARNsi de doble cadena dirigido contra el ARNm de la transtiretina	Tratamiento de la amiloidosis asociada a latranstiretina
Swedish	Syntetisk dubbelsträngad siRNA-oligonukleotid riktad mot transtyretin mRNA	Behandling av transtyretin- amyloidos
Norwegian	Syntetisk dobbeltstrenget sIRNA-oligonukleotid rettet mot transtyretin mRNA	Behandling av transtyretinmediert amyloidose
Icelandic	Tilbúið tveggja þátta siRNA fákirni sem beinist gegn thýretín mRNA	Meðferð við transtýretín-miðluðu mýlildi