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EMA/COMP/30845/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Phosphorothioate oligonucleotide targeted to apolipoprotein C-III for the treatment of familial chylomicronaemia syndrome

On 19 February 2014, orphan designation (EU/3/14/1249) was granted by the European Commission to Isis USA Ltd, United Kingdom, for phosphorothioate oligonucleotide targeted to apolipoprotein C-III for treatment of familial chylomicronaemia syndrome.

What is familial chylomicronaemia syndrome?

Familial chylomicronaemia syndrome (also known as type I hyperlipoproteinaemia) is an inherited disease where patients have abnormally high levels of some types of fat called triglycerides in their blood. The excess fat accumulates in organs such as the spleen and liver, which become abnormally enlarged. Fat accumulation can also cause repeated bouts of pancreatitis (inflammation of the pancreas) and xanthomas (formation of yellow fatty deposits just under the skin, generally around joints).

The cause of the disease is often the body's failure to produce enough of an enzyme called lipoprotein lipase, which is involved in breaking down fats from the diet.

Familial chylomicronaemia syndrome is a debilitating and life threatening disease because the bouts of pancreatitis can be severe and sometimes fatal.

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

At the time of designation, familial chylomicronaemia syndrome affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 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 511,100,000 (Eurostat 2014).

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What treatments are available?

At the time of designation, the medicine Glybera (alipogene tiparvovec) was authorised for the treatment of lipoproteinlipase deficiency in patients who suffer from multiple episodes of pancreatitis despite fat dietary restrictions (avoiding foods that contain a high level of fat). Patients were also advised to avoid the use of substances known to increase the level of triglycerides in the blood, such as alcohol, diuretics or oestrogens.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with familial chylomicronaemia syndrome because early studies suggest that the medicine works in a different way to existing treatment and it may benefit a wider population. 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 RNA (a type of genetic material). It has been designed to block the production of a protein called apolipoprotein C-III, which when found at high levels in the blood is thought to prevent the breaking down of fats in the blood. By blocking the production of this protein, the medicine is expected to reduce fat accumulation in the various organs and the number of pancreatitis attacks, thus reducing the severity of the disease.

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 familial chylomicronaemia syndrome were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for familial chylomicronaemia syndrome 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 9 January 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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Phosphorothioate oligonucleotide targeted to apolipoprotein C-III	Treatment of familial chylomicronaemia syndrome
Bulgarian	Фосфоротиоатен олигонуклеотид, насочен към аполипопротеин С-III	Лечение на синдром на фамилна хиломикронемия
Czech	Fosforothioat oligonucleotid cílenýna apolipoproteinu C-III	Léčba syndromu familiární chylomikronemie
Croatian	Fosforotioat oligonukleotid usmjeren na apolipoprotein C-III	Liječenje sindroma obiteljske hilomikronemije
Danish	Phosphorothioat oligonucleotid rettet mod apolipoprotein C-III	Behandling af familiær chylomikronæmi syndrom
Dutch	Phosphorothioate oligonucleotide gericht tegen apolipoproteïne C-III	Behandeling van familiaal chylomicronemie syndroom
Estonian	Fosfortioaat oligonukleotiid sihtmärgiga apolipoproteiin C-III	Perekondliku külomikroneemia sündroomi ravi.
Finnish	Apolipoproteiini C-III:a vähentävä fosforotioaatti-oligonukleotidi	Suvuittaisen kylomikronemia-oireyhtymän hoito
French	Oligonucléotide de phosphorothiate ciblant l'apolipoprotéine C-III	Traitement du syndrome de chylomicronémie familiale
German	Apolipoprotein C-III spezifisches Phosphortioat-Oligonukleotid	Behandlung des familiären Chylomikronämie-Syndroms
Greek	Φωσφορο-θειοϊκό ολιγονουκλεοτίδιο έναντι της απολιποπρωτεϊνης C-III	Θεραπεία του συνδρόμου οικογενούς χυλομικροναιμίας
Hungarian	Apolipoprotein C-III-ra ható foszfotioát oligonukleotid	Familiáris chylomicronemia szindróma kezelése
Italian	Oligonucleotide fosforotioato contro la apolipoproteina C-III	Trattamento della chilomicronemia familiare
Latvian	Pret apolipoprotīnu C-III vērsts tiofosfāta oligonukleotīds	Iedzimtās hilomikronēmijas sindroma ārstēšana
Lithuanian	Fosforotioato oligonukleotidas nukreiptas į apolipoproteiną C III	Šeiminio chilomikronemijos sindromo gydymas
Maltese	Oligonukleotide phosphothioate immirat għall-apolipoproteina Ċ-III	Kura tas-sindrome tal-kilomikronemija li tintiret
Polish	Oligonulkeotyd tiofosforanowy hamujący wytwarzanie apolipoproteiny C-III	Leczenie zespołu rodzinnej chylomikronemii
Portuguese	Oligonucleótido fosforotioato anti apolipoproteína C-III	Tratamento do sindrome da quilomicronémia familiar
Romanian	Oligonucleotidă fosforotiolată care vizează apolipoproteina C-III	Tratamentul sindromului chilomicronemiei familiale
Slovak	Fosforotioátový oligonukleotid namierený na apolipoproteín C-III	Liečba syndrómu familiárnej chylomikronémie

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Fosforotioatni oligonukleotid usmerjen za apolipoprotein C-III	Zdravljenje sindroma familiarne hilomikronemije
Spanish	Oligonucleótido fosforotioato anti apolipoproteína C-III	Tratamiento del sindrome de la quilomicronémia familiar
Swedish	Fosfortioat-oligonukleotid riktad mot apolipoprotein C-III	Behandling av familjär kylomikronemi syndrom
Norwegian	Fosfortioat oligonukleotid rettet mot apolipoprotein C-III	Behandling av familiær kylomikronemi syndrom
Icelandic	Fosfóróthíóat ólígónúkleótíð sem beinist gegn apólípópróteini C-III	Meðferð við ættgengum chýlómíkróndreyra heilkenni