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EMA/COMP/345427/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Triheptanoin for the treatment of very long-chain acyl-CoA dehydrogenase deficiency

On 19 June 2015, orphan designation (EU/3/15/1508) was granted by the European Commission to Ultragenyx UK Limited, United Kingdom, for triheptanoin for the treatment of very long-chain acyl-CoA dehydrogenase deficiency.

What is very long-chain acyl-CoA dehydrogenase deficiency?

Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency is an inherited disease caused by the lack of an enzyme called VLCAD. VLCAD is one of the enzymes needed by the mitochondria (the energy-producing components within cells) to break down certain long fatty acids in order to generate energy. If this enzyme is not present, cells cannot function normally, causing a wide range of signs and symptoms including tiredness, hypoglycaemia (low blood sugar levels), muscle wasting and damage to the heart.

The condition is chronically debilitating and life threatening, particularly as it causes damage to the heart.

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

At the time of designation, VLCAD deficiency affected less than 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 21,000 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).

What treatments are available?

At the time of orphan designation, no satisfactory method had been authorised in the European Union for the treatment of VLCAD deficiency. Treatment of patients primarily involved restriction of dietary

*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 512,900,000 (Eurostat 2015).

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fat to less than 30% of the total calories and the substitution of long-chain fatty acids with medium-chain fatty acids. However, these dietary regimens were of unproven value or only partially successful.

How is this medicine expected to work?

Triheptanoin is a synthetic (artificially produced) fat, which is broken down in the liver into substances that can be used by cells to generate energy without the need for VLCAD. By bypassing the need for VLCAD, this medicine is expected to restore the generation of energy and ultimately improve the overall outcome of patients with VLCAD deficiency.

What is the stage of development of this medicine?

The effects of triheptanoin have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with triheptanoin in patients with VLCAD deficiency were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for VLCAD deficiency. Orphan designation of triheptanoin 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 13 May 2015 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	Triheptanoin	Treatment of very long-chain acyl-CoA dehydrogenase deficiency
Bulgarian	Трихептаноин	Лечение на дефицит на дълговерижна ацил-CoA дехидрогеназа
Croatian	Triheptanoin	Liječenje nedostatka acil-CoA-dehidrogenaze vrlo dugog lanca
Czech	Triheptanoin	Léčba deficitu acyl-CoA dehydrogenázy mastných kyselin s velmi dlouhým řetězcem
Danish	Triheptanoin	Behandling af meget-langkædet-acyl-CoA-dehydrogenase mangel
Dutch	Triheptanoin	Behandeling van Zeer lange keten acyl-CoA dehydrogenase deficiëntie
Estonian	Triheptanoiin	Väga pika ahelaga atsüül-CoA-dehüdrogenaasi defitsiidi ravi
Finnish	Triheptanoiini	Hyvin pitkäketjuisten rasvahappojen asyyli-CoA-dehydrogenaasin puutoksen puutoksen hoito
French	Triheptanoïne	Traitement du déficit en acyl-CoA déshydrogénase des acides gras à chaîne très longue
German	Triheptanoin	Behandlung eines Very-Long-Chain-Acyl-CoA-Dehydrogenase-Mangels (VLCAD-Mangel)
Greek	Τριεπτανοΐνη	Θεραπεία της ανεπάρκειας ακυλο-CoA αφυδρογονάσης πολύ μακράς αλύσου
Hungarian	Triheptanoin	Nagyon hosszú-láncú acil-CoA dehidrogenáz hiány (VLCAD) kezelése
Italian	Trieptanoina	Trattamento del deficit di acil-CoA deidrogenasi a catena molto lunga
Latvian	Triheptanoīns	Ļoti garo ķēžu acil-CoA dehidrogenāzes deficīta ārstēšana
Lithuanian	Triheptanoinas	Labai ilgų grandinių acil-KoA dehidrogenazės (angl. VLCAD) stokos gydymas
Maltese	Triheptanoin	Kura ta' nuqqas ta' acyl-CoA dehydrogenase b'katina twila ħafna
Polish	Triheptanoina	Leczenie niedoboru dehydrogenazy acylokoenzymu A bardzo długołańcuchowych kwasów tłuszczowych
Portuguese	Tri-heptanoína	Tratamento da deficiência da desidrogenase de acil-coA de cadeia muito longa
Romanian	Triheptanoin	Tratamentul deficienţei de acil-CoA-dehidrogenază cu lanţ foarte lung
Slovak	Triheptanoín	Liečbadeficitu acyl-CoA dehydrogenázy mastných kyselín s veľmi dlhým reťazcom
Slovenian	Triheptanoin	Zdravljenje pomanjkanja zelo dolgoverižne acil-CoA dehidrogenaze
Spanish	Triheptanoína	Tratamiento de la deficiencia de acil-CoA deshidrogenasa de cadena muy larga
Swedish	Triheptanoin	Behandling av mycket långkedjigt acyl-CoA-dehydrogenasbrist
Norwegian	Triheptanoin	Behandling av meget langkjedet acyl-CoA-dehydrogenasedefekt
Icelandic	Tríheptanóín	Meðferð við skorti á mjög langkeðju asýl-CoA dehýdrógenasa

[1] At the time of designation