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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Triheptanoin for the treatment of very long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 6 December 2012, orphan designation (EU/3/12/1081) was granted by the European Commission to B. Braun Melsungen AG, Germany, for triheptanoin for the treatment of very long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency.

What is very long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency?

Very long-chain 3-hydroxyacyl-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 not more than 0.32 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 16,000 people*, and is below the

*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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

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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 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 to generate energy without the need for VLCAD. By bypassing the need for VLCAD, this medicine is expected to restore the normal energy generation and ultimately improve the overall outcome of the patients.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of triheptanoin in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with triheptanoin in patients with VLCAD deficiency had been started.

At the time of submission, triheptanoin was not authorised anywhere in the EU for VLCAD deficiency. Orphan designation of triheptanoin had been granted in the United States of America for fatty acid oxidation disorders.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 November 2012 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 substance	Indication
English	Triheptanoin	Treatment of very-long-chain-acyl-CoA dehydrogenase deficiency
Bulgarian	Трихептаноин	Лечение наДефицит на Ацил-CoA дехидрогеназата с много дълга верига
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

[1] At the time of designation

Language	Active substance	Indication
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