16 November 2020
EMADOC-628903358-2624

Public summary of opinion on orphan designation

Triheptanoin for the treatment of carnitine-acylcarnitine translocase deficiency

On 27 July 2020, orphan designation EU/3/20/2302 was granted by the European Commission to Ultragenyx Germany GmbH, Germany, for triheptanoin for the treatment of carnitine-acylcarnitine translocase deficiency.

What is carnitine-acylcarnitine translocase deficiency?

Carnitine-acylcarnitine translocase deficiency is an inherited disease caused by the lack of an enzyme called carnitine-acylcarnitine translocase (CACT). CACT is one of the enzymes needed by the mitochondria (the energy-producing components within cells) to break down certain fatty acids to generate energy. If this enzyme is lacking, cells cannot function normally causing a wide range of signs and symptoms including hypoglycaemia (low blood sugar levels), muscle pain, muscle breakdown leading to kidney damage, increased blood levels of ammonia (a sign of liver damage) and damage to the heart muscle.

The condition is chronically debilitating due to tiredness, hypoglycaemia and muscle damage and symptoms such as damage to the heart can be life-threatening.

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

At the time of designation, carnitine-acylcarnitine translocase deficiency affected less than 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 500 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 designation, no satisfactory methods were authorised in the EU for the treatment of CACT deficiency. Treatment of patients primarily involved avoidance of fasting and following a low-fat,

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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high-carbohydrate diet supplemented with 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 CACT. By bypassing the need for CACT, this medicine is expected to restore normal energy generation and ultimately improve the overall outcome of patients with CACT 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 CACT deficiency were ongoing.

At the time of submission, triheptanoin was not authorised anywhere in the EU for the treatment of carnitine-acylcarnitine translocase deficiency. Orphan designation of triheptanoin had been granted in the United States for fatty acid oxidation disorders.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 18 June 2020, recommending the granting of this designation.

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

Contact details of the current sponsor for this orphan designation can be found on EMA website.

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 carnitine-acylcarnitine translocase deficiency
Bulgarian	Трихептаноин	Лечение на дефицит на карнитин-ацилкарнитин транслоказа
Croatian	Triheptanoin	Liječenje nedostatka karnitin-acilkarnitin translokaze
Czech	Triheptanoin	Léčba deficitu karnitinacylkarnitintranslokázy
Danish	Triheptanoin	Behandling af carnitine-acylcarnitine translocase mangel
Dutch	Triheptanoin	Behandeling van carnitine-acylcarnitine translocasedeficiëntie
Estonian	Triheptanoiin	Karnitiini-atsüülkarnitiini translokaasi puudulikkuse ravi
Finnish	Triheptanoiini	Karnitiini-asyylikarnitiini-translokaasin puutoksen hoito
French	Triheptanoïne	Traitement du déficit en carnitine-acylcarnitine translocase
German	Triheptanoin	Behandlung der Carnitin-Acylcarnitin Translocase Deifizienz
Greek	Τριεπτανοΐνη	Θεραπεία της ανεπάρκειας της τρανσλοκάσης καρνιτίνης-ακυλοκαρνιτίνης
Hungarian	Triheptanoin	Karnitin-acilkarnitin transzlokáz hiány kezelése
Italian	Trieptanoina	Trattamento del deficit di carnitina- acetilcarnitina translocasi
Latvian	Triheptanoīns	Kanitīna-acilkarnitīna translokāzes trūkuma ārstēšana
Lithuanian	Triheptanoinas	Karnitino–acilkarnitino translokazės stokos gydymas
Maltese	Triheptanoin	Kura ta' defiċjenza ta' translokaži karnitina-aċilkarnitina
Polish	Triheptanoina	Leczenie niedoboru translokazy karnitynoacylokarnitynowej
Portuguese	Tri-heptanoína	Tratamento da deficiência de carnitina-acilcarnitina translocase
Romanian	Triheptanoin	Tratamentul deficienței de carinitn-acilcarnitină translocază
Slovak	Triheptanoín	Liečba deficitu karnitín-acylkarnitíntranslokázy
Slovenian	Triheptanoin	Zdravljenje pomanjkanja translokaze karnitin-acilkarnitina
Spanish	Triheptanoína	Tratamiento de la deficiencia de la translocase de carnitina-acilcarnitina
Swedish	Triheptanoin	Behandling av karnitin-acylkarnitintranslokas-brist
Norwegian	Triheptanoin	Behandling av karnitin-acylkarnitin translokase mangel
Icelandic	Tríheptanóín	Meðferð við skorti á karnitín-asýlkarnitín-translókasa (CACT)

[1] At the time of designation