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Public summary of opinion on orphan designation

Sodium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetate for the treatment of long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

On 21 August 2020, orphan designation EU/3/20/2319 was granted by the European Commission to Scendea (NL) B.V, Netherlands, for sodium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetate (also known as REN001) for the treatment of long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency.

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

Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency is an inherited disease. LCHAD is one of the enzymes needed by the mitochondria (the energy-producing components in cells) to break down certain long-chain fatty acids in order to generate energy. If this enzyme is lacking, the long-chain fatty acids build up in cells and the cells cannot function normally, causing a wide range of effects including tiredness, hypoglycaemia (low blood sugar levels), muscle wasting, abnormalities in the retina (the light-sensitive tissue at the back of the eye) and damage to the liver, brain, nerves and heart.

The condition is chronically debilitating and life threatening particularly since it causes hypoglycaemia and damage to the nerves and various organs.

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

At the time of designation, LCHAD deficiency affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 26,000 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).

*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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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What treatments are available?

At the time of orphan designation, no satisfactory methods had been authorised in the European Union for the treatment of LCHAD deficiency. Treatment of patients mainly involved changes to the diet, including eating frequently, restriction of dietary fat and the substitution of long-chain fatty acids with medium-chain fatty acids.

How is this medicine expected to work?

The medicine activates a receptor (target) called PPAR delta which leads to an increase in enzymes involved in converting fatty acids to energy. This is expected to improve energy production and reduce build-up of fatty acids and so reduce symptoms of LCHAD deficiency.

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 LCHAD deficiency were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of LCHAD deficiency or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 16 July 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	Sodium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetate	Treatment of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency
Bulgarian	Натрий (4-{(E)-3-(4-флуорофенил)-3-[4-(3-морфолин-4-ил-пропинил)фенил]алилокси}-2-метилфенокси)ацетат	Лечение на дефицит на дълговерижна 3-хидроксиацил-коензим А дехидрогеназа
Croatian	Natrij (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloksi}-2-metilfenoksi)acetat	Liječenje nedostatka 3-hidroksiacil-koenzima A dehidrogenaze dugog lanca
Czech	(4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolin-4-yl-prop1ynyl)fenyl]allyloxy}-2-methylfenoxy)acetát sodný	Léčba deficitu 3-hydroxyacyl-CoA dehydrogenázy mastných kyselin s dlouhým řetězcem
Danish	Natrium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetat	Behandling af langkædede 3-hydroxyacyl-CoA dehydrogenase mangel
Dutch	Natrium(4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetaat	Behandeling van lange-keten 3-hydroxyacyl-coënzyme A dehydrogenasedeficiëntie
Estonian	Naatrium (4-{(E)-3-(4-fluorofenüül)-3-[4-(3-morfoliin-4-üül-prop1ünüül)fenüül]allüüloksü}-2-metüülfenoksü)atsetaat	Pikaahelalise 3-hüdroksüatsüül-koensüüm A-dehüdrogenaasi puudulikkuse ravi
Finnish	Natrium (4 - {(E) -3- (4-fluorofenyyli) -3- [4- (3-morfoliini-4-yyli-prop1ynyyli) fenyyli] allyylioksi} -2-metyylifenoksi) asetaatti	Pitkäketjuisen 3-hydroksiasyylikoentsyymi A -dehydrogenaasipuutoksen hoito
French	(4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy) acétate de sodium	Traitement du déficit en 3-hydroxyacyl-coenzyme A déshydrogénase à longue chaîne
German	Natrium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetat	Behandlung von langkettigem 3-Hyrdoxacyl-Coenzym-A-Dehydrogenase-Mangel

[1] At the time of designation

Language	Active ingredient	Indication
Greek	Νατριο (4-{(E)-3-(4-φθοροφαινυλ)-3-[4-(3-μορφολιν-4-υλ-προπ1υνυλ)φαινυλ]αλλυλοξυ}-2-μεθυλφαινοξυ)οξικό	Θεραπεία της ανεπάρκειας της αφυδρογονάσης του 3-υδροξυακυλ-συνενζύμου Α μακριάς αλύσου
Hungarian	Nátrium (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]alliloxi}-2-metilfenoxi)acetát	Hosszú láncú 3-hydroxyacyl-koenzim-A-dehidrogenáz-hiány kezelése
Italian	Sodio (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1ynil)fenil]allilossi}-2-metilphenossi)acetato	Trattamento del deficit di idrossiacil-coenzima A deidrogenasi
Latvian	Nātrija (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolīn-4-il-prop1inil)fenil]alliloksi}-2-metilfenoksi)acetāts	Garo ķēžu 3-hidroksiacil-koenzīma A dehidrogenāzes nepietiekamības ārstēšana
Lithuanian	Natrio (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloksi}-2-metilfenoksi)acetatas	Ilgųjų grandinių 3-hidroksi-acil-koenzimo A dehidrogenazės stokos gydymas
Maltese	Aċetat (4-{(E)-3-(4-fluworofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]allilossi}-2-metilfenossi)tas-sodju	Kura ta’ defiċjenza deidroġenaži ta’ katina-twila 3-idrossiaċil-koenzima A
Polish	(4-{(E)-3-(4-fluorofenylo)-3-[4-(3-morfolino-4-yl-prop1ynyl)fenyl] allyloksy}-2-metylofenoksy) octan sodu	Leczenie niedoboru dehydrogenazy 3-hydroksyacylo-koenzymu A długołańcuchowych kwasów tłuszczowych
Portuguese	Acetato de (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-propinil)fenil]aliloxi}-2-metilfenoxi) sódio	Tratamento da deficiência da desidrogenase de 3-hidroxi-acil- coenzima A de cadeia longa
Romanian	Sodiu (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloxi}-2-metilfenoxi)acetat	Tratamentul deficienţei de 3-hidroxiacil-CoA-dehidrogenază cu lanţ lung
Slovak	(4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolín-4-yl-prop1ynyl)fenyl]allyloxy}-2-metylfenoxy)acetát sodný	Liečba deficiencie dlhých reťazcov 3-hydroxyacyl-koenzým A dehydrogenázy
Slovenian	Natrijev (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloksi}-2-metifenoksi)acetat	Zdravljenje pomanjkanja dolgoverižne dehidrogenaze 3-hidroksiacil koencima A

Language	Active ingredient	Indication
Spanish	(4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloxi}-2-metilfenoxi)acetate de sodio	Tratamiento de la deficiencia de cadena larga 3 hudroxiacil-coenzima A deshidrogenica
Swedish	natrium (4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolin-4-yl-prop1ynyl)fenyl]allyloxy}-2-metylfenoxy)acetat	Behandling av LCHAD-brist
Norwegian	Natrium(4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolin-4-yl-prop-1-ynyl)fenyl]allyloksy}-2-metylfenoksy)acetat	Behandling av langkjedet 3-hydroksyacyl-koenzym A dehydrogenase mangel
Icelandic	Natríum (4-{(E)-3-(4-flúorófenýl)-3-[4-(3-morfólín-4-ýl-própýnýl)fenýl]allýloxý}-2-metýlfenoxý)asetat	Meðferð við skorti á langkeðju 3-hýdroxýasýl-Co-A-dehýdrógenasa