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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 mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

On 21 August 2020, orphan designation EU/3/20/2311 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 mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS).

What is mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes?

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) is an inherited disease caused by genetic abnormalities in the mitochondria, the energy-producing components within cells. The disease causes reduced energy production in the cells and can lead to symptoms such as muscle weakness and pain, headaches, loss of appetite, vomiting and seizures (fits) usually in childhood. By the age of 40, most patients experience stroke-like episodes that can lead to vision loss, problems with movement and loss of intellectual function.

The condition is life threatening and debilitating in the long term due to symptoms such as seizures, stroke-like episodes, and the recurring headaches, vomiting and weakness.

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

At the time of designation, MELAS 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).

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What treatments are available?

No satisfactory methods of treatment were authorised in the EU at the time of orphan designation. Patients received supportive therapy to deal with the symptoms.

How is this medicine expected to work?

The medicine is expected to activate a protein known as PGC-1 alpha, which is involved in the production of mitochondria. By activating this protein, it will be able to increase the number of mitochondria in the cells. As a result, it is expected to improve energy production within the cells and improve symptoms of the disease.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

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

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of MELAS 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 mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes
Bulgarian	Натрий (4-{(E)-3-(4-флуорофенил)-3-[4-(3-морфолин-4-ил-пропинил)фенил]алилокси}-2-метилфенокси)ацетат	Лечение на митохондриална енцефаломиопатия, лактатна ацидоза и инсулт подобни епизоди
Croatian	Natrij (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloksi}-2-metilfenoksi)acetat	Liječenje mitohondijske encefalomiopatije, laktične acidoze i epizoda nalik na moždani udar
Czech	(4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolin-4-yl-prop1ynyl)fenyl]allyloxy}-2-methylfenoxy)acetát sodný	Léčba mitochodnriální encefalomyopatie, laktátové acidózy a iktoidní episody
Danish	Natrium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetat	Behandling af MELAS syndrom (mitokondriel myopati, encephalopati, mælkesyreose og slagtilfælde)
Dutch	Natrium(4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetaat	Behandeling van mitochondriale encephalomyopathy, lactaatacidosis en neurologische beroerte-achtige episodes
Estonian	Naatrium (4-{(E)-3-(4-fluorofenüül)-3-[4-(3-morfoliin-4-üül-prop1ünüül)fenüül]allüüloksü}-2-metüülfenoksü)atsetaat	Mitokondriaalse entsefalomüopaatia, laktaatatsidoosi ja insuldisarnaste episoodide ravi
Finnish	Natrium (4 - {(E) -3- (4-fluorofenyyli) -3- [4- (3-morfoliini-4-yyli-prop1ynyyli) fenyyli] allyylioksi} -2-metyylifenoksi) asetaatti	Mitokondriaalisen enkefalomyopatian, maitohappoasidoosin ja kohtauksellisten aivoverenkiertohäiriöitä muistuttaven aivotoiminnan häiriöiden hoito
French	(4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy) acétate de sodium	Traitement de l'encéphalomyopathie mitochondriale, l'acidose lactique et des épisodes stroke-like
German	Natrium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetat	Behandlung von mitochondriale Enzephalopathie, Laktatazidose und Schlaganfall-ähnliche Episoden

[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 μιτοχοχονδριακής εγκεφαλομυοπάθειας, γαλακτικής οξέωσης και επεισοδείων που ομοιάζουν εγκεφαλικών (σύνδρομο MELAS)
Hungarian	Nátrium (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]alliloxi}-2-metilfenoxi)acetát	Mitokondriális enkefalomiopátia, laktátacidózis és stroke-szerű epizódok kezelése
Italian	Sodio (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1ynil)fenil]allilossi}-2-metilphenossi)acetato	Trattamento dell'encefalomiopatia mitocondriale con acidosi lattica ed episodi tipo ictus
Latvian	Nātrija (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolīn-4-il-prop1inil)fenil]alliloksi}-2-metilfenoksi)acetāts	Mitohondriālās encefalomiopātijas, pienskābās acidozes un insultam līdzīgo epizožu ārstēšana
Lithuanian	Natrio (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloksi}-2-metilfenoksi)acetatas	Mitochondrinės encefalomiopatijos, laktatacidozės ir į insultą panašių priepuolių epizodų gydymas
Maltese	Aċetat (4-{(E)-3-(4-fluworofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]allilossi}-2-metilfenossi)tas-sodju	Kura ta' enċefalomijopatija mitokondrijali, aċidożi lattika u episodji li jixbhu lill-attakki ta' puplesija
Polish	(4-{(E)-3-(4-fluorofenylo)-3-[4-(3-morfolino-4-yl-prop1ynyl)fenyl] allyloksy}-2-metylofenoksy) octan sodu	Leczenie zespołu miopatii mitochondrialnej, encefalopatii, kwasicy mleczanowej oraz występowania incydentów podobnych do udarów
Portuguese	Acetato de (4-{(*E*)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-propinil)fenil]aliloxi}-2-metilfenoxi) sódio	Tratamento da encefalomiopatia mitocondrial, acidose lática e episódios do tipo acidente vascular cerebral
Romanian	Sodiu (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloxi}-2-metilfenoxi)acetat	Tratamentul encefalomiopatiei mitocondriale, acidozei lactice şi al episoadelor de tip accident vascular cerebral
Slovak	(4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolín-4-yl-prop1ynyl)fenyl]allyloxy}-2-metylfenoxy)acetát sodný	Liečba mitochondriálnej encefalomyopatie, laktátovej acidózy a infarktu podobných epizód
Slovenian	Natrijev (4-{(E)-3-(4-fluorofenil)-3-[4-(3-morfolin-4-il-prop1inil)fenil]aliloksi}-2-metifenoksi)acetat	Zdravljenje mitohondijske encefalomiopatije, laktacidoze in kapi podobnih epizod

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 encefalomiopatía mitocondrial, acidosis láctica y episodios tipo ictus
Swedish	natrium (4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolin-4-yl-prop1ynyl)fenyl]allyloxy}-2-metylfenoxy)acetat	Behandling av mitokondriell hjärn-och muskelsjukdom med stegrad mjölksyrahalt i blodet och strokeliknande attacker
Norwegian	Natrium(4-{(E)-3-(4-fluorofenyl)-3-[4-(3-morfolin-4-yl-prop-1-ynyl)fenyl]allyloksy}-2-metylfenoksy)acetat	Behandling av mitokondrie encefalomyopati, laktacidose og slagliknende episoder
Icelandic	Natríum (4-{(E)-3-(4-flúórófenýl)-3-[4-(3-morfólín-4-ýl-própýnýl)fenýl]allýloxý}-2-metýlfenoxý)asetat	Meðferð hvatbera heilavöðvakvilla, mjólkursýringu og heilaáfalls- líkum köstum