



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride for the treatment of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

On 10 August 2015, orphan designation (EU/3/15/1543) was granted by the European Commission to Khondrion BV, the Netherlands, for (S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride for the treatment of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes.

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

MELAS is an inherited disease caused by genetic abnormalities in the mitochondria, the energy-producing components within cells. Symptoms of the condition usually appear in childhood and include muscle weakness and pain, headaches, loss of appetite, vomiting and fits (seizures). By the age of 40, most patients experience stroke-like episodes that can lead to brain problems, vision loss and problems with movement.

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 approximately 0.06 in 10,000 people in the European Union (EU). This was equivalent to a total of around 3,000 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).

^{*}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).



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 defects in mitochondria that occur in MELAS are known to result in the production of 'free radicals', molecules that cause damage to cells (known as 'oxidative stress'). The medicine is a small molecule which is capable of entering the cells, where it acts as an antioxidant, reducing oxidative stress. This antioxidant activity is expected to protect cells, thereby reducing the symptoms of the disease.

What is the stage of development of this medicine?

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

At the time of the application for orphan designation, clinical trials with the medicine were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for MELAS. Orphan designation of the medicine had been granted in the United States for treatment of inherited mitochondrial respiratory chain diseases.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 July 2015 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

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride	Treatment of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes
Bulgarian	(S)-6-хидрокси-2,5,7,8-тетраметил-N-((R)-пиперидин-3-ил)хроман-2-карбоксамид хидрохлорид	Лечение на митохондриална енцефаломиопатия, лактацидоза и инсултopodobни пристъпи
Croatian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)kroman-2-karboksamid klorid	Liječenje mitohondrijske encefalomiopatije, laktacidoze i epizoda nalik moždanom udaru
Czech	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-karboxamid hydrochlorid	Léčba mitochondriální encefalomyopatie, laktátové acidózy a stroke-like epizod
Danish	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamidhydrochlorid	Behandling af mitokondriel encefalomyopati, laktatacidose og apopleksilignende episoder
Dutch	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidine-3-yl)chromaan-2-carboxamidehydrochloride	Behandeling van mitochondriële encefalomyopathie, lactaatacidose en stroke (=beroerte)-achtige episodes
Estonian	(S)-6-hüdroksü-2,5,7,8-tetrametüül-N-((R)-piperidiin-3-üül)kromaan-2-karboksamiid hüdrokloriid	Mitokondriaalse entsefalomüopaatia, laktatsidoosi ja insuldisarnaste episoodide ravi
Finnish	(S)-6-hidroksi-2,5,7,8-tetrametyyli-N-((R)-piperidin-3-yyli)kromaani-2-karboksiamidihydrokloridi	Mitokondriaalisen enkefalomyopatian, Maitohappoasidoosin sekä aivohalvauksen kaltaisten episodien hoito
French	Chlorhydrate de (S)-6-hydroxy-2,5,7,8-tétraméthyl-N-((R)-pipéridine-3-yl)chroman-2-carboxamide	Traitement de l'encéphalomyopathie mitochondriale, de l'acidose lactique et des pseudo-épisodes vasculaires cérébraux
German	(S)-6-Hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamidhydrochlorid	Behandlung des Krankheitsbildes der mitochondrialen Enzephalomyopathie mit Laktatazidose und Schlaganfall-ähnlichen Episoden
Greek	υδροχλωρικό (S)-6-υδροξυ-2,5,7,8-τετραμεθυλ-N-((R)-πιπεριδιν-3-υλ)χρωμαν-2-καρβοξαμίδιο	Θεραπεία της μιτοχονδριακής εγκεφαλομυοπάθειας, γαλακτικής οξέωσης και επεισοδίων που μοιάζουν με εγκεφαλικά (σύνδρομο MELAS)
Hungarian	(S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)kromán-2-karboxamid-hidroklorid	Mitokondriális encefalomyopathia, laktát-acidózis és stroke-szerű epizódok kezelése

¹ At the time of designation

Language	Active ingredient	Indication
Italian	(S)-6-idrossi-2,5,7,8-tetrametil-N-((R)-piperidina-3-il)croman-2-carbossamide cloridrato	Trattamento dell'encefalomiopatia mitocondriale, acidosi lattica ed episodi ictus-like
Latvian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidīn-3-il)hromān-2-karboksamīda hidrohlorīds	Mitohondriālas encefalomiopātijas, laktacidozes un insultam līdzīgu epizožu ārstēšana
Lithuanian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)chroman-2-karboksamido hidrochloridas	Mitochondrinės encefalomiopatijos, laktatacidozės ir į insultą panašių epizodų gydymas
Maltese	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride	Kura ta' encefalomijopatija mitokondrijali, acidozi lattika, u episodji simili għal puplesija
Polish	Chlorowodorek (S)-6-hydroksy-2,5,7,8-tetrametylo-N-((R)-piperidyno-3-ylo)chromano-2-karboksyamidu	Leczenie encefalomiopatii mitochondrialnej, kwasicy mleczanowej i incydentów udaropodobnych.
Portuguese	Cloridrato de (S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)croman-2-carboxamida	Tratamento de encefalomiopatia mitocondrial, acidose láctica e episódios do tipo AVC
Romanian	Clorhidrat de (S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)croman-2-carboxamidă	Tratamentul encefalomiopatiei mitocondriale, al acidozei lactice și al pseudo-accidentelor vasculare cerebrale
Slovak	(S)-6-hydroxy-2,5,7,8-tetrametyl-N-((R)-piperidín-3-yl)chróman-2-karboxamid hydrochlorid	Liečba mitochondriálnej encefalomyopatie, laktátovej acidózy a epizód podobných cievnej mozgovej príhode
Slovenian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)kroman-2-karboksamid hidroklorid	Zdravljenje mitohondrijske encefalomiopatije, laktacidoze, in epizod, podobnih možganski kapi
Spanish	(S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)croman-2-carboxamida hidrocloruro	Tratamiento de la encefalomiopatia mitocondrial, acidosis láctica y episodios tipo ictus
Swedish	(S)-6-hydroxi-2,5,7,8-tetrametyl-N-((R)-piperidin-3-yl)kroman-2-karboxamidhydroklorid	Behandling av mitokondriell encefalomyopati, laktatacidos och strokeliknande episoder
Norwegian	(S)-6-hydroksy-2,5,7,8-tetrametyl-N-((R)-piperidin-3-yl)-kroman-2-karboksamid-hydroklorid	Behandling av mitokondriell encefalomyopati, melkesyreacidose, og slagliknende episoder
Icelandic	(S)-6-hýdroxý-2,5,7,8-tetrametyl-N-((R)-píperidín-3-ýl)króman-2-karboxamíð hýdroklóríð	Meðferð við MELAS-heilkenni (hvatberatengdum heila- og vöðvakvilla, mjólkursýrublóðsýringu og heilablóðfallslíkum köstum)