

10 November 2014
EMA/COMP/557459/2014
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 Leigh syndrome

On 15 October 2014, orphan designation (EU/3/14/1336) 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 Leigh syndrome.

What is Leigh syndrome?

Leigh syndrome, also known as subacute necrotising encephalomyelopathy, is an inherited disease of the brain and the nervous system leading to problems such as poor motor function (movement), weakness, lack of muscle tone and difficulty breathing. Symptoms typically start before the age of 12 months. The disease has many genetic causes, all of which are linked to defects in the mitochondria, the energy-producing components within cells, which lead to the death of nerve cells.

Leigh syndrome is debilitating and life threatening due to progressive worsening of nervous system function as well as problems with heart, kidney and hormonal glands.

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

At the time of designation, Leigh syndrome affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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).

What treatments are available?

At the time of designation, there were no satisfactory methods of treatment authorised in the EU for Leigh syndrome. Patients received supportive therapy to deal with the symptoms, such as mechanical support with breathing, vitamins and supplements.

^{*}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 511,100,000 (Eurostat 2014).

How is this medicine expected to work?

The defects in mitochondria that occur in Leigh syndrome 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 cell and acts as an antioxidant, reducing oxidative stress. This antioxidant activity is expected to prevent nerve cell death, 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 submission of the application for orphan designation, no clinical trials with the medicine in patients with Leigh syndrome had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 4 September 2014 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 Leigh syndrome
Bulgarian	(S)-6-хидрокси-2,5,7,8-тетраметил-N-((R)-пиперидин-3-ил)хроман-2-карбоксаμид хидрохлорид	Лечение на синдрома на Leigh
Croatian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)kroman-2- karboksamidklorid	Liječenje Leighovog sindroma
Czech	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-karboxamid hydrochlorid	Léčba syndromu Leigh
Danish	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamidhydrochlorid	Behandling af Leighs syndrom
Dutch	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidine-3-yl)chromaan-2-carboxamidehydrochloride	Behandeling van Leigh syndroom
Estonian	(S)-6-hüdroksü-2,5,7,8-tetrametüül-N-((R)-piperidiin-3-üül)kromaan-2-karboksamiid hüdrokloriid	Leigh sündroomi ravi
Finnish	(S)-6-hydroksi-2,5,7,8-tetrametyyli-N-((R)-piperidin-3-yyli)kromaani-2-karboksiamidihydrokloridi	Leigh:n oireyhtymän hoito
French	Chlorhydrate de (S)-6-hydroxy-2,5,7,8-tétraméthyl-N-((R)-pipéridine-3-yl)chroman-2-carboxamide	Traitement de syndrome de Leigh
German	(S)-6-Hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamidhydrochlorid	Behandlung des Leigh-Syndroms
Greek	υδροχλωρικό (S)-6-υδροξυ-2,5,7,8-τετραμεθυλ-N-((R)-πιπεριδιν-3-υλ)χρωμαν-2-καρβοξαμίδιο	Θεραπεία του συνδρόμου Leigh
Hungarian	(S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)kromán-2-karboxamid-hidroklorid	Leigh-szindróma kezelése
Italian	(S)-6-idrossi-2,5,7,8-tetrametil-N-((R)-piperidina-3-il)croman-2-carbossamide cloridrato	Trattamento della sindrome di Leigh
Latvian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidīn-3-il)hromān-2-karboksamīda hidrohlorīds	Leiga (Leigh) sindroma ārstēšana

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)chroman-2-karboksamido hidrochloridas	Leigh sindromo gydymas
Maltese	(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride	Kura tas-sindrome ta' Leigh
Polish	Chlorowodorek (S)-6-hydroksy-2,5,7,8-tetrametylo-N-((R)-piperydino-3-ylo)chromano-2-karboksyamidu	Leczenie zespołu Leigha
Portuguese	Cloridrato de (S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)croman-2-carboxamida	Tratamento da síndrome de Leigh
Romanian	Clorhidrat de (S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidină-3-il)croman-2-carboxamidă	Tratamentul sindromului Leigh
Slovak	(S)-6-hydroxy-2,5,7,8-tetrametyl-N-((R)-piperidín-3-yl)chróman-2-karboxamid hydrochlorid	Liečba Leighovho syndrómu
Slovenian	(S)-6-hidroksi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)kroman-2-karboksamid hidroklorid	Zdravljenje sindroma Leigh
Spanish	(S)-6-hidroxi-2,5,7,8-tetrametil-N-((R)-piperidin-3-il)croman-2-carboxamida hidrocloruro	Tratamiento del síndrome de Leigh
Swedish	(S)-6-hydroxi-2,5,7,8-tetrametyl-N-((R)-piperidin-3-yl)chroman-2-karboxamidhydroklorid	Behandling av Leighs syndrom
Norwegian	(S)-6-hydroksy-2,5,7,8-tetrametyl-N-((R)-piperidin-3-yl)-kroman-2-karboksamid-hydroklorid	Behandling av Leighs syndrom
Icelandic	(S)-6-hýdroxý-2,5,7,8-tetrametýl-N-((R)-píperidín-3-ýl)króman-2-karboxamíð hýdróklóríð	Meðferð á Leigh heilkenni