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EMA/754098/2017

Public summary of opinion on orphan designation

4-hydroxy-2,2,6,6-tetramethylpiperidine-N-oxyl for the treatment of familial cerebral cavernous malformation

On 12 December 2017, orphan designation (EU/3/17/1948) was granted by the European Commission to Premier Research Group Limited, United Kingdom, for 4-hydroxy-2,2,6,6-tetramethylpiperidine-N-oxyl (also known as Tempol) for the treatment of familial cerebral cavernous malformation.

What is familial cerebral cavernous malformation?

Familial cerebral cavernous malformation is a condition in which patients have clusters of enlarged, abnormal blood vessels in the brain that can cause symptoms such as seizures (fits), headache, weakness of arms or legs, impaired vision, and problems with memory and attention.

The condition is caused by mutations (changes) in certain genes that control the way that blood vessels grow. As a result, patients have blood vessels with thin, fragile walls that leak blood and damage surrounding brain tissue.

Familial cerebral cavernous malformation is a debilitating condition that is long lasting and may be life threatening due to severe bleeding inside the brain.

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

At the time of designation, familial cerebral cavernous malformation affected not more than 3 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 155,000 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 515,700,000 (Eurostat 2017).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

What treatments are available?

At the time of application, no satisfactory methods were authorised in the EU for the treatment of familial cerebral cavernous malformation. Patients were given treatment as required for symptoms such as seizures. Patients with certain symptoms had surgery to remove the abnormal blood vessels.

How is this medicine expected to work?

This medicine is expected to work by reducing oxidative stress, which is thought to be involved in the formation of clusters of abnormal blood vessels. Oxidative stress is when high levels of certain highly reactive molecules in the body damage cells and tissues. By reducing the activity of these molecules, the medicine is expected to reduce the formation of abnormal vessels and thereby improve symptoms of patients with familial cerebral cavernous malformation.

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 familial cerebral cavernous malformation had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for familial cerebral cavernous malformation. Orphan designation had been granted in the United States for cerebral cavernous malformation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 31 October 2017 recommending the granting of this designation.

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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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	4-hydroxy-2,2,6,6-tetramethylpiperidine-N-oxyl	Treatment of familial cerebral cavernous malformations
Bulgarian	4-хидрокси-2,2,6,6-тетраметилпиперидин-N-оксил	Лечение на фамилни церебрални кавернозни малформации
Croatian	4-hidroksi-2,2,6,6-tetrametilpiperidin-N-oksi	Liječenje obiteljskog tipa cerebralnih kavernoznih malformacija
Czech	4-hydroxy-2,2,6,6-tetramethylpiperidin-N-oxyl	Léčba familiární mozkových kavernózní malformací
Danish	4-hydroxy-2,2,6,6-tetramethylpiperidin-N-oxyl	Behandling af familiær cerebral cavernous misdannelser
Dutch	4-hydroxy-2,2,6,6-tetramethylpiperidin-N-oxyl	Behandeling van familiale cerebraal caverneuze malformaties
Estonian	4-hüdroksü-2,2,6,6-tetrametüülpiperidiin-N-oksüül	Perekondliku aju kavernoossete väärarengute ravi
Finnish	4-hydroksi-2,2,6,6-tetrametyylipiperidin-N-oksyyli	Aivoverisuonten suvuttaisen ontelomuodostumia aiheuttavan kehityshäiriön hoito
French	4-hydroxy-2,2,6,6-tétraméthylpipéridine-N-oxyle	Traitement des malformations familiales cérébraux caverneuses
German	4-hydroxy-2,2,6,6-tetramethylpiperidin-N-oxyl	Behandlung von familiären zerebralen kavernösen Fehlbildungen
Greek	4-υδροξυ-2,2,6,6-τετραμεθυλπιπεριδιν-N-οξύλιο	Θεραπεία των οικογενών εγκεφαλικών σηραγγωδών δυσπλασιών
Hungarian	4-hidroxi-2,2,6,6-tetrametil-piperidin-N-oxil	Familiásis agyi cavernosus fejlődési rendellenesség kezelése
Italian	4-idrossi-2,2,6,6-tetrametilpiperidin-N-ossile	Trattamento delle malformazioni cavernose cerebrali familiari
Latvian	4-hidroksi-2,2,6,6-tetrametilpiperidīn-N-oksils	Iedzimtu cerebrālu kavernozu malformāciju ārstēšana
Lithuanian	4-hidroksi-2,2,6,6-tetrametilpiperidin-N-oksilas	Šeiminių smegenų kaverninių malformacijų gydymas
Maltese	4-idrossi-2,2,6,6-tetrametilpiperidina-N-ossil	Kura ta' deformazzjonijiet kavernużi (fil-kapillari) tal-moħħ li jintirtu
Polish	4-hydroksy-2,2,6,6-tetrametylopiperydyno-N-oksyl	Leczenie rodzinnych naczyniaków jamistych mózgu

[1] At the time of designation

Language	Active ingredient	Indication
Portuguese	4-hidroxi-2,2,6,6-tetrametilpiperidin-N-oxil	Tratamento da malformação cavernosa cerebral familiar
Romanian	4-hidroxi-2,2,6,6-tetrametilpiperidin-N-oxil	Tratamentul familiale cerebrale cavernos malformații
Slovak	4-hydroxy-2,2,6,6-tetrametylpiperidín-N-oxyl	Liečba familiárnych mozgových kavernóznych malformácií
Slovenian	4-hidroksi-2,2,6,6-tetrametilpiperidin-N-oksil	Zdravljenje familiarne možganske kavernozne malformacije
Spanish	4-hidroxi-2,2,6,6-tetrametilpiperidin-N-oxilo	Tratamiento de familiares cerebrales cavernosos malformaciones
Swedish	4-hydroxi-2,2,6,6-tetrametylpiperidin-N-oxyl	Behandling av familjär cerebral cavernous missbildningar
Norwegian	4-hydroksy-2,2,6,6-tetrametylpiperidin-N-oksyl	Behandling av familiær cerebral kavernøse malformasjoner
Icelandic	4-hýdroxý-2,2,6,6-tetrametýlpíperidín-N-oxýl	Meðferð ættgengs heila holu vansköpunar