



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public summary of opinion on orphan designation

2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)]amino-N-(4-chlorocinnamyl)-N-methylbenzylamine for the treatment of Charcot-Marie-Tooth disease

On 16 October 2017, orphan designation (EU/3/17/1915) was granted by the European Commission to Repositioning SAS, France, for 2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)]amino-N-(4-chlorocinnamyl)-N-methylbenzylamine (also known as KN-93) for the treatment of Charcot-Marie-Tooth disease.

What is Charcot-Marie-Tooth disease?

Charcot-Marie-Tooth disease is a group of inherited disorders of the peripheral nerves (the nerves outside the brain and spinal cord). The symptoms include muscle weakness, tremor and sensory loss (numbness, tingling, burning sensation), and usually first appear in the first or second decade of life.

The disease can be caused by many different mutations (changes) in the genes responsible for producing proteins essential for the make up of the peripheral nerves. Because of these mutations, the peripheral nerves are damaged and this leads to problems in the transmission of nerve signals.

Charcot-Marie-Tooth disease is a long-term debilitating disease because the progressive deterioration of nerves leads to disability and reduced quality of life.

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

At the time of designation, Charcot-Marie-Tooth disease affected approximately 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 134,000 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).



What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for the treatment of Charcot-Marie-Tooth disease. Supportive treatments were available such as pain medications, physical therapy and corrective surgery.

How is this medicine expected to work?

The medicine blocks the action of a protein called calmodulin-dependent protein kinase II (CaMKII). The amount of CaMKII is too high in certain patients with Charcot-Marie-Tooth disease, which causes damage to myelin, a substance that surrounds nerves and helps them transmit nerve signals. By blocking CaMKII activity, the medicine is expected to reduce damage to myelin and relieve 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 Charcot-Marie-Tooth disease had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Charcot-Marie-Tooth disease 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 7 September 2017 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:

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)amino-N-(4-chlorocinnamyl)-N-methylbenzylamine	Treatment of Charcot-Marie-Tooth disease
Bulgarian	2-[N-(2-хидроксиетил)]-N-(4-метоксибензенесулфонил)амино-N-(4-хлороцинамил)-N-метилбензиламин	Лечение на болест на Шарко-Мари-Тут
Croatian	2-[N-(2-hidroksietil)]-N-(4-metoksibenzenesulfonyl)amino-N-(4-klorocinamil)-N-metilbenzilamin	Liječenje Charcot-Marie-Tothove bolesti
Czech	2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)amino-N-(4-chlorocinnamyl)-N-methylbenzylamin	Léčba Charcot-Marie-Tooth choroby
Danish	2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)amino-N-(4-chlorocinnamyl)-N-methylbenzylamin	Behandling af Charcot-Marie-Tooth sygdom
Dutch	2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)amino-N-(4-chlorocinnamyl)-N-methylbenzylamine	Behandeling van Ziekte van Charcot-Marie-Tooth
Estonian	2-[N-(2-hüdroksüetüül)]-N-(4-metoksübenzeensulfonyl)amino-N-(4-klorotsinnamüül)-N-metüülbenzülamiin	Charcot-Marie-Toothi haiguse ravi
Finnish	2-[N-(2-hydroksietyyli)]-N-(4-metoksibentseenisulfonyyli)amino-N-(4-klorosinnamyyli)-N-metyylibensyyliamini	Charcot-Marie-Toothin taudin hoito
French	2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)amino-N-(4-chlorocinnamyl)-N-methylbenzylamine	Traitement de la maladie de Charcot-Marie-Tooth
German	2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)amino-N-(4-chlorocinnamyl)-N-methylbenzylamin	Behandlung des Morbus Charcot-Marie-Tooth
Greek	2-[N-(2-υδροξυαιθυλ)]-N-(4-μεθοξυβενζενισουλφονυλ)αμινο-N-(4-χλωροκινναμυλ)-N-μεθυλβενζυλαμίνη	Θεραπεία της περονιαίας μυϊκής ατροφίας (Charcot-Marie-Tooth)
Hungarian	2-[N-(2-hidroxietyl)]-N-(4-metoxibenzénsulfonyl)amino-N-(4-klorocinamil)-N-metilbenzilamin	Charcot-Marie-Tooth-betegség kezelése
Italian	2-[N-(2-idrossietil)]-N-(4-metossibenzenesulfonyl)amino-N-(4-clorocinamil)-N-metilbenzilamina	Tattamento della malattia di Charcot-Marie-Tooth
Latvian	2-[N-(2-hidroksietil)]-N-(4-metoksibenzēnsulfonyl)amino-N-(4-hlorocinamil)-N-metilbenzilamīns	Charcot-Marie-Tooth slimības (jeb iedzimtas neiralģiskās amiotrofijas) ārstēšana

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	2-[N-(2-hidroksietil)]-N-(4-metoksibenzosulfonil)]amino-N-(4-chlorocinamil)-N-metilbenzilaminas	Šarko–Mari–Tuto ligos gydymas
Maltese	2-[N-(2-idrossietil)]-N-(4-metossibenzensulfonil)]ammino-N-(4-kloroċinnamil)-N-metilbenžilamina	Kura tal-marda ta' Charcot-Marie-Tooth
Polish	2-[N-(2-hydroksyetylo)]-N-(4-metoksybenzenosulfonylo)]amino-N-(4-chlorocynamylo)-N-metylbenzylamina	Leczenie choroby Charcota, Mariego i Tootha
Portuguese	2-[N-(2-hidroxietyl)]-N-(4-metoxibenzosulfonil)]amino-N-(4-clorocinamil)-N-metilbenzilamina	Tratamento da doença de Charcot-Marie-Tooth
Romanian	2-[N-(2-hidroxietyl)]-N-(4-metoxibenzensulfonil)]amino-N-(4-clorocinamil)-N-metilbenzilamină	Tratamentul bolii Charcot-Marie-Tooth
Slovak	2-[N-(2-hydroxyethyl)]-N-(4-metoxybenzénésulfonyl)]amino-N-(4-chlorocinnamyl)-N-metylbenzylamín	Liečba Charcotovej-Marieovej-Toothovej choroby
Slovenian	2-[N-(2-hidroksi)]-N-(4-metoksibenzensulfonil)]amino-N-(4-klorocinamil)-N-metilbenzilamin	Zdravljenje Charcot-Marie-Toothove bolezni
Spanish	2-[N-(2-hidroxietyl)]-N-(4-metoxibenzosulfonil)]amino-N-(4-clorocinamil)-N-metilbenzilamina	Tratamiento de la enfermedad de Charcot-Marie-Tooth
Swedish	2-[N-(2-hydroxyethyl)]-N-(4-metoxybenzenesulfonyl)]amino-N-(4-chlorocinnamyl)-N-metylbenzylamin	Behandling av Charcot-Marie-Tooths sjukdom
Norwegian	2-[N-(2-hydroksyetyl)]-N-(4-metoksybenzensulfonyl)]amino-N-(4-klorocinnamyl)-N-metylbenzylamine	Behandling av Charcot-Marie-Tooths sykdom
Icelandic	2-[N-hýdroxyetýl)]-N-(4-metoxýbenzensúlfónýl)]amínó-N-(4-klórócinamýl)-N-metýlbenzýlamín	Meðferð við Charcot-Marie-Tooth sjúkdómi