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EMA/COMP/94332/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Fixed-dose combination of (R-S) baclofen, naltrexone hydrochloride and D-sorbitol for the treatment of Charcot-Marie-Tooth disease type 1A

On 26 March 2014, orphan designation (EU/3/14/1260) was granted by the European Commission to Pharnext SAS, France, for fixed-dose combination of (R-S) baclofen, naltrexone hydrochloride and D-sorbitol for the treatment of Charcot-Marie-Tooth disease type 1A.

What is Charcot-Marie-Tooth disease type 1A?

Charcot-Marie-Tooth disease (CMT) is a group of inherited disorders of the nervous system. The symptoms include muscle weakness, tremor and sensory loss (identifiable as numbness, tingling, burning sensation), and usually first appear in the first or second decade of life.

CMT is classified in 5 groups and one of them, CMT1, is by far the most common form of the disease. Approximately 70%-80% of CMT1 patients have the type called CMT1A, which is caused by an extra copy of the gene responsible for producing the protein PMP22. This protein is a component of myelin (the protective sheath around nerves). Patients with CMT1A produce too much PMP22, and this causes the structure and function of the myelin sheath to be abnormal and leads to problems in the transmission of nerve signals.

CMT1A 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, CMT1A affected approximately 1.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 72,000 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 511,100,000 (Eurostat 2014).

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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for the treatment of CMT1A. Supportive treatments were available such as pain medications, physical therapy and corrective surgery.

How is this medicine expected to work?

This medicine consists of a low-dose combination of three substances: (R-S) baclofen, naltrexone hydrochloride and D-sorbitol, which are thought to act in different ways to limit the production of PMP22 in patients with CMT1A. The combined actions of the three substances are expected to help improve the function of the myelin sheath, improving signal transmission between nerve cells and relieving 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, clinical trials with the medicine in patients with CMT1A were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for CMT1A or designated as an orphan medicinal product elsewhere for this condition. The three individual components of the medicine have been individually authorised at higher doses in the EU for other indications.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 February 2014.

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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:

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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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Fixed-dose combination of (R-S) baclofen, naltrexone hydrochloride and D-sorbitol	Treatment of Charcot-Marie-Tooth disease type 1A
Bulgarian	комбинация с фиксиранаи дози от (R-S) баклофен, налтрексон хидрохлорид и D-сорбитол	Лечение на болест на Шарко-Мари-Тут тип 1А
Czech	Fixní kombinace (R-S) baclofenu,naltrexonu hydrochloridu a D-sorbitolu,	Léčba Charcot-Marie-Tooth choroby typu 1A
Croatian	Fiksna kombinacija (RS)-baklofena, naltreksonklorida i D-sorbitola	Liječenje Charcot-Marie-Tothove bolesti tip 1A
Danish	Fast dosis kombination af (R-S) baclofen, naltrexon hydroklorid og D-sorbitol	Behandling af Charcot-Marie-Tooth sygdom type 1A
Dutch	Vast combinatiepreparaat van (R-S) baclofen, naltrexone hydrochloride en D-sorbitol	Behandeling van Ziekte van Charcot-Marie- Tooth type 1A
Estonian	Fikseeritud doosiga kombinatsioon (R-S) baklofeenist, naltreksoonhüdrokloriidist ja D-sorbitoolist	1A tüüpi Charcot-Marie-Toothi haiguse ravi
Finnish	(R-S)-baklofeenin, naltreksonihydrokloridin ja D-sorbitolin kiinteä yhdistelmä	Tyypin 1A Charcot-Marie-Toothin taudin hoito
French	Combinaison de baclofen (R-S), chlorhydrate de naltrexone et Sorbitol D à dose fixe	Traitement de la maladie de Charcot-Marie-Tooth de type 1A
German	Kombinationspräparat aus (R-S) Baclofen, Naltrexonhydrochlorid und D-Sorbitol	Behandlung des Morbus Charcot-Marie-Tooth Typ 1A
Greek	Συνδυασμός σταθερής δόσης (R-S) Βακλοφαίνης, υδροχλωρικής ναλτρεξόνης και D-σορβιτόλης	Θεραπεία της περονιαίας μυϊκής ατροφίας τύπου 1Α
Hungarian	(R-S)baklofen, naltrexon HCl és D-szorbitol fix-dózisú kombinációban	1A-. típusú Charcot-Marie-Tooth-betegség kezelése
Italian	Combinazione a dosaggio fisso di (R-S) baclofene, naltrexone cloridrato e D-sorbitolo	Trattamento della malattia di Charcot-Marie-Tooth di tipo 1A
Latvian	(R-S) baklofēna, naltreksona hidrohlorīda un D-sorbitola fiksētu devu kombinācija	1A tipa Charcot-Marie-Tooth slimības (jeb iedzimtas neiralģiskās amiotrofijas) ārstēšana
Lithuanian	(R-S) baklofeno, naltreksono hidrochlorido ir D – sorbitolio fiksuotos dozės derinys	Šarko – Mari – Tuto ligos I A tipo gydymas
Maltese	(R-S) baclofen, naltrexone hydrochloride u D-sorbitol magħqudin f'doża fissa	Kura tal-marda ta' Charcot-Marie-Tooth tat-tip 1A

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Preparat złożony o ustalonych dawkach (R-S) baklofenu, chlorowodorku naltreksonu i D-sorbitolu	Leczenie typu 1A choroby Charcota, Mariego i Tootha
Portuguese	Combinação fixa de (R-S) baclofeno, cloridrato de naltrexona e D-sorbitol	Tratamento da doença de Charcot-Marie-Tooth, Tipo 1A
Romanian	Combinaţie in doza fixa de (R-S) baclofen, clorhidrat de naltrexonă şi D-sorbitol	Tratamentul bolii Charcot-Marie-Tooth de tip 1 A
Slovak	Kombinácia fixnej dávky (R-S) baklofenu, chloridu naltrexonu a D-sorbitolu	Liečba Charcotovej-Marieovej-Toothovej choroby typu 1A
Slovenian	Kombiniran fiksni odmerek (R-S) baklofena, naltreksonijevega hidroklorida in D-sorbitola	Zdravljenje Charcot-Marie-Toothove bolezeni tipa 1 A
Spanish	Combinacion fija de (R-S) baclofeno, cloridrato de naltrexona e D-sorbitol	Tratamiento de la enfermedad de Charcot-Marie-Tooth tipo 1A
Swedish	Kombinationspreparat innehållande (R-S) baklofen, naltrexonhydroklorid och D-sorbitol	Behandling av Charcot-Marie-Tooths sjukdom av typ 1A
Norwegian	Kombinasjonspreparat med (R-S) baklofen, naltreksonhydroklorid og D-sorbitol	Behandling av Charcot-Marie-Tooths sykdom type 1A
Icelandic	Blanda í föstum skammti af baklófeni, naltrexón hýdróklóríði og D-sorbitóli	Meðferð við Charcot-Marie-Tooth gerð 1A sjúkdómi