27 March 2017
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Public summary of opinion on orphan designation

26 base synthetic single-stranded fully phosphorothioated 2'-O-methyl-RNA and DNA mixmer oligonucleotide-based compound for the treatment of Dravet syndrome

On 27 February 2017, orphan designation (EU/3/17/1829) was granted by the European Commission to EirGen Pharma Limited, Ireland, for 26 base synthetic single-stranded fully phosphorothioated 2'-O-methyl-RNA and DNA mixmer oligonucleotide-based compound (also known as CUR-1916) for the treatment of Dravet syndrome.

What is Dravet syndrome?

Dravet syndrome, also called severe myoclonic epilepsy of infancy (SMEI), is a severe form of epilepsy that affects children and adults. It is caused by defects in genes required for the proper function of brain cells.

In Dravet syndrome, the seizures (fits) begin in the first year of life, and are most often associated with a high temperature (febrile convulsions). Later, other types of seizures typically occur, including status epilepticus (seizure lasting at least 5 minutes and requiring emergency medical care). From the age of 2 years, the child's development begins to decline or reverse, leading to problems such as impaired mental and motor (movement) skills.

Dravet syndrome is debilitating in the long term because of the poor development of mental and motor skills. It is also life threatening particularly because of the occurrence of major seizures.

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

At the time of designation, Dravet syndrome affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 26,000 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 designation, the medicine Diacomit (stiripentol) was authorised in the EU as add-on treatment for generalised tonic-clonic seizures (major fits, including loss of consciousness) in children with Dravet syndrome. Various epilepsy medicines were used to prevent fits and to treat long-lasting fits.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Dravet syndrome because laboratory studies showed that it may improve mental and motor skills and anxiety. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Most patients with Dravet syndrome have defects (mutations) in a gene called *SCN1A*. This gene is responsible for the production of proteins (voltage-gated sodium channels) that control transmission of electrical impulses within the brain.

This medicine is made of a small strand of synthetic genetic material. When injected into the space that surrounds the spinal cord, the medicine is expected to attach to genetic material inside brain cells and thereby increase the production of voltage-gated sodium channels. This is expected to restore normal electrical activity in the brain and hence improve not only seizures but also other symptoms of Dravet syndrome.

What is the stage of development of this medicine?

The effects of this 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 Dravet syndrome had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Dravet 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 19 January 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	26 base synthetic single-stranded fully phosphorothioated 2'-O-methyl-RNA and DNA mixmer oligonucleotide-based compound	Treatment of Dravet syndrome
Bulgarian	Синтетично олигонуклеотидно съединение на едноверижна, напълно фосфоротиоирана 2'-О-метил-РНК и миксмер на ДНК , съдържащо се от 26 бази	Лечение на синдром на Dravet
Croatian	Sintetski, jednolančani potpuno fosforotiolirani 2'-O-metil-RNA i DNA miksmer baziran na oligonukleotidu spoj, dužine od 26 baza	Liječenje Dravetovog sindroma
Czech	26-bazový syntetický, jednovláknový, plně phosphorothioated 2'-O-methyl-RNA a DNA mixmer oligonukleotidová na bázi sloučeniny	Léčba Dravetova syndromu
Danish	En 26 baser, syntetisk, enkeltstrenget, fuldt phosphorthioleret 2'-O-methyl-RNA og DNA mixmer oligonukleotid-baseret forbindelse.	Behandling af Dravet syndrom
Dutch	26 basen synthetische, enkelstrengs, volledig phosphorothioated 2'-O-methyl-RNA-en DNA-oligonucleotide mixmer gebaseerde verbinding	Behandeling van het syndroom van Dravet
Estonian	26-aluspaariline sünteetiline üheahelaline täielikult fosforotioaaditud 2'-O-metüül-RNA ja DNA mixmeri oligonukleotiidil baseeruv ühend	Dravet' sündroomi ravi
Finnish	26 emästä sisältävä, synteettinen, yksijuosteinen, täysin fosforotioaattimuodossa oleva 2'-O-metyyli-RNA-ja DNA-mixmer oligonukleotidi-pohjainen yhdiste	Dravet'n oireyhtymän hoito
French	Oligonucléotidemixmer de 26 bases, synthétique simple brin, entièrement sous forme de phosphorothioate 2'-O-méthyl-ARN et ADN.	Traitement du syndrome de Dravet
German	Eine synthetische einzelsträngige, vollständig phosphorthioierte 26 Basen oligonukleotid-basierte Verbindung aus 2'-O-Methyl-RNA und DNA Mixmer.,	Behandlung des Dravet-Syndroms
Greek	Ένωση βασισμένη σε ένα συνθετικό, μονόκλωνο, πλήρως φωσφοροθειοϊκό 2'-Ο-μεθυλο-RNA και DNA μεικτό ολιγονουκλεοτιδιο μήκους 26 βάσεων	Θεραπεία συνδρόμου Dravet
Hungarian	26 bázis hosszúságú szintetikus, egyszálú, teljesen phosphorothioált 2'-O-metil-RNS és DNS mixmer oligonukleotid-alapú vegyület	Dravet-szindróma kezelése
Italian	Oligonucleotide sintetico misto 2'-O-metil-RNA e DNA, a singolo filamento, completamente tiofosfato, di 26 basi di lunghezza	Trattamento della sindrome di Dravet
Latvian	26 bāžu uz sintētiska vienķēdes pilnībā fosfortioātizēta 2'-O-metil-RNS un DNS miksmēra oligonukleotīda balstīts savienojums	Draveta sindroma ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	26-ių bazių sintetinis, viengrandis, visiškai fosforotiorilintas 2'-O-metil-RNR ir DNR oligonukleotidų mišiniu paremtas junginys	*Dravet* sindromo gydymas
Maltese	26 bażi sintetika bi strand waħda fosforotioata kompletament 2'-O-methyl-RNA u DNA mixmer kompost b'bażi ta 'oligonucleotide	Kura tas-sindrome ta' Dravet
Polish	26-zasadowy, syntetyczny, jednoniciowy, w pełni fosforotiolowany mixmer oligonukleotydów 2'-O-metyl-RNA i DNA	Leczenie zespołu Draveta
Portuguese	Estrutura de cadeia simples composta por 26 oligonucleotídeos 2'-O-metil-RNA fosforotioato e DNA *mixmer*	Tratamento da síndrome de Dravet
Romanian	Oligonucleotid sintetic mixt 2'-O-metil-ARN si ADN, cu filament unic, complet sub formă de tiofosfat, cu lungimea de 26 de baze	Tratamentul sindromului Dravet
Slovak	26 bázová syntetická jednovláknová plne fosfotiovaná oligonukleotidová zlúčenina na báze 2'-O-metyl-RNA a DNA mixmeru	Liečba Dravetovej syndrómu
Slovenian	26-bazna sintetična enoverižna, v celoti fosforotioatizirana 2'-O-metil-RNK in DNK miksmer, spojina na oligonukleotidni osnovi	Zdravljenje Dravetovega sindroma
Spanish	Estrutura de cadena simple compuesta por 26 oligonucleotídeos 2'-O-metil-RNA fosforotioato e DNA *mixmer*	Tratamiento del síndrome de Dravet
Swedish	26 bassyntetisk, enkelsträngad, fullt phosphorothioated 2'-O-metyl-RNA och DNA mixmer oligonukleotid-baserad förening	Behandling av Dravets syndrom
Norwegian	26 base syntetisk, enkeltkjedet, fullt fosforotioert 2'-O-metyl-RNA og DNA miksmer oligonukleotid-basert forbindelse	Behandling av Dravet-syndrom
Icelandic	26 basa einkeðju að fullu fosfóróthíóerað 2'-Ó-methýl-RNA og DNA mixmer fánúkleótíð-baserað	Meðferð við Dravet heilkenni