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Public summary of opinion on orphan designation

1-(2,2-diphenyltetrahydrofuran-3-yl)-N,N-dimethylmethanamine hydrochloride for the treatment of Rett syndrome

On 21 August 2019, orphan designation EU/3/19/2195 was granted by the European Commission to Anavex Germany GmbH, Germany, for 1-(2,2-diphenyltetrahydrofuran-3-yl)-N,N-dimethylmethanamine hydrochloride (also known as ANAVEX2-73) for the treatment of Rett syndrome.

What is Rett syndrome?

Rett syndrome is a genetic disease characterised by intellectual disability as well as by loss of speech and of acquired skills between 6 and 18 months of age. Other features include difficulty breathing, irregular heartbeat, gradual loss of the ability to move, feeding difficulties, sleeping problems, constipation, repetitive hand movements and seizures (fits).

The syndrome is caused by spontaneous mutations (changes) in the *MECP2* gene and is not passed on from the parents. The *MECP2* gene is important for the normal functioning of nerve cells. It is found on the X chromosome, one of the two chromosomes (X and Y) that determine a person's sex. Rett syndrome occurs almost exclusively in girls (who have two X chromosomes), as baby boys (who have only one X chromosome) do not usually survive.

Rett syndrome is a debilitating and life-threatening disease mainly because of problems with breathing and heart rhythm.

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

At the time of designation, Rett syndrome affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 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 518,400,000 (Eurostat 2019).

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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for treating Rett syndrome. Girls with the disease were given physiotherapy, speech therapy and nutritional support to help relieve the symptoms of the disease. Medicines were used to manage seizures, heart rhythm disturbances, breathing problems, heartburn and constipation.

How is this medicine expected to work?

The medicine attaches to sigma-1 receptors, which are involved in protecting nerve cells from damage and inflammation. Sigma-1 receptors have been shown to play a role in Rett syndrome. The medicine is expected to activate sigma-1 receptors thereby restoring normal cell functioning. This medicine is expected to improve survival and functioning of nerve cells and thereby improve patients' symptoms.

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 Rett syndrome were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of Rett syndrome. Orphan designation had been granted in the United States for Rett syndrome.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 18 July 2019, 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.

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	1-(2,2-diphenyltetrahydrofuran-3-yl)-N,N-dimethylmethanamine hydrochloride	Treatment of Rett syndrome
Bulgarian	1-(2, 2-дифенилтетрахидрофуран-3-ил)-N, N-диметилметамин хидрохлорид)	Лечение на синдром на Rett
Croatian	1-(2, 2-dipheniltetrahidrofuran-3-il)-N, N-dimetilmetanamin hidroklorid)	Liječenje Rettovog sindroma
Czech	1-(2, 2-difenyltetrahydrofuran-3-yl)-N, N-dimethylmethanamin hydrochlorid	Léčba Rett-syndromu
Danish	1-(2, 2-diphenyltetrahydrofuran-3-YL)-N, N-dimethylmethaninhydrochlorid)	Behandling af Rett syndrom
Dutch	1-(2, 2-diphenyltetrahydrofuran-3-YL)-N, N-dimethylmethanamine hydrochloride)	Behandeling van het Syndroom van Rett
Estonian	1-(2, 2-difenüültetrahüdrofuran-3-ÜÜL)-N, N-dimetüülmethanamiinvesinikkloriid	Rett' sündroomi ravi
Finnish	1-(2, 2-difenyylitetrahydrofuraani-3-YYLI)-N, N-dimetyylimetenamiini hydrokloridi)	Rettin oireyhtymän hoito
French	1-(2, 2-diphényltétrahydrofurane-3-YL)-N, N-chlorhydrate de diméthylméthanamine)	Traitement du syndrome de Rett
German	1-(2,2-Diphenyltetrahydrofuran-3-YL)-N, N-dimethylmethanamin Hydrochlorid)	Behandlung des Rett-Syndroms
Greek	1-(2, 2-διφαινυλοτετραϋδροφολο-3-υλ)-N, N-διμεθυλομεθαμίνη υδροχλωρική	θεραπεία του συνδρόμου Rett
Hungarian	1-(2,2-difenil-tetrahidrofurán-3-Il)-N, N-dimetil-metanamin-hidroklorid)	Rett szindróma kezelése
Italian	1-(2, 2-difenilltetraidrofurano-3-il)-N, N-dimetilmetanamina cloridrato)	Trattamento della sindrome di Rett
Latvian	1-(2,2-difeniltetrahidrofurāna3-IL)-N, N-dimetilmetanamīna hidrohlorīds	Retta sindroma terapija
Lithuanian	1-(2,2 '-difeniltetrahidrofurano-3-il)-N, N-dimetilmetanamino hidrochloridas)	Rett'o sindromo gydymas
Maltese	1-(2, 2-difeniltetraidrofuran-3-YL)-N, N-dimetilmetanamina kloridrata)	Kura tas-sindrome ta' Rett
Polish	chlorowodorek 1-(2, 2-difenylotetrahydrofuran-3-yL)-N, N-dimetylometanaminy)	Leczenie zespołu Retta
Portuguese	Cloridrato de 1-(2, 2-difeniltetra-hidrofuran-3-il)-N,N-dimetilmetanamina	Tratamento do síndrome de Rett
Romanian	Clorhidrat de 1-(2, 2-difeniltetrahidrofuran-3-il)-N, N-dimetilmetanamină	Tratamentul sindromului Rett
Slovak	1-(2, 2-difenyltetrahydrofuran-3-YL)-N, N-dimetylmetanamín hydrochlorid)	Liečba Rettovho syndrómu

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	1-(2, 2-difeniltetrahidrofuran-3-Il)-N, N-dimetilmetanamin hidroklorid)	Zdravljenje Rettovega sindroma
Spanish	1-(2, 2-difeniltetrahidrofurano-3-YL)-N, clorhidrato de N-dimethylmethanamine)	Tratamiento del síndrome de Rett
Swedish	1-(2, 2-difenyltetrahydrofuran-3-YL)-N, N-dimetylmetanaminhydroklorid)	Behandling av Rett syndrom
Norwegian	1-(2,2-difenyltetrahydrofuran-3-yl)-N,N-dimetylmetanaminhydroklorid)	Behandling av Retts syndrom
Icelandic	1-(2, 2-diphenyltetrahydrofuran-3-YL)-N, N-dímetýlmetanín hýdróklóríð)	Meðferð á Rett heilkenni