15 March 2019
EMADOC-628903358-233

Public summary of opinion on orphan designation

Mercaptamine-pantetheine disulfide for the treatment of Rett syndrome

On 11 January 2019, orphan designation (EU/3/18/2128) was granted by the European Commission to Thiogenesis Therapeutics S.A.R.L., France, for mercaptamine-pantetheine disulfide for the treatment of Rett syndrome.

What is Rett syndrome?

Rett syndrome is a 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, a gradual loss of the ability to move, feeding difficulties, sleeping problems, constipation, repetitive hand movements and seizures (fits).

The syndrome is most commonly 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. This gene is in 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).

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

[*]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 517,400,000 (Eurostat 2018).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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?

Mercaptamine-pantetheine disulfide breaks down gradually to cysteamine, which has several protective actions in the body. It may also be involved in increasing the release of a protein called brain-derived neurotrophic factor (BDNF). Nerve cells need BDNF to help them grow and develop, but BDNF may be reduced in the brain of patients with mutations in the *MECP2* gene. By increasing the release of BDNF, 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 mercaptamine-pantetheine disulfide 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 Rett syndrome had been started.

At the time of submission, mercaptamine-pantetheine disulfide was not authorised anywhere in the EU for Rett 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 6 December 2018 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 the 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 orphan condition in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Mercaptamine-pantetheine disulfide	Treatment of Rett syndrome
Bulgarian	Меркаптамин-пантетеин дисулфид	Лечение на синдром на Rett
Croatian	Merkaptamin-pantetein disulfid	Liječenje Rettovog sindroma
Czech	Merkaptamin-pantethein asymetrického sulfidu	Léčba Rett-syndromu
Danish	Mercaptamin-pantetheindisulfid	Behandling af Rett syndrom
Dutch	Mercaptamine-pantetheïne disulfide	Behandeling van het Syndroom van Rett
Estonian	Merkaptamiinpanteteiindisulfiid	Rett' sündroomi ravi
Finnish	Merkaptamiini-panteteiini disulfidi	Rettin oireyhtymän hoito
French	Disulfure asymétrique mercaptamine-pantéthéine	Traitement du syndrome de Rett
German	Mercaptamin-Pantethein Disulfid	Behandlung des Rett-Syndroms
Greek	Μερκαπταμίνη-παντεθείνη ασύμμετρο δισουλφίδιο	θεραπεία του συνδρόμου Rett
Hungarian	Merkaptamin-pantethein diszulfid	Rett szindróma kezelése
Italian	Disolfuro asimmetrico di mercaptamina-panteteina	Trattamento della sindrome di Rett
Latvian	Merkaptamīna-panteteīna disulfīds	Retta sindroma terapija
Lithuanian	Merkaptamino-panteteino disulfidas	Rett'o sindromo gydymas
Maltese	Merkaptamina-panteteina disulfid	Kura tas-sindrome ta' Rett
Polish	Asymetryczny dwusiarczek merkaptaminy-panteteiny	Leczenie zespołu Retta
Portuguese	Mercaptamina-pantefeína dissulfido	Tratamento do síndrome de Rett
Romanian	Mercaptamină-panteteină disulfid	Tratamentul sindromului Rett
Slovak	Merkaptamín-panteteín asymetrického sulfidu	Liečba Rettovho syndrómu
Slovenian	Merkaptamin pantetein disulfid	Zdravljenje Rettovega sindroma
Spanish	Disulfuro asimétrico de mercaptamina-pantetheine	Tratamiento del síndrome de Rett
Swedish	Merkaptamin-pantetein asymmetrisk disulfid	Behandling av Rett syndrom
Norwegian	Merkaptamin-pantetein asymmetrisk disulfid	Behandling av Retts syndrom
Icelandic	Mercaptamín-pantethein tvísúlfíð	Meðferð á Rett heilkenni

[1] At the time of designation