30 September 2015
EMA/COMP/494145/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Glycyl-L-2-methylprolyl-L-glutamic acid for the treatment of Rett syndrome

On 10 August 2015, orphan designation (EU/3/15/1534) was granted by the European Commission to QRC Consultant Ltd., United Kingdom, for glycyl-L-2-methylprolyl-L-glutamic acid 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 regression of acquired skills between 6 and 18 months of age. Other symptoms 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 caused by abnormalities in the *MECP2* gene, which 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 the gender. Rett syndrome is seen almost exclusively in girls (who have two X chromosomes), as the male babies (who have only one X chromosome) do not usually survive. Although the disease is genetic, most girls affected (over 95%) do not inherit it from their parents.

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

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

At the time of designation, Rett syndrome affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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 512,900,000 (Eurostat 2015).

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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 to control seizures were also used, as well as laxatives and painkillers.

How is this medicine expected to work?

This medicine is made up of a molecule derived from a protein in the body called insulin-like growth factor 1 (or IGF-1), which is important for the correct development and functioning of the nervous system. In Rett syndrome, IGF-1 in the brain is lower than normal and it is thought that nerve function is affected as a result. This medicine is expected to restore IGF-1 activity in the brain, thus restoring normal functioning of brain cells and improving 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, a clinical trial with the medicine in patients with Rett syndrome had been completed.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 July 2015 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:

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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	Glycyl-L-2-methylprolyl-L-glutamic acid	Treatment of Rett syndrome
Bulgarian	Глицил-L-2-метилпропил-L-глутаминова киселина	Лечение на синдром на Rett
Croatian	Glicil-L-2-metilprolil-L-glutamatna kiselina	Liječenje Rettovog sindroma
Czech	Glycyl-L-2-methylprolyl-L-glutamová kyselina	Léčba Rett-syndromu
Danish	Glycyl-L-2-methylprolyl-L-glutaminsyre	Behandling af Rett syndrom
Dutch	Glycyl-L-2-methylprolyl-L-glutaminezuur	Behandeling van het Syndroom van Rett
Estonian	Glütsüül-L-2-metüülprolüül-L-glutamiinhape	Rett' sündroomi ravi
Finnish	Glysyyli-L-2-metyyliprolyyli-L-glutamiinihappo	Rettin oireyhtymän hoito
French	Acide glycyl-L-2-méthylprolyl-L- glutamique	Traitement du syndrome de Rett
German	Glycyl-L-2-Methylprolyl-L-Glutaminsäure	Behandlung des Rett-Syndroms
Greek	Γλυκυλ-L-2-μεθυλπρολυλ-L-γλουταμινικό οξύ	θεραπεία του συνδρόμου Rett
Hungarian	Glicil-L-2-metilprolil-L-glutámsav	Rett szindróma kezelése
Italian	Acido glicil-L-2-metilprolil-L-glutammico	Trattamento della sindrome di Rett
Latvian	Glicil-L-2-metilprolil-L-glutamīnskābe	Retta sindroma terapija
Lithuanian	Glicil-L-2-metilprolil-L-glutamo rūgštis	Rett'o sindromo gydymas
Maltese	Glycyl-L-2-methylprolyl-L-glutamic acid	Kura tas-sindrome ta' Rett
Polish	Kwas glicylo-L-2-metylo prolilo-L-glutaminowy	Leczenie zespołu Retta
Portuguese	Ácido glicil-L-2-metilpropil-L-glutâmico	Tratamento do síndrome de Rett
Romanian	Acid glicil-L-2-metilprolil-L-glutamic	Tratamentul sindromului Rett
Slovak	Glycyl-L-2-methylprolyl-L-glutamová kyselina	Liečba Rettovho syndrómu
Slovenian	Glicil-L-2-metilpropil-L-glutaminska kislina	Zdravljenje Rettovega sindroma
Spanish	Ácido glicil-L-2-metilprolil-L-glutámico	Tratamiento del síndrome de Rett
Swedish	Glycyl-L-2-metylprolyl-L-glutaminsyra	Behandling av Rett syndrom
Norwegian	Glycyl-L-2-metylprolyl-L-glutaminsyre	Behandling av Retts syndrom
Icelandic	Glýsýl-L-2-metýlprólýl-L-glútamínsýra	Meðferð á Rett heilkenni

[1] At the time of designation