12 August 2015
EMA/COMP/425722/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

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

On 28 July 2015, orphan designation (EU/3/15/1529) was granted by the European Commission to QRC Consultants Ltd., United Kingdom, for glycyl-L-2-methylprolyl-L-glutamic acid for the treatment of fragile X syndrome.

What is fragile X syndrome?

Fragile X syndrome is a genetic disease characterised by moderate to severe learning disability. Other symptoms include difficulty communicating and socialising, anxiety, hyperactivity, and repetitive and stereotyped behaviours.

The disease is caused by a defect in a gene on the X chromosome. The gene is responsible for the production of a protein called fragile X mental retardation protein (FMRP), which is necessary for the development of the brain. In patients with fragile X syndrome, the defective gene cannot produce normal levels of the FMRP protein and this leads to learning disability and other neurological symptoms. Women are normally less severely affected than men, because they have a second X chromosome that usually has a normal copy of the gene.

Fragile X syndrome is a long-term debilitating disease because of the behavioural and mental health problems it causes.

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

At the time of designation, fragile X syndrome affected approximately 2.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 113,000 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).

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, no satisfactory methods were authorised in the EU for the treatment of fragile X syndrome. Patients were given general support, such as behavioural therapy and special education, and in some cases, antidepressants, stimulants and antipsychotics were used to treat the symptoms of the disease. Genetic counselling (discussion of the risks of passing the condition on to children) was recommended for families with a history of fragile X syndrome.

How is this medicine expected to work?

The medicine is a modified version of a substance called glypromate. Glypromate is naturally present in the brain where it is thought to regulate the activity of two protein cascades that are believed to be affected in fragile X syndrome (the so-called PI3-Akt-mTOR and Ras-MAPK pathways), helping to protect the normal functioning of brain cells. Once given by mouth, the medicine is expected to be able to reach the brain by crossing the 'blood-brain barrier' that separates the nervous system from the bloodstream.

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 fragile X syndrome were ongoing.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 June 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:

QRC Consultants Ltd.
Silvaco Technology Centre
Compass Point
St Ives
Cambridgeshire PE27 5JL
United Kingdom
Tel. +44 (0)1480 309 349
Fax +44 (0)1480 309 332
E-mail: enquiries@qrcc.co.uk

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 fragile X syndrome
Bulgarian	Глицил-L-2-метилпропил-L-глутаминова киселина	Лечение на синдрома на чупливата X хромозома
Croatian	Glicil-L-2-metilprolil-L-glutamatna kiselina	Liječenje sindroma fragilnog X kromosoma
Czech	Glycyl-L-2-methylprolyl-L-glutamová kyselina	Léčba syndromu fragilního X
Danish	Glycyl-L-2-methylprolyl-L-glutaminsyre	Behandling af fragilt X-syndrom
Dutch	Glycyl-L-2-methylprolyl-L-glutaminezuur	Behandeling van het fragiele-X-syndroom
Estonian	Glütsüül-L-2-metüülprolüül-L-glutamiinhape	Fragiilse X sündroomi ravi
Finnish	Glysyyli-L-2-metyyliprolyyli-L-glutamiinihappo	Särö-X-oireyhtymän hoito
French	Acide glycyl-L-2-méthylprolyl-L-glutamique	Traitement du syndrome de l'X fragile
German	Glycyl-L-2-Methylprolyl-L-Glutaminsäure	Zur Behandlung des Fragilen-X-Syndroms
Greek	Γλυκυλ-L-2-μεθυλπρολυλ-L-γλουταμινικό οξύ	Θεραπεία του συνδρόμου εύθραυστο X
Hungarian	Glicil-L-2-metilprolil-L-glutámsav	A fragilis X-szindróma kezelésére
Italian	Acido glicil-L-2-metilprolil-L-glutammico	Trattamento della sindrome dell'X fragile
Latvian	Glicil-L-2-metilprolil-L-glutamīnskābe	Trauslā X sindroma ārstēšanai
Lithuanian	Glicil-L-2-metilprolil-L-glutamo rūgštis	Lūžiosios X chromosomos sindromo gydymas
Maltese	Glycyl-L-2-methylprolyl-L-glutamic acid	Kura tas-sindrome ta' X fraġli
Polish	Kwas glicylo-L-2-metylo prolilo-L-glutaminowy	Leczenie zespołu łamliwego chromosomu X
Portuguese	Ácido glicil-L-2-metilpropil-L-glutâmico	Tratamento da síndrome do X frágil
Romanian	Acid glicil-L-2-metilprolil-L-glutamic	Tratamentul sindromului cromozomului X fragil
Slovak	Glycyl-L-2-methylprolyl-L-glutamová kyselina	Liečba syndrómu fragilného chromozómu X
Slovenian	Glicil-L-2-metilpropil-L-glutaminska kislina	Zdravljenje sindroma fragilnega kromosoma X
Spanish	Ácido glicil-L-2-metilprolil-L-glutámico	Tratamiento del síndrome de X frágil
Swedish	Glycyl-L-2-metylprolyl-L-glutaminsyra	Behandling av Fragil X-syndrom
Norwegian	Glycyl-L-2-metylprolyl-L-glutaminsyre	Behandling av Fragilt X-syndrom
Icelandic	Glýsýl-L-2-metýlprólýl-L-glútamínsýra	Meðferð við heilkenni brotgjarns X (fragile X syndrome)

[1] At the time of designation