25 July 2016
EMA/396049/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pyridoxine and L-pyroglutamic acid for the treatment of fragile X syndrome

On 27 June 2016, orphan designation (EU/3/16/1673) was granted by the European Commission to FGK Representative Service Ltd, United Kingdom, for pyridoxine and L-pyroglutamic acid (the combination is also called metadoxine) for the treatment of fragile X syndrome.

What is fragile X syndrome?

Fragile X syndrome is an inherited 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 problems and learning disabilities it causes.

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

At the time of designation, fragile X syndrome affected approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 103,000*, 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 513,700,000 (Eurostat 2016).

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 on the condition to children) was recommended for families with a history of fragile X syndrome.

How is this medicine expected to work?

This medicine is intended to increase the transmission of GABA between nerve cells. GABA is a substance that reduces the activity of brain cells. In fragile X syndrome GABA transmission is impaired, leading to the behavioural problems associated with the disease.

By binding to GABA transporters on the nerve cells and blocking the action of enzymes that break down GABA, the medicines is expected to increase the effects of GABA in the nerve cells and thereby reduce some symptoms of the condition.

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 authorised in Hungary, Italy, Lithuania and Portugal for treating alcohol dependence and fatty liver due to alcoholism.

At the time of submission, the medicine was not authorised anywhere in the EU for fragile X syndrome. Orphan designation 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 19 May 2016 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, 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	Pyridoxine and L-pyroglutamic acid	Treatment of fragile X syndrome
Bulgarian	Пиридоксин и L-пироглутамова киселина	Лечение на синдрома на чупливата X хромозома
Croatian	Piridoksin i L-piroglutamička kiselina	Liječenje sindroma fragilnog X kromosoma
Czech	Pyridoxin a L-pyroglutamová kyselina	Léčba syndromu fragilního X
Danish	Pyridoxin og L-pyroglutamsyre	Behandling af fragilt X-syndrom
Dutch	Pyridoxine en L-pyroglutaminezuur	Behandeling van het fragiele-X-syndroom
Estonian	Püridoksiin ja L-püroglutaamhape	Fragiilse X sündroomi ravi
Finnish	Pyridoksiini ja L-pyroglutamiinihappo	Särö-X-oireyhtymän hoito
French	Acide pyridoxine et L-pyroglutamique	Traitement du syndrome de l'X fragile
German	Pyridoxine und L-Pyroglutaminsäure	Zur Behandlung des Fragilen-X-Syndroms
Greek	Πυριδοξινη και L-πυρογλουταμικό οξύ	Θεραπεία του συνδρόμου εύθραυστο X
Hungarian	Piridoxin és L-pyroglutamátsav	A fragilis X-szindróma kezelésére
Italian	Piridossina e acido L-piroglutamico	Trattamento della sindrome dell'X fragile
Latvian	Piridoksīns un L-piroglutamīnskābe	Trauslā X sindroma ārstēšanai
Lithuanian	Piridoksinas ir L-piroglutamo rūgštis	Lūžiosios X chromosomos sindromo gydymas
Maltese	Pyridoxine u L-pyroglutamic acid	Kura tas-sindrome ta' X fraġli
Polish	Pirydoksyna i kwas L-pyroglutaminowy	Leczenie zespołu łamliwego chromosomu X
Portuguese	Piridoxina e ácido L-piroglutâmico	Tratamento da síndrome do X frágil
Romanian	Piridoxină şi acid L-piroglutamic	Tratamentul sindromului cromozomului X fragil
Slovak	Pyridoxín a L-pyroglutámová kyselina	Liečba syndrómu fragilného chromozómu X
Slovenian	Piridoksin in L-piroglutaminska kislina	Zdravljenje sindroma fragilnega kromosoma X
Spanish	Piridoxina y Ácido piroglutámico-L	Tratamiento del síndrome de X frágil
Swedish	Pyridoxine och L-pyroglutamatsyra	Behandling av Fragil X-syndrom
Norwegian	Pyridoksin og L-pyroglutamin syre	Behandling av Fragilt X-syndrom
Icelandic	Pýridoxín og pýróglútamik sýra	Meðferð við heilkenni brotgjarns X (fragile X syndrome)

[1] At the time of designation