10 November 2014
EMA/COMP/556117/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Acamprosate calcium for the treatment of fragile X syndrome

On 15 October 2014, orphan designation (EU/3/14/1337) was granted by the European Commission to Real Regulatory Limited, Ireland, for acamprosate calcium for the treatment of fragile X syndrome.

What is fragile X syndrome?

Fragile X syndrome is a genetic disease characterised by moderate to severe mental retardation. 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 the mental retardation and other neurological symptoms. Men are usually more severely affected than women as they have only one X chromosome.

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 in 10,000 people in the European Union (EU). This was equivalent to a total of around 102,000 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 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

*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 511,100,000 (Eurostat 2014).

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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?

FMRP is thought to regulate the production of various proteins in nerve cells. These include receptors for a substance called glutamate, which stimulates the activity of nerve cells in the brain, and receptors for another substance called GABA, which helps to reduce brain cell activity. The lack of FMRP in patients with fragile X syndrome results in an increase in the effect of glutamate and a reduction in the effect of GABA, which eventually alters brain function.

Acamprosate calcium acts by increasing the effects of GABA in the brain and normalising several of the functions of glutamate. This is expected to help improve the symptoms in patients with fragile X syndrome. The medicine may also reduce the excessive transmission of signals in the amygdala, the region in the brain involved in the processing and memory of emotional reactions.

Acamprosate calcium is authorised in the EU for the treatment of alcohol dependence.

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 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 4 September 2014 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	Acamprosate calcium	Treatment of fragile X syndrome
Bulgarian	Акампрозат калций	Лечение на синдрома на чупливата Х хромозома
Croatian	Akamprozatkalcij	Liječenje sindroma fragilnog X kromosoma
Czech	Acamprosatum calcicum	Léčba syndromu fragilního X
Danish	Acamprosatcalcium	Behandling af fragilt X-syndrom
Dutch	Acamprosaat calcium	Behandeling van het fragiele-X-syndroom
Estonian	Akamprosaatkaltsium	Fragiilse X sündroomi ravi
Finnish	Akamprosaattikalsium	Särö-X-oireyhtymän hoito
French	Acamprosate calcique	Traitement du syndrome de l'X fragile
German	Acamprosat calcium	Zur Behandlung des Fragilen-X-Syndroms
Greek	Ασβεστιούχος ακαρποσάτη	Θεραπεία του συνδρόμου εύθραυστου Χ
Hungarian	Akamprozát-kalcium	A fragilis X-szindróma kezelésére
Italian	Calcio acamprosate	Trattamento della sindrome dell'X fragile
Latvian	Akamprosāta kalcija sāls	Trauslā X sindroma ārstēšanai
Lithuanian	Akamprosato kalcis	Lūžiosios X chromosomos sindromo gydymas
Maltese	Acamprosate calcium	Kura tas-sindrome ta' X fraġli
Polish	Akamprozat wapnia	Leczenie zespołu łamliwego chromosomu X
Portuguese	Cálcio acamprosato	Tratamento da síndrome do X frágil
Romanian	Acamprosat de calciu	Tratamentul sindromului cromozomului X fragil
Slovak	Akamprozát vápnika	Liečba syndrómu fragilného chromozómu X
Slovenian	Kalcijev akamprozat	Zdravljenje sindroma fragilnega kromosoma X
Spanish	Calcio acamprosato	Tratamiento del síndrome de X frágil
Swedish	Akamprosat kalcium	Behandling av Fragil X-syndrom
Norwegian	Akamprosatkalsium	Behandling av Fragilt X-syndrom
Icelandic	Akamprósat kalsíum	Meðferð við heilkenni brotgjarns X (fragile X syndrome)

[1] At the time of designation