



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

R-baclofen for the treatment of fragile X syndrome

On 15 April 2011, orphan designation (EU/3/11/858) was granted by the European Commission to Lakeside Regulatory Consulting Services Ltd, United Kingdom, for R-baclofen 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 social withdrawal, 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 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 is equivalent to a total of around 101,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 506,300,000 (Eurostat 2011).



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 acts as a 'brake' in the brain processes that involve certain receptors called 'glutamate receptors'. The lack of FMRP in patients with fragile X syndrome results in an overactivation of these processes, which eventually affects brain function.

R-baclofen activates a different type of receptors (GABA-B receptors) that are expected to make up for the lack of FMRP by decreasing the activation of glutamate receptors. This is expected to help correct the brain dysfunction in patients with fragile X syndrome.

It is also thought that R-baclofen could work by reducing the excessive transmission of signals in the amygdala, the region in the brain involved in the processing and memory of emotional reactions.

What is the stage of development of this medicine?

The effects of R-baclofen have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with R-baclofen in patients with fragile X syndrome were ongoing.

At the time of submission, R-baclofen was not authorised anywhere in the EU for fragile X syndrome. Orphan designation of the medicine had been granted in the United States of America for the treatment of the behavioural abnormalities associated with fragile X syndrome.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 January 2011 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:

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	R-baclofen	Treatment of fragile X syndrome
Bulgarian	R-баклофен	Лечение на синдрома на чупливата X хромозома
Czech	R-baklofen	Léčba syndromu fragilního X chromozomu
Danish	R-baclofen	Behandling af fragilt X-syndrom
Dutch	R-baclofen	Behandeling van fragiel-X-syndroom
Estonian	R-baklofeen	Fragiilse X-i sündroomi ravi
Finnish	R-baklofeeni	Fragiilin X-oireyhtymän hoito
French	R-baclofen	Traitement du syndrome de l'X fragile
German	R-Baclofen	Behandlung des Fragilen X-Syndroms
Greek	R-μπακλοφένη	Θεραπεία Συνδρόμου Εύθραυστο X (Fragile X)
Hungarian	R-baklofen	Fragilis X-szindróma kezelése
Italian	R-baclofene	Trattamento della sindrome dell'X fragile
Latvian	R-baklofēns	Trauslās X hromosomas sindroma ārstēšana
Lithuanian	R-baklofenas	Trapiosios X chromosomos sindromo gydymas
Maltese	R-baclofen	Kura tas-sindrome ta' X fragli
Polish	R-baklofen	Leczenie zespołu łamliwego chromosomu X
Portuguese	R-Baclofeno	Tratamento de Síndrome do X Frágil
Romanian	R-baclofen	Tratamentul sindromului cromozomului X fragil
Slovak	R-baklofen	Liečba syndrómu fragilného X chromozómu
Slovenian	R-baklofen	Zdravljenje sindroma krhkega kromosoma X
Spanish	R-baclofeno	Tratamiento del síndrome del cromosoma X frágil
Swedish	R-baklofen	Behandling av fragilt X-syndrom
Norwegian	R-baklofen	Behandling av fragilt X-syndrom
Icelandic	R-baklófen	Meðferð við heilkenni brotgjarns X-litnings

¹ At the time of designation