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Public summary of opinion on orphan designation

Alpha-tocopherol and ascorbic acid for treatment of fragile X syndrome

On 27 February 2017, orphan designation (EU/3/17/1832) was granted by the European Commission to Advanced Medical Projects, Spain, for alpha-tocopherol and ascorbic acid for treatment of fragile X syndrome.

What is fragile X syndrome?

Fragile X syndrome is an inherited disease that causes 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 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 2.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 129,000 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

*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 515,700,000 (Eurostat 2017).

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education, and in some cases, medicines were used to treat the symptoms of the disease such as anxiety, hyperactivity and depression. 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?

Patients with fragile X syndrome have high amounts of highly reactive (oxidising) chemicals in the body, which can be harmful to cells, especially in the brain. Although the body is normally exposed to these substances, it is usually able to neutralise them and prevent any damage to cells.

This medicine contains alpha-tocopherol (a form of vitamin E) and ascorbic acid (vitamin C), which are antioxidants that can neutralise oxidising chemicals and are expected to help reduce some of the patient's symptoms.

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 or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 January 2017 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:

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	Alpha-tocopherol and ascorbic acid	Treatment of fragile X syndrome
Bulgarian	Алфа токоферол и аскорбинова киселина	Лечение на синдрома на чупливата Х хромозома
Croatian	Alfa tokoferol I askorbinska kiselina	Liječenje sindroma fragilnog X kromosoma
Czech	Alfa-tokoferol a kyselina askorbova	Léčba syndromu fragilního X
Danish	Alfa-tocopherol og ascorbinsyre	Behandling af fragilt X-syndrom
Dutch	Alfa-tocoferol en ascorbinezuu	Behandeling van het fragiele-X-syndroom
Estonian	Alfatokoferool ja askorbiinhape	Fragiilse X sündroomi ravi
Finnish	Alfa-tokoferoli ja askorbiinihappo	Särö-X-oireyhtymän hoito
French	Alpha-tocophérol et acide ascorbique	Traitement du syndrome de l'X fragile
German	Alpha-Tocopherol und Ascorbinsäure	Zur Behandlung des Fragilen-X-Syndroms
Greek	α-τοκοφερόλη και ασκορβικό οξύ	Θεραπεία του συνδρόμου εύθραυστο Χ
Hungarian	Alfa-tokoferol és aszkorbinsav	A fragilis X-szindróma kezelésére
Italian	Alfa-tocoferolo e acido ascorbico	Trattamento della sindrome dell'X fragile
Latvian	Alfa tokoferols un askorbīnskābe	Trauslā X sindroma ārstēšanai
Lithuanian	Alfa-tokoferolis ir askorbo rūgštis	Lūžiosios X chromosomos sindromo gydymas
Maltese	Alpha tokoferol u aċidu askorbiku	Kura tas-sindrome ta' X fraġli
Polish	Alfa-tokoferol i kwas askorbinowy	Leczenie zespołu łamliwego chromosomu X
Portuguese	Alfatocoferol e ácido ascórbico	Tratamento da síndrome do X frágil
Romanian	Alfa-tocoferol şi acid ascorbic	Tratamentul sindromului cromozomului X fragil
Slovak	Alfa-tokoferol a kyselina askorbová	Liečba syndrómu fragilného chromozómu X
Slovenian	Alfa-tokoferol in askorbinska kislina	Zdravljenje sindroma fragilnega kromosoma X
Spanish	Tocoferol alfa y ácido ascórbico	Tratamiento del síndrome de X frágil
Swedish	Alfa-tokoferol och askorbinsyra	Behandling av Fragil X-syndrom
Norwegian	Alfa-tokoferol og askorbinsyre	Behandling av Fragilt X-syndrom
Icelandic	Alfa-tókóferól og askorbínsýra	Meðferð við heilkenni brotgjarns X (fragile X syndrome)

[1] At the time of designation