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Public summary of opinion on orphan designation

Fenfluramine hydrochloride for the treatment of Lennox-Gastaut syndrome

On 27 February 2017, orphan designation (EU/3/17/1836) was granted by the European Commission to Zogenix International Limited, United Kingdom, for fenfluramine hydrochloride for the treatment of Lennox-Gastaut syndrome.

What is Lennox-Gastaut syndrome?

Lennox-Gastaut syndrome is a severe form of epilepsy that starts in childhood between 2 and 5 years of age. Patients have different types of seizures (fits), including tonic seizures (muscle contraction lasting few seconds to minutes), atypical absence seizures (during which the person has a blank stare but is still partly aware of their surroundings) and drop seizures (brief loss of muscle tone and consciousness, causing abrupt falls). Most children with Lennox-Gastaut syndrome experience some degree of learning disability and developmental delays, along with behavioural problems such as hyperactivity and aggression.

Lennox-Gastaut syndrome is long-term debilitating due to the seizures, effects on mental function and behavioural problems.

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

At the time of designation, Lennox-Gastaut syndrome affected approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 103,000 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, several epilepsy medicines were authorised in the EU for treatment of seizures in patients with Lennox-Gastaut syndrome, including clonazepam, felbamate, lamotrigine, nitrazepam, rufinamide, sodium valproate and topiramate.

*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).

The sponsor has provided sufficient information to show that fenfluramine hydrochloride might be of significant benefit for patients with Lennox-Gastaut syndrome. Preliminary data showed that adding fenfluramine hydrochloride to previous treatment reduced the number of seizures in patients in whom previous treatment alone was not sufficient. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Epilepsy is caused by excessive electrical activity in the brain. The exact way in which fenfluramine hydrochloride works is still unclear but it seems to stimulate certain receptors in the brain that are involved in the release of the chemical messenger serotonin from nerve cells. By increasing serotonin levels, fenfluramine is thought to help stabilise electrical activity in the brain and prevent seizures.

What is the stage of development of this medicine?

The effects of fenfluramine hydrochloride have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial with fenfluramine hydrochloride in patients with Lennox-Gastaut syndrome was ongoing.

At the time of submission, fenfluramine hydrochloride was not authorised anywhere in the EU for Lennox-Gastaut syndrome or designated as an orphan medicinal product elsewhere for this condition. Orphan designation has been granted in the EU for Dravet syndrome, another form of epilepsy.

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.

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Fenfluramine hydrochloride	Treatment of Lennox-Gastaut syndrome
Bulgarian	Фенфлурамин хидрохлорид	Лечение на синдром на Ленокс-Гасто
Croatian	Fenfluraminklorid	Liječenje sindroma Lennox-Gastaut
Czech	Fenfluramin hydrochlorid	Léčba Lennox-Gastautova syndromu
Danish	Fenfluraminhydrochlorid	Behandling af Lennox-Gastaut syndrom
Dutch	Fenfluramine hydrochloride	Behandeling van het Lennox-Gastaut syndroom
Estonian	Fenfluramiinvesinikkloriid	Lennox-Gastaut´ sündroomi raviks
Finnish	Fenfluramiinihydrokloridi	Lennox-Gastautin oireyhtymän hoito
French	Chlorhydrate de fenfluramine	Traitement du syndrome de Lennox-Gastaut
German	Fenfluraminhydrochlorid	Behandlung des Lennox-Gastaut-Syndroms
Greek	Φαινφλουραμίνη υδροχλωρική	θεραπεία του Συνδρόμου Lennox-Gastaut
Hungarian	Fenfluramin hidroklorid	Lennox-Gastaut szindróma kezelése
Italian	Fenfluramina cloridrato	Trattamento della sindrome di Lennox-Gastaut
Latvian	Fenfluramīna hidrohlorklīds	Lenoksa–Gasto sindroma terapija
Lithuanian	Fenfluramino hidrochloridas	Lenokso–Gasto sindromo gydymas
Maltese	Fenfluramina idroklorida	Kura tas-sindromu Lennox-Gastaut
Polish	Chlorowodorek fenfluraminy	Leczenie zespołu Lennox-Gastauta
Portuguese	Cloridrato de fenfluramina	Tratamento do síndrome de Lennox-Gastaut
Romanian	Clorhidrat de fenfluramină	Tratamentul sindromului Lennox-Gastaut
Slovak	Fenfluramín hydrochlorid	Liečba Lennox-Gastautovho syndrómu
Slovenian	Fenfluraminijev hidroklorid	Zdravljenje Lennox-Gastautovega sindroma
Spanish	Clorhidrato de fenfluramina	Tratamiento del síndrome de Lennox-Gastaut
Swedish	Fenfluraminhydroklorid	Behandling av Lennox-Gastaut syndrom
Norwegian	Fenfluraminhydroklorid	Behandling av Lennox-Gastaut syndromet
Icelandic	Fenflúramín hydróklóríð	Meðferð á Lennox-Gastaut heilkenni

¹ At the time of designation