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EMA/COMP/700717/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Fenfluramine hydrochloride for the treatment of Dravet syndrome

On 16 January 2014, orphan designation (EU/3/13/1219) was granted by the European Commission to Brabant Pharma Limited, United Kingdom, for fenfluramine hydrochloride for the treatment of Dravet syndrome.

What is Dravet syndrome?

Dravet syndrome, also called severe myoclonic epilepsy of infancy (SMEI), is a severe form of epilepsy that affects children and adults. It is caused by defects in genes required for the proper function of brain cells.

In Dravet syndrome, the seizures (fits) begin in the first year of life, and are most often associated with a high temperature (febrile convulsions). Later, other types of seizures typically occur, including status epilepticus (a state of continuous seizure requiring emergency medical care). From the second year of life, the child's development begins to decline or reverse, leading to problems such as impaired mental and motor (movement) skills.

Dravet syndrome is debilitating in the long term because of the poor development of mental and motor skills. It is also life threatening particularly because of the occurrence of major seizures.

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

At the time of designation, Dravet syndrome affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 26,000 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).

*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 512,200,000 (Eurostat 2013).

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What treatments are available?

At the time of designation, the medicine Diacomit (stiripentol) was authorised in the EU as add-on treatment for generalised tonic-clonic seizures (major fits, including loss of consciousness) in children with Dravet syndrome.

The sponsor has provided sufficient information to show that fenfluramine hydrochloride might be of significant benefit for patients with Dravet syndrome because it works in a different way to existing treatments and early studies show that it might improve the outcome of patients when used as add-on to other treatments. 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?

Although the way fenfluramine hydrochloride works is not clearly understood, this medicine is expected to increase the levels of the neurotransmitter serotonin in the brain. This may have a role in preventing the seizures in Dravet syndrome and fenfluramine hydrochloride has been shown to reduce seizures in experimental models.

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, no clinical trials with fenfluramine hydrochloride in patients with Dravet syndrome were ongoing.

Fenfluramine hydrochloride had been previously authorised in several countries worldwide as an appetite suppressant for the treatment of obesity. The medicine was withdrawn from the EU market in 1997.

At the time of submission, fenfluramine hydrochloride was not authorised anywhere in the EU for Dravet 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 6 November 2013 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Fenfluramine hydrochloride	Treatment of Dravet syndrome
Bulgarian	Фенфлурамин хидрохлорид	Лечение на синдром на Dravet
Czech	Fenfluramin hydrochlorid	Léčba Dravetova syndromu
Croatian	Fenfluraminklorid	Liječenje Dravetovog sindroma
Danish	Fenfluraminhydrochlorid	Behandling af Dravet syndrom
Dutch	Fenfluramine hydrochloride	Behandeling van het syndroom van Dravet
Estonian	Fenfluramiinvesinikkloriid	Dravet' sündroomi ravi
Finnish	Fenfluramiinihydrokloridi	Dravet'n oireyhtymän hoito
French	Chlorhydrate de fenfluramine	Traitement du syndrome de Dravet
German	Fenfluraminhydrochlorid	Behandlung des Dravet-Syndroms
Greek	Φαινφλουραμίνη υδροχλωρική	Θεραπεία συνδρόμου Dravet
Hungarian	Fenfluramin hidroklorid	Dravet-szindróma kezelése
Italian	Fenfluramina cloridrato	Trattamento della sindrome di Dravet
Latvian	Fenfluramīna hidrohlorīds	Draveta sindroma ārstēšana
Lithuanian	Fenfluramino hidrochloridas	*Dravet* sindromo gydymas
Maltese	Fenfluramine hydrochloride	Kura tas-sindrome ta' Dravet
Polish	Chlorowodorek fenfluraminy	Leczenie zespołu Draveta
Portuguese	Cloridrato de fenfluramina	Tratamento da síndrome de Dravet
Romanian	Clorhidrat de fenfluramină	Tratamentul sindromului Dravet
Slovak	Fenfluramín hydrochlorid	Liečba Dravetovej syndrómu
Slovenian	Fenfluramin hidroklorid	Zdravljenje Dravetovega sindroma
Spanish	Clorhidrato de fenfluramina	Tratamiento del síndrome de Dravet
Swedish	Fenfluraminhydroklorid	Behandling av Dravets syndrom
Norwegian	Fenfluraminhydroklorid	Behandling av Dravet-syndrom
Icelandic	Fenflúramín hýdróklóríð	Meðferð við Dravet heilkenni

[1] At the time of designation