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EMA/COMP/787361/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sodium valproate for the treatment of Wolfram syndrome

On 15 January 2015, orphan designation (EU/3/14/1428) was granted by the European Commission to Alan Boyd Consultants Ltd, United Kingdom, for sodium valproate for the treatment of Wolfram syndrome.

What is Wolfram syndrome?

Wolfram syndrome is a group of inherited disorders that usually appears in childhood and causes diabetes, optic atrophy (when the optic nerve that connects the eye to the brain wastes away) leading to loss of vision, deafness and often 'diabetes insipidus', a condition in which the kidneys cannot retain water, resulting in excessive amounts of urine. Other complications that affect the nervous system may also occur, such as problems with balance and coordination, loss of taste and smell, breathing problems, fits and intellectual impairment.

Wolfram syndrome is a long-term debilitating condition that may be life threatening because of its complications, such as respiratory failure caused by the brain's inability to control breathing.

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

At the time of designation, Wolfram syndrome affected not more than 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 10,000 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 Wolfram syndrome. Treatment was supportive and aimed at managing the complications of the condition, and included medicines for diabetes, to prevent fits or to treat other problems with the brain and nerves, as well as hearing aids.

*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).

How is this medicine expected to work?

Most patients with Wolfram syndrome lack a protein called wolframin, which is present at high levels in certain organs such as the brain and pancreas. Wolframin is thought to play a role in maintaining the correct functioning of a structure (called the endoplasmic reticulum) within cells involved in the elimination of defective proteins. If cells are unable to get rid of defective proteins they become 'stressed' and die. In patients with Wolfram syndrome, the death of specific cells in the pancreas that make insulin causes diabetes, the gradual loss of cells along the optic nerve eventually leads to blindness, and the death of cells in other organs causes the various signs and symptoms of the disease.

Sodium valproate is a well-known medicine used to treat epilepsy (fits). In patients with Wolfram syndrome it is thought to increase the production of a protein called p21, which prevents cells from dying. Sodium valproate is also thought to increase the production of wolframin. This is expected to reduce cell death, therefore slowing down the progression of the disease.

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, no clinical trials with the medicine in patients with Wolfram syndrome had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Wolfram 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 11 December 2014 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

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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	Sodium valproate	Treatment of Wolfram syndrome
Bulgarian	Натриев валпроат	Лечение на синдром на Волфрам
Croatian	Natrijev valproat	Liječenje Wolframovog sindroma
Czech	Valproát sodný	Léčba Wolframova syndromu
Danish	Natriumvalproat	Behandling af Wolframs syndrom
Dutch	Natriumvalproaat	Behandeling van het Syndroom van Wolfram
Estonian	Naatriumvalproaat	Wolframi sündroomi ravi
Finnish	Natriumvalproaatti	Volframioireyhtymän hoitoon
French	Valproate de sodium	Le traitement du syndrome de Wolfram
German	Natriumvalproat	Behandlung des Wolfram-Syndroms
Greek	Βαλπροϊκό νάτριο	Θεραπεία του συνδρόμου Wolfram
Hungarian	Nátrium valproat	Wolfram-szindróma kezelése
Italian	Valproato di sodio	Trattamento della Sindrome di Wolfram
Latvian	Nātrija valproāts	Volframa sindroma ārstēšana
Lithuanian	Natrio valproatas	Wolfram sindromo gydymas
Maltese	Sodium valproate	Kura tas-sindrome ta' Wolfram
Polish	Sodu walproinian	Leczenie zespołu Wolframa
Portuguese	Valproato de sódio	Tratamento da Síndrome de Wolfram
Romanian	Valproat de sodiu	Tratamentul sindromului Wolfram
Slovak	Natrii valproas	Liečba Wolframovho syndrómu
Slovenian	Natrijev valproate	Zdravljenje Wolframovega sindroma
Spanish	Valproato sódico	Tratamiento del síndrome de Wolfram
Swedish	Natriumvalproat	Behandling av Wolframs syndrom
Norwegian	Natriumvalproat	Behandling av Wolfram syndrom
Icelandic	Natríum valpróat	Meðferð við Wolfram-heilkenni

¹ At the time of designation