



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

6 January 2017
EMA/756214/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Dantrolene sodium for the treatment of Wolfram syndrome

On 12 December 2016, orphan designation (EU/3/16/1800) was granted by the European Commission to Alan Boyd Consultants Ltd, United Kingdom, for dantrolene sodium for the treatment of Wolfram syndrome.

What is Wolfram syndrome?

Wolfram syndrome is a group of inherited disorders that usually appear in childhood and cause 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 513,700,000 (Eurostat 2016).



How is this medicine expected to work?

Most patients with Wolfram syndrome lack a protein called wolframin, which is thought to play a role in the function of a structure called the endoplasmic reticulum inside cells, particularly in cells of the pancreas and nervous system. This lack causes the cells to become 'stressed' and die, leading to the various signs and symptoms of the disease.

Dantrolene sodium is a medicine used for many years as a muscle relaxant that acts by regulating the flow of calcium in and out of cells. In patients with Wolfram syndrome, controlling the calcium flow in this way is thought to stabilise the endoplasmic reticulum. This is expected to prevent cells from dying, therefore slowing down the progression of the disease.

What is the stage of development of this medicine?

The effects of dantrolene sodium 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, dantrolene 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 4 November 2016 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	Dantrolene sodium	Treatment of Wolfram syndrome
Bulgarian	Дантролен натрий	Лечение на синдром на Волфрам
Croatian	Dantrolennatrij	Liječenje Wolframovog sindroma
Czech	Dantrolen sodný	Léčba Wolframova syndromu
Danish	Dantrolennatrium	Behandling af Wolframs syndrom
Dutch	Dantroleennatrium	Behandeling van het Syndroom van Wolfram
Estonian	Dantroleennaatrium	Wolframi sündroomi ravi
Finnish	Dantroleeninatrium	Volframioireyhtymän hoitoon
French	Dantrolène sodique	Le traitement du syndrome de Wolfram
German	Dantrolen-Natrium	Behandlung des Wolfram-Syndroms
Greek	Νατρίουχος δαντρολένη	Θεραπεία του συνδρόμου Wolfram
Hungarian	Dantrolén nátrium	Wolfram-szindróma kezelése
Italian	Dantrolene sodico	Trattamento della Sindrome di Wolfram
Latvian	Dantrolēna nātrija sāls	Volframa sindroma ārstēšana
Lithuanian	Natrio dantrolenas	Wolfram sindromo gydymas
Maltese	Dantrolene sodium	Kura tas-sindrome ta' Wolfram
Polish	Dantrolen sodu	Leczenie zespołu Wolframa
Portuguese	Sal sódico de dantroleno	Tratamento da Síndrome de Wolfram
Romanian	Dantrolen sare sodică	Tratamentul sindromului Wolfram
Slovak	Dantrolén sodný	Liečba Wolframovho syndrómu
Slovenian	Natrijev dantrolen	Zdravljenje Wolframovega sindroma
Spanish	Dantroleno sódico	Tratamiento del síndrome de Wolfram
Swedish	Dantrolennatrium	Behandling av Wolframs syndrom
Norwegian	Dantrolennatrium	Behandling av Wolfram syndrom
Icelandic	Dantrólen natrím	Meðferð við Wolfram-heilkenni

¹ At the time of designation