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EMA/COMP/652841/2014  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### Dantrolene sodium for the treatment of malignant hyperthermia

On 19 November 2014, orphan designation (EU/3/14/1379) was granted by the European Commission to Eagle Laboratories Ltd, United Kingdom, for dantrolene sodium for the treatment of malignant hyperthermia.

#### What is malignant hyperthermia?

Malignant hyperthermia is an inherited disorder marked by rapid, uncontrolled muscle contractions and a rise in body temperature.

Symptoms can be triggered by certain medicines such as some general anaesthetics or the muscle relaxant succinylcholine, which cause the sudden release of abnormally high amounts of calcium within muscle cells. The release of calcium then makes the muscles to contract uncontrollably, leading to high body temperature, and other problems such as a rapid heart rate and muscle breakdown.

Malignant hyperthermia is a life-threatening condition due to heart arrhythmias (irregular heart beat), acidosis (high blood levels of acid) and muscle rigidity.

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

At the time of designation, malignant hyperthermia affected less than 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer 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, dantrolene sodium given by injection was already authorised in the EU for the treatment of malignant hyperthermia. However, the medicine was formulated in a way that does not allow the medicine to be given quickly in an emergency situation.

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\*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).

The sponsor has provided sufficient information to show that this medicine is a new formulation of dantrolene sodium which might be of significant benefit for patients with malignant hyperthermia because it is expected to be given quickly to patients with malignant hyperthermia thereby reducing morbidity and mortality associated with treatment delay. 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?**

Dantrolene is a muscle relaxant that decreases the release of calcium from within muscle cells, helping the muscles to relax again.

It is expected that the new formulation will allow for a faster preparation of the medicine, as well as for a lower volume to be given to patients, which would allow for the medicine to be given without delay.

### **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, a clinical trial with the new formulation of dantrolene sodium in healthy volunteers had finished and no further studies were planned.

At the time of submission, this medicine was not authorised anywhere in the EU for malignant hyperthermia. The medicine has received orphan designation and has been approved in the United States for malignant hyperthermia.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 October 2014 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:

Eagle Laboratories Ltd  
The Clockhouse Station Approach  
Marlow SL7 1NT  
United Kingdom  
Tel. +44 (0)162 847 7709  
Fax +44 (0)162 847 7719  
E-mail: [info@pink-accounts.co.uk](mailto:info@pink-accounts.co.uk)

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Dantrolene sodium	Treatment of malignant hyperthermia
Bulgarian	Дантролен натрий	Лечение на малигна хипертермия
Croatian	Dantrolennatrij	Liječenje maligne hipertermije
Czech	Dantrolen sodný	Léčba maligní hypertermie
Danish	Dantrolennatrium	Behandling af malign hypertermi
Dutch	Dantroleennatrium	Behandeling van maligne hyperthermie
Estonian	Dantroleennaatrium	Pahaloomulise hüpertermia ravi
Finnish	Dantroleeninatrium	Pahanlaatuisten hypertermian hoito
French	Dantrolène sodique	Traitement de l'hyperthermie maligne
German	Dantrolen-Natrium	Behandlung der malignen Hyperthermie
Greek	Νατρίουχος δαντρολένη	Θεραπεία της κακοήθους υπερθερμίας
Hungarian	Dantrolén nátrium	Malignus hyperthermia kezelése
Italian	Dantrolene sodico	Trattamento dell'ipertermia maligna
Latvian	Dantrolēna nātrija sāls	Ļaundabīgas hipertermijas ārstēšana
Lithuanian	Natrio dantrolenas	Piktybinės hipertermijos gydymas
Maltese	Dantrolene sodium	Kura tal-ipertermija malinna
Polish	Dantrolen sodu	Leczenie hipertermii złośliwej
Portuguese	Sal sódico de dantroleno	Tratamento de hipertermia maligna
Romanian	Dantrolen sare sodică	Tratamentul hipertermiei maligne
Slovak	Dantrolén sodný	Liečba malígnej hypertermie
Slovenian	Natrijev dantrolen	Zdravljenje maligne hipertermije
Spanish	Dantroleno sódico	Tratamiento de la hipertermia maligna
Swedish	Dantrolennatrium	Behandling av malign hypertermi
Norwegian	Dantrolennatrium	Behandling av malign hypertermi
Icelandic	Dantrólen natríum	Meðferð við illkynja háhita

<sup>1</sup> At the time of designation