



**COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS**

**PUBLIC SUMMARY OF  
POSITIVE OPINION FOR ORPHAN DESIGNATION  
OF  
cholest-4-en-3-one, oxime  
for the treatment of 5 q spinal muscular atrophy**

On 10 March 2005, orphan designation (EU/3/05/264) was granted by the European Commission to TROPHOS SA, France for cholest-4-en-3-one, oxime for the treatment of 5 q spinal muscular atrophy.

**What is 5q spinal muscular atrophy?**

5q spinal muscular atrophy (SMA) is an inherited disease. The abnormal gene is located on a portion of chromosome number 5 called "the q arm" (hence the name "5q") and the disease occurs if both parents pass an abnormal version of this gene onto their offspring (this type of disease transmission is called "autosomal recessive transmission"). Due to this genetic defect, a molecule called "spinal motor neuron" (SMN) protein is lacking. Normally, SMN protein is essential to the normal functioning and survival of motor neurons (the cells of the nervous system which allow the body to move) and without this protein these neurons may deteriorate and eventually die, resulting in muscle weakness.

In 5q SMAs muscle weakness is found most often at the level of proximal muscles (the muscles closest to the trunk), but in the most severe cases respiratory muscles can be affected too leading to increased risk of pneumonia and breathing problems. The disease is life-threatening and chronically debilitating.

**What are the methods of treatment available?**

No satisfactory methods exist that were authorised at the time of application. Several treatment methods consisting of medicines or non-medicinal approaches have been tried or are currently under investigation.

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

According to the information provided by the sponsor, 5q spinal muscular atrophy was affecting about 12,000 persons in European Union.

**How is this medicinal product expected to act?**

Cholest-4-en-3-one, oxime is a substance that derives from cholesterol and is supposed to protect the motor neurons either by stimulating their repair and delaying their death. The exact mechanism of action is not known; effects on cellular structures called "mitochondria" may be involved.

**What is the stage of development of this medicinal product?**

The effects of cholest-4-en-3-one, oxime were evaluated in experimental models. At the time of submission of the application for orphan designation, no clinical trials in patients with 5q spinal muscular atrophy were initiated.

Cholest-4-en-3-one, oxime was not marketed anywhere worldwide for 5q spinal muscular atrophy or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 3 February 2005 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

**For more information:**

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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**Translations of the active ingredient and indication in all EU languages  
and Norwegian and Icelandic**

<b>Language</b>	<b>Active Ingredient</b>	<b>Indication</b>
English	Cholest-4-en-3-one, oxime	Treatment of 5q spinal muscular atrophy
Czech	Cholest-4-en-3-one, oxim	Léčba 5q spinální muskulární atrofie
Danish	Cholest-4-en-3-on, oxim	Behandling af 5q spinal muskeltrofi
Dutch	Cholest-4-en-3-on, oxime	Behandeling van 5q spinale spieratrofie
Estonian	Cholest-4-en-3-one, oksiid	5q spinaalse lihaskatroofia ravi
Finnish	Kolest-4-ja-3-yksi, oksimi	Selkärangan 5q lihassurkastuman hoito
French	Cholest-4-ène-3-one, oxime	Traitement de l'amyotrophie spinale 5q
German	Cholest-4-in-3-one, Oxime	Behandlung der 5q spinalen Muskelatrophie
Greek	Χοληστ-(4)-εν-(3)-όνη, οξίμη	Θεραπεία της νωτιαίας μυϊκής ατροφίας (5q)
Hungarian	Cholest-4-en-3-on, oxim	5q spinális izomatrophia kezelése
Italian	4-colesten-3-one, ossima	Trattamento dell'atrofia muscolare spinale 5q
Latvian	Holest-4-en-3-ons, oksīms	Léčba 5q spinální muskulární atrofie
Lithuanian	Cholest-4-en-3-vienas, oksimas	Nugaros raumenų atrofijos gydymas, esant 5q srities delecijoms
Polish	Cholest-4-eno-3-onu oksym	Leczenie rdzeniowego zaniku mięśni 5q
Portuguese	Colest-4-en-3-ona,oximo	Tratamento da atrofia muscular espinal 5q
Slovak	Cholest-4-en-3-one, oxím	Liečba 5q spinálnej svalovej atrofie
Slovenian	Kolestenon, oksim	Zdravljenje 5q spinalne mišične atrofije
Spanish	Colest-4-en-3-ona, oxima	Tratamiento de la atrofia muscular espinal 5q
Swedish	Cholest-4-en-3-on, oxim	Behandling av 5q spinal muskeltrofi
Norwegian	Kolest-4-en-3-on,oksim	Behandling av 5q spinal muskeltrofi
Icelandic	Kólesteról -4- en-3-einn, oxím	Meðhöndlun vöðvarýrnunar í mænu