



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### L-threo-3,4-dihydroxyphenylserine for the treatment of orthostatic hypotension in patients with pure autonomic failure

On 2 August 2007, orphan designation (EU/3/07/465) was granted by the European Commission to The Weinberg Group LLC, United Kingdom, for L-threo-3,4-dihydroxyphenylserine for the treatment of orthostatic hypotension in patients with pure autonomic failure.

The sponsorship was transferred to The Weinberg Group Limited, United Kingdom, in March 2009 and to Diamond BioPharm Limited, United Kingdom, in March 2011.

#### What is pure autonomic failure?

The autonomic nervous system regulates blood pressure, heart rate, sleep, and bladder function. Pure autonomic failure is a progressive disorder of the autonomic central nervous system with symptoms such as constipation, impotence in men, urinary incontinence and orthostatic (postural) hypotension. Orthostatic hypotension is an excessive drop in blood pressure when the patient stands, which causes dizziness or momentary blackouts. The condition is chronically debilitating to the patient and life-threatening due to loss of consciousness.

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

At the time of designation, pure autonomic failure affected less than 0.1 in 10,000 people in the European Union (EU)\*. This is equivalent to a total of fewer than 5,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

#### What treatments are available?

Orthostatic hypotension in patients with pure autonomic failure can be treated by increasing water and salt intake, using compression stockings, and by the use of medication authorised for the condition in

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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 27), Norway, Iceland and Liechtenstein. This represents a population of 498,000,000 (Eurostat 2006).



some countries in the Community at the time of submission of the application for orphan drug designation.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that the medicinal product might be of potential significant benefit for the treatment of orthostatic hypotension in patients with pure autonomic failure.

The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

### **How is this medicine expected to work?**

When a person stands up, gravity causes blood to settle in the veins in the legs, so less blood reaches the heart for pumping, and as a result the blood pressure drops. The body normally responds automatically to the drop in blood pressure by increasing the rate at which the heart beats and by narrowing the veins to return more blood to the heart. In patients with postural hypotension, this compensating reflex fails to occur, resulting in symptomatic low blood pressure. L-threo-3,4-dihydroxyphenylserine treatment is expected to restore the normal reflex by acting on both, the heart and blood vessels.

### **What is the stage of development of this medicine?**

At the time of submission of the application for orphan designation, the effects of L-threo-3,4-dihydroxyphenylserine had been evaluated in experimental models but no clinical trials in patients with pure autonomic failure had been initiated.

L-threo-3,4-dihydroxyphenylserine was not authorised anywhere worldwide for treatment of orthostatic hypotension in patients with pure autonomic failure, at the time of submission. Orphan designation of L-threo-3,4-dihydroxyphenylserine was granted in the United States for the treatment of symptomatic neurogenic orthostatic hypotension in patients with primary autonomic failure, dopamine- $\beta$ -dehydroxylase deficiency or nondiabetic autonomic neuropathy.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 27 June 2007 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:

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

Language	Active Ingredient	Indication
English	L-threo-3,4-dihydroxyphenylserine	Treatment of orthostatic hypotension in patients with pure autonomic failure
Bulgarian	L-трео-3,4-дихидроксифенилсерин	Лечение на ортостатична хипотензия при пациенти с чиста автономна отпадналост
Czech	L-threo-3,4-dihydroxyfenylserin	Léčba ortostatické hypotenze u pacientů s čistě autonomním selháním
Danish	L-threo-3,4-dihydroxyphenylserin	Behandling af ortostatisk hypotension hos patienter med autonom insufficiens
Dutch	L-threo-3,4-dihydroxyphenylserine	Behandeling van orthostatische hypotensie bij patiënten met puur autonoom falen
Estonian	L-treo-3,4-dihüdoksüfeenülseriin	Ortostaatilise hüpotensiooni ravi ainult autonoomse puudulikkusega patsientidel
Finnish	L-treo-3,4-dihydroksifenyyliiseriini	Oireisen ortostaattisen hypotonian hoito, kun potilaalla on autonomisen hermoston toiminnanvaja
French	L-thréo-3,4-dihydroxyphénylsérine	Traitement de l'hypotension orthostatique des patients ayant une défaillance autonome.
German	L-threo-3,4-Dihydroxyphenylserin	Behandlung der orthostatischen Hypotonie bei Patienten mit reiner autonomer Dysfunktion
Greek	L-θρεο-3,4-διυδροξυφενυλσερίνη	Θεραπεία ορθοστατικής υπέρτασης σε ασθενείς με αμιγή αυτόνομη ανεπάρκεια
Hungarian	L-treo-3,4-dihidroxifenilszerin	Ortosztatikus hipotónia kezelése kizárólagos vegetatív elégtelenségben szenvedő betegeknel
Italian	L-treo-3,4-diidrossidrossifenilserine,	Trattamento dell'ipotensione ortostatica neurogena sintomatica nei pazienti affetti da disautonomia pura
Latvian	L-treo-3,4-dihidroksifenilserīns	Ortostātiskās hipotensijas ārstēšana pacientiem ar veģetatīvās nervu sistēmas traucējumiem
Lithuanian	L-threo-3,4-dihidroksifenilserinas	Pacientų su tikroju autonominiu sutrikimu ortostatinės hipotonijos gydymas
Maltese	L-threo-3,4-dihydroxyphenylserine	Kura tal-pressjoni baxxa ortostatika f'pazzjenti li għandhom inkapaċità awtonomika pura
Polish	L-treo-3,4-dihydroksyfenyloserine	Leczenie objawowego neurogenego niedociśnienia ortostatycznego u pacjentów z czystą niewydolnością układu autonomicznego
Portuguese	L-threo-3,4-dihydroxyphenylserine	Tratamento da hipotensão ortostática nos pacientes com insuficiência autonómica pura
Romanian	L-treo-3,4-dihidroxifenilserină	Tratamentul hipotensiunii ortostatice la pacienții cu insuficiență vegetativă pură
Slovak	L-treo-3,4-dihydroxyfenylserín	Liečba ortostatickej hypertenzie u pacientov s čisto autonómnym zlyhaním

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

Language	Active Ingredient	Indication
Slovenian	L-treo-3, 4-dihidroksifenilserin	Zdravljenje ortostatične hipotenzije pri bolnikih s čisto avtonomno okvaro
Spanish	L-treo-3,4-dihidroxifenilserina	Tratamiento de la hipotensión ortostática en pacientes con insuficiencia autonómica pura.
Swedish	L-treo-3,4-dihydroxyfenylserin	Behandling av ortostatiskt lågt blodtryck hos patienter med nedsatt funktion i autonoma nervsystemet
Norwegian	L-treo-3,4-dihydroksyfenylserin	Behandling av ortostatisk hypotensjon hos pasienter med ren autonom svikt
Icelandic	L-threó-3,4-tvíhýdroxýphenýlserín3,4-	Meðferð sjúklinga með taugatengdt réttstöðuprýstingsfall með einkennum vegna hreinnar bilunar í ósjálfráða kerfinnu