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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

cardiotrophin-1 for the prevention of the ischemia/reperfusion injury associated with solid organ transplantation

On 28 August 2006, orphan designation (EU/3/06/396) was granted by the European Commission to Digna Biotech S.L., Spain, for cardiotrophin-1 for the prevention of the ischemia/reperfusion injury associated with solid organ transplantation.

What is ischemia/reperfusion injury associated with solid organ transplantation?

Organs for transplantation (grafts) face a period of having to survive outside the donor and recipient. During that time, although grafts are preserved by cooling and other measures, they are short of blood supply (ischemia). Prolonged ischemia can be damaging because of lack of oxygen and nutrients. When the graft organ is attached to the blood circulation of the recipient, the tissue is suddenly reperfused with blood (reperfusion). However, instead of restoring normal function, reperfusion can result in inflammation and damage, an event known as reperfusion injury. Inflammation can further destroy an already damaged/ischemic graft. Depending on the severity of the initial ischemia, the tissue can subsequently be seriously damaged. There is an increased risk of graft dysfunction and even rejection from the recipient. Ischemia/reperfusion injury associated to solid organ transplantation is a life-threatening condition.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of ischemia/reperfusion injury associated with solid organ transplantation was estimated to be approximately 1 people in 10,000 in the European Union (EU) [*]. This is equivalent to a total of around 46,000 people, which 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 the knowledge of the Committee for Orphan Medicinal Products (COMP).

[*]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 459,700,000 (Eurostat 2004).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What methods of prevention are available?

Graft organs are preserved in cold (hypothermic) conditions and various solutions to reduce the effects of the ischemia. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that cardiotrophin-1 might be of potential significant benefit for the prevention of ischemia/reperfusion injury associated with solid organ transplantation, mainly because it has a new mechanism of action which could avoid the graft organ damage caused by the condition. This 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?

The naturally occurring (endogenous) cardiotrophin-1 has been shown to stimulate the survival and recovery of cells after damage. According to the sponsor, these effects of cardiotrophin-1 medicinal product will help protect the graft organ from ischemia/reperfusion injury.

What is the stage of development of this medicine?

The effects of cardiotrophin-1 were evaluated in experimental models. At the time of submission of the application for orphan designation, no clinical trials in patients at risk of ischemia/reperfusion injury were initiated.

Cardiotrophin-1 was not authorised anywhere worldwide for the prevention of ischemia/reperfusion injury nor designated as orphan medicinal product elsewhere for this condition, at the time of submission.

The product was designated in June 2008 as an orphan product by the FDA for the following indication: "to protect the liver from ischemia/reperfusion injury inherent to the procedure of transplantation".

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 July 2007 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 European Union) 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:

Digna Biotech S.L.
Avenida Pio XII, 22
Oficina 2
31008 Pamplona
Navarra
Spain
Telephone: +34 91 18 52 510
Telefax: +34 91 18 52 519
E-mail: info@dignabiotech.com

Patient associations' contact points

None available.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Cardiotrophin-1	Prevention of the ischemia/reperfusion injury associated with solid organ transplantation
Czech	Kardiotropin-1	Prevence ischemie/ reperfuzního poškození u transplantace solidních orgánů
Danish	Kardiotrophin-1	Prævention af den iskæmi/reperfusionsskade associeret med transplantation af solide organer
Dutch	Cardiotrofine-1	Preventie van ischemie- / reperfusieletsel geassocieerd aan soliede orgaantransplantatie
Estonian	Kardiotrofiin-1	Soliidorganite siirdamisega seotud isheemia/reperfusioonvigastuse ennetamine
Finnish	Kardiotropiini-1	Iskemia-/reperfuusiovaurion esto elinsiirtoleikkauksessa
French	Cardiotrophine-1	Prévention des lésions d'ischémie-reperfusion associées aux transplantations d'organes solides
German	Cardiotrofine-1	Prävention (Vorbeugung) der Ischämie/Organperfusion verursacht durch die Transplantation solider Organe
Greek	καρδιοτροφίνη-1	Πρόληψη της ισχαιμίας/ τραυματισμού λόγω επαναιμάτωσης που συσχετίζεται με τη μεταμόσχευση συμπαγών οργάνων
Hungarian	Cardiotrophin-1	Szervátültetéssel összefüggő ischemiás/reperfúziós károsodás megelőzése
Italian	Cardiotrofina-1	Prevenzione del danno da ischemia/riperfusione associato all'intervento di trapianto di organi solidi
Latvian	Kardiotrofīns-1	Išēmisko/reperfūzijas bojājumu novēršana saistībā ar orgānu transplantāciju
Lithuanian	Kardiotrofinas-1	Išemijos / reperfuzijos pažeidimo prevencija, susijusi su parenchiminių organų transplantacija
Polish	Kardiotropina-1	Zapobieganie uszkodzeniu narządu spowodowanego niedokrwieniem/reperfuzją związanym z przeszczepem narządów litych
Portuguese	Cardiotrofina-1	Prevenção da lesão de isquémia/reperfusão associada ao transplante de órgãos sólidos
Slovak	Kardiotrofín-1	Prevencia ischemicko-reperfúzneho poškodenia súvisiaceho s postupom pri transplantácii solídneho orgánu
Slovenian	Kardiotrofin-1	Preprečevanje ishemične/reperfuzijske poškodbe, povezane s presaditvijo parenhimskih organov
Spanish	Cardiotrofina-1	Prevención del daño por isquemia/reperfusión asociado al transplante de órganos sólidos
Swedish	Cardiotrophin-1	Förebyggande av ischemia/reperfusionsskada i samband med organtransplantation

[1] At the time of designation

Language	Active Ingredient	Indication
Norwegian	Kardiotrofin-1	Forebygging av iskemi/reperfusjonsskade forbundet med solid organ-transplantasjon
Icelandic	Kardíótrófín-1	Forvörn gegn blóðþurrðar/endurblóðvæðingar skaða í tengslum við líffæraígræðslu.