European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF pyridoxalated hemoglobin polyoxyethylene for the treatment of cardiogenic shock

On 2 August 2007, orphan designation (EU/3/07/463) was granted by the European Commission to Curacyte AG, Germany, for pyridoxalated hemoglobin polyoxyethylene for the treatment of cardiogenic shock.

What is cardiogenic shock?

Shock is defined by inadequate delivery of oxygen to the tissues of the body. Cardiogenic shock is a form of shock that occurs due to the weakened pumping function of the heart. A sudden decrease in the strength of the heart pump (e.g. due to a heart attack or heart disease) combined with an inadequate response of the tone of the vascular system (the system composed of arteries and veins, which serves to transport the blood around the body), resulting in a lowered blood pressure. This may lead to a reduction of oxygen brought to the vital organs of the body by the blood, which will ultimately lead to shock and possibly death. Nitric oxide (NO) is a naturally produced substance, released by certain cells such as the endothelial cells (the cells that line the inside surface of the blood vessels). NO is known to be a powerful substance that can cause widening of blood vessels (vasodilatation) and thus reduction the blood pressure. It is hypothesized that the production of an excessive amount of NO by the body might play an important role in the development of the cardiogenic shock process. Cardiogenic shock is a life-threatening condition.

What are the methods of treatment available?

Several products were authorised for treatment of the condition in the Community at the time of submission of the application for orphan drug designation. Treatment included medicines to support the blood pressure and to stimulate the heart to contract more forcefully. In addition, other measures were used such as revascularisation (cardiac bypass surgery) to treat possible causes.
Satisfactory argumentation has been submitted by the sponsor to justify the assumption that pyridoxalated hemoglobin polyoxyethylene might be of potential significant benefit for the treatment of cardiogenic shock, mainly because it has a new mechanism of action and might possibly be used in combination with other treatments. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, cardiogenic shock was considered to affect approximately 4 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 200,000 persons in total.

*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 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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How is this medicinal product expected to act?
Pyridoxalated hemoglobin polyoxyethylene is designed to bind to NO in the blood and inhibit vasodilation caused by NO release. According to the sponsor, the blood pressure will thus be maintained at a high enough level to prevent the lack of oxygen in tissues and the development of cardiogenic shock.

What is the stage of development of this medicinal product?
The effects of pyridoxalated hemoglobin polyoxyethylene were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with cardiogenic shock were ongoing.

Pyridoxalated hemoglobin polyoxyethylene was not authorised anywhere worldwide for the treatment of cardiogenic shock nor 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 27 June 2007 a positive opinion recommending the grant of the above-mentioned designation.

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.

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

Language	Active Ingredient	Indication
English	Pyridoxalated haemoglobin polyoxyethylene	Treatment of cardiogenic shock
Bulgarian	Пиридоксилиран хемоглобин полиоксиетилен	Лечение на кардиогенен шок
Czech	Pyridoxalát-hemoglobin-polyoxyethylen	Léčba kardiogenního šoku
Danish	Pyridoxyleret hæmoglobin polyoxyethylen	Behandling af kardiogent shock
Dutch	Gepyridoxaleerd hemoglobine polyoxyethyleen	Behandeling van cardiogene shock
Estonian	Püridoksaleeritud hemoglobiin polüoksüetüleen	Kardiogeense šoki ravi
Finnish	Pyridoksaloitu polyoksyetyleeni-hemoglobiini	Kardiogeenisen sokin hoito
French	Polyoxyéthylène d'hémoglobine pyridoxalatée	Traitement du choc cardiogénique
German	Pyridoxaliertes Hämoglobin-Polyoxyethylen	Behandlung des kardiogenen Schocks
Greek	Πυριδοξαλιωμένη αιμοσφαιρίνη-πολυοξυαιθυλένιο	Θεραπεία καρδιογενούς καταπληξίας
Hungarian	Piridoxál-hemoglobin-polioxietilén	Cardiogen shock kezelése
Italian	Emoglobina poliossietilene piridossilata	Trattamento dello shock cardiogenico
Latvian	Hemoglobīna konjugāts ar piridoksālu un polioksietilēnu	Kardiogēnā šoka ārstēšana
Lithuanian	Pyridoxalát hemoglobín-polyoxyetylénu	Kardiogeninio šoko gydymas
Maltese	Pyridoxalated hemoglobin polyoxyethylene	Kura tax-xokk kardjoġeniku
Polish	Koniugat hemoglobiny z pirydoksalem i polioksyetylenem	Leczenie wstrząsu kardiogennego
Portuguese	Polioxietileno de hemoglobina piridoxalatada	Tratamento do choque cardiogénico
Romanian	Hemoglobină polioxietilen piridoxalată	Tratamentul şocului cardiogenic
Slovak	Pyridoxal hemoglobín polyoxyetylén	Liečba kardiogénneho šoku
Slovenian	Piridoksaliran hemoglobin polioksietilen	Zdravljenje kardiogenega šoka
Spanish	Compuesto de piridoxalato de hemoglobina y polioxietileno	Tratamiento del shock cardiogénico
Swedish	Pyridoxalerat hemoglobin-polyoxyetylen	Behandling av kardiogen chock
Norwegian	Pyridoksintilsatt hemoglobin-polyoksyetylen	Behandling av kardiogent sjokk
Icelandic	Pýrídoxaltengt hemóglóbín pólýoxýetýlen	Meðferð við hjartalosti