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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Synthetic peptide L-cysteine, L-cysteinylglycyl-L-glutaminy-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide for the treatment of primary graft dysfunction following lung transplantation

On 9 October 2015, orphan designation (EU/3/15/1549) was granted by the European Commission to Apeptico Forschung und Entwicklung GmbH, Austria, for synthetic peptide L-cysteine, L-cysteinylglycyl-L-glutaminy-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide for the treatment of primary graft dysfunction following lung transplantation.

What is primary graft dysfunction following lung transplantation?

Organ transplantation refers to the transfer of organs from a donor's to a recipient's body. The transplanted organ is called a graft. Transplanted organs may suffer damage during transplantation; in some cases, the damage stops the graft from working normally.

The graft may stop working properly in the first 72 hours after transplantation and this is known as primary graft dysfunction. It is thought that interruption and resumption of blood supply during transplantation can damage the transplanted lungs.

Primary graft dysfunction following lung transplantation is a life-threatening condition because the transplanted organ may fail.

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

At the time of designation, primary graft dysfunction following lung transplantation affected approximately 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of around 500 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This

*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 512,900,000 (Eurostat 2015).

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, no satisfactory methods were authorised in the EU for the treatment of primary graft dysfunction following lung transplantation.

How is this medicine expected to work?

During transplantation, interruption and resumption of blood supply to transplanted lungs can lead to the formation of reactive oxygen species (ROS, toxic molecules containing oxygen) which can damage the cells and the function of the transplanted lungs.

Although its mechanism of action is not fully understood, this medicine is thought to reduce the production of ROS and thereby prevent cells in the transplanted lung from being damaged. It is also thought to restore the impaired exchange of oxygen between the blood and airways in the lung.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial with the medicine in patients with primary graft dysfunction following lung transplantation had been completed.

At the time of submission, the medicine was not authorised anywhere in the EU for primary graft dysfunction following lung transplantation or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 3 September 2015 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 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

For details of the current sponsor of the orphan designation please refer to the information on the main web page of this Public Summary of Opinion.

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Synthetic peptide L-cysteine, L-cysteinylglycyl-L-glutamyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Treatment of primary graft dysfunction following lung transplantation
Bulgarian	Синтетичен пептид съдържащ L-цистеин, L-цистеинилглицил-L-глутамил-L-аргинил-L-алфа-глутамил-L-треонил-L-пролил-L-алфа-глутамилглицил-L-аланил-L-алфа-глутамил-L-аланил-L-лизил-L-пролил-L-триптофил-L-тирозил-, цикличен (1.fwdarw.17)-дисулфид	Лечение на първична дисфункция на присадката след трансплантация на бял дроб
Croatian	Sintetički peptid L-cistein, L-cisteinilglicil-L-glutaminil-L-arginil-L-.alfa.-glutamyl-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamyl-L-alanil-L-lizil-L-prolil-L-triptofil-L-tirozil-, ciklični (1.fwdarw.17)-disulfid	Liječenje primarne disfunkcije presatka nakon transplantacije pluća
Czech	Syntetický peptid L-Cysteine, L-cysteinylglycyl-L-glutamyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfid	Léčba primární dysfunkce štěpu po transplantaci plic
Danish	Syntetisk peptid L-ystein, L-cysteinylglycyl-L-glutamyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfid	Behandling af primær graft-dysfunktion efter lungetransplantation
Dutch	Synthetisch peptide L-Cysteine, L-cysteinylglycyl-L-glutamyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Behandeling van primaire transplantaatdysfunctie na longtransplantatie
Estonian	Süntetiline peptiid L-tsüsteiin, L-tsüsteinüülglüküül-L-glutaminüül-L-arginüül-L-.alfa.-glutamüül-L-threonüül-L-prolül-L-.alfa.-glutamüülglicüül-L-alanüül-L-.alfa.-glutamüül-L-alanüül-L-lüsüül-L-prolül-L-trüptofüül-L-türosüül-, tsüklikc (1.fwdarw.17)-disulfiid	Ravi primaarne siiriku düsfunktsioon järgmised kopsusiire

¹ At the time of designation

Language	Active ingredient	Indication
Finnish	Synteettinen L-kysteiini, L-kysteiinylglysyli-L-glutaminyli-L-arginyli-L-.alpha.-glutamyyli-L-treonyyli-L-prolyli-L-.alpha.-glutamylglysyli-L-alanyyli-L-.alpha.-glutamyyli-L-alanyyli-L-lysyli-L-prolyli-L-tryptofyli-L-tyrosyli-, syklinen (1.fwdarw.17)-disulfiidi peptidipeptide	Keuhkonsiirron jälkeinen siirrännäisen toimintahäiriön hoito
French	Peptide synthétique L-Cysteine, L-cysteinylglycyl-L-glutaminyli-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Traitement de la dysfonction primaire du greffon après transplantation pulmonaire
German	Synthetisches Peptid L-Cysteine, L-cysteinylglycyl-L-glutaminyli-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfid	Behandlung der primären Transplantatdysfunktion nach einer Lungentransplantation
Greek	Συνθετικό πεπτιδιο L-Cysteine, L-cysteinylglycyl-L-glutaminyli-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Θεραπεία της πρωτογενούς δυσλειτουργίας του μοσχεύματος μετά από μεταμόσχευση πνεύμονα
Hungarian	Szintetikus L-Cysteine, L-cysteinylglycyl-L-glutaminyli-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-diszulfid peptid	Tüdőtranszplantációt követő elsődleges graft diszfunkció kezelése
Italian	Peptide sintetico L-Cysteine, L-cysteinylglycyl-L-glutaminyli-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Trattamento della disfunzione dell'innesto primitiva dopo il trapianto del polmone
Latvian	Sintētisks L-cisteīna, L-cisteīnīlglicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamīlglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lizil-L-prolil-L-triptofil-L-tirozil-, ciklisks (1.fwdarw.17)-disulfīda peptīds	Primāras transplantāta disfunkcijas pēc plaušu transplantācijas ārstēšana
Lithuanian	Sintetinis L-cisteino, L-cisteinilglycil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglycil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lysyl-L-prolil-L-triptofil-L-tirozil-, ciklic (1.fwdarw.17)-disulfido peptidas	Pirminio transplantato funkcijos sutrikimo po plaučių transplantacijos gydymas
Maltese	Peptide L-cysteine, L-cysteinylglycyl-L-glutaminyli-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide sintetiku	Kura ta' taħsir ta' funzjoni ta' trapijant primarju wara trapijant tal-pulmun

Language	Active ingredient	Indication
Polish	Syntetyczny peptyd L-Cysteine, L-cysteinyglycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Leczenie pierwotnej dysfunkcji przeszczepu po transplantacji płuc
Portuguese	Peptídeo sintético L-cisteína, L-cisteinilglicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lisil-L-prolil-L-triptofil-L-tirosil-, ciclico (1.fwdarw.17)-dissulfeto	Tratamento da disfunção primária do enxerto após transplante do pulmão
Romanian	Peptid sintetic L-Cistein, L-cisteinilglicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lizil-L-prolil-L-triptofil-L-tirozil-, ciclic (1.fwdarw.17)-disulfid	Tratamentul disfuncției primare de grefonpost transplant pulmonar
Slovak	Syntetický L-Cysteine, L-cysteinyglycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide peptid	Liečba primárnej disfunkcie štepú po transplantácii pľúc
Slovenian	Sintetični peptid L-cistein, L-cisteinilglicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lisil-L-prolil-L-triptofil-L-tirosil-, ciklični (1.fwdarw.17)-disulfid	Zdravljenje primarne disfunkcije presadka pri trasplantaciji pljuč
Spanish	Peptido sintético L-cisteína, L-cisteinilglicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lisil-L-prolil-L-triptofil-L-tirosil-, ciclico (1.fwdarw.17)-disulfuro	Tratamiento de la disfunción primaria del injerto tras el transplante de pulmón
Swedish	Synthetisk peptid L-Cysteine, L-cysteinyglycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Behandling av primär graft-dysfunktion efter lungtransplantat
Norwegian	Syntetisk peptid L-Cysteine, L-cysteinyglycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Behandling av primær graft-dysfunksjon etter lungetransplantasjon
Icelandic	Samtengt peptíð L-Cýstein, L-cýsteinýlglycýl-L-glútamínýl-L-arginýl-L-.alfa.-glútamýl-L-threónýl-L-prólýl-L-.alfa.-glútamýlglycýl-L-alanýl-L-.alfa.-glútamýl-L-alanýl-L-lýsýl-L-prólýl-L-trýptóphýl-L-týrósfýl-, cýclic (1.fwdarw.17)-dísúlfíð	Meðferð frumkominnar ígræðslu vanstarfsemi eftir lungna-ígræðslu