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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Ciclosporin (inhalation use) for the prevention of graft rejection after lung transplantation

On 29 July 2004 orphan designation (EU/3/04/209) was granted by the European Commission to PARI Aerosol Research Institute, Germany, for ciclosporin (for inhalation use) for the prevention of graft rejection after lung transplantation.

The name of the sponsor changed to PARI Pharma GmbH in 2007.

What is graft rejection in lung transplantation?

Lung transplantation is performed when, because of underlying conditions, the lungs are so damaged that one or both need to be replaced. It is most commonly performed in pulmonary emphysema, idiopathic pulmonary fibrosis, pulmonary hypertension and cystic fibrosis.

Rejection is the process by which the organ recipient's defence (immune) system recognises, becomes sensitised against, and attempts to eliminate the foreign donor organ.

It has been observed that at least one episode of rejection is common within the first year after a transplant. More than 80% of people who receive a lung transplant develop some symptoms of rejection within a month of transplantation. Symptoms include fever, shortness of breath, and weakness due to the non-optimal functioning of the transplanted lungs. Scar tissue may form in the small airways and gradually block them, possibly indicating gradual rejection.

The condition can be chronically debilitating and life threatening due to the high incidence of severe infections and graft rejection.

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 graft rejection after lung transplantation was estimated to be approximately 0.01 people in 10,000 in the European Union (EU)*. This is

*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.

equivalent to a total of around 460 people, which is below the ceiling 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).

What methods of prevention are available?

In order to preserve the new lung(s) in the recipient's body a suppression of the patient's defence potential (immunosuppression) is induced after lung transplantation. The immunosuppressive agents already authorized for the use in the prevention of graft rejection are represented by ciclosporin (oral and intravenous administration) and corticosteroids. Other therapies that can be used are medicinal products called antibodies that are aimed at targeting and blocking the cells that produce the immune response: antithymocyte globulins or monoclonal CD3 antibodies.

Inhaled ciclosporin might be of potential significant benefit for the prevention of graft rejection after lung transplantation due to its new route of administration. 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?

Ciclosporin for inhalation use is an immunosuppressive drug used to prevent the body from rejecting transplanted organs, as it suppresses the body's natural reaction to the transplanted organ and is a component of most of the post transplant regimens. Ciclosporin acts by inhibiting some special defence cells called lymphocyte T cells. It inhibits also the production of some special substances called lymphokines, which play a role in the defence reactions of the body. Ciclosporin for inhalation is meant to be used in patients to prevent development of a rejection against lung transplants by delivering the medicinal product directly to the lungs.

What is the stage of development of this medicine?

The effects of ciclosporin for inhalation use were evaluated in experimental models. At the time of submission of the application for orphan designation, no clinical trials in patients with lung transplantation were initiated.

Ciclosporin for inhalation use was not marketed anywhere worldwide for graft rejection in lung transplantation or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 of June 2004 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

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Ciclosporin (inhalation use)	Prevention of graft rejection after lung transplantation
Czech	Ciclosporin (k inhalaci)	Prevence rejekce transplantátu plic
Danish	Ciclosporin (til inhalation)	Forebyggelse af afstødning af transplantat efter lungetransplantation
Dutch	Ciclosporine (inhalatie)	Preventie van een afstotingsreactie na longtransplantatie
Estonian	Tsüklosporiin (inhalatsiooniks)	Äratõukereaktsiooni ennetamine peale kopsu transplantatsiooni
Finnish	Siklosporiini (inhalaatioon)	Siirännäisen hylkimisreaktion ehkäisy keuhkonsiirron jälkeen
French	Ciclosporine (voie inhalée)	Prevention du rejet du greffon après transplantation pulmonaire
German	Ciclosporin (zur Inhalation)	Vorbeugung von Abstoßungsreaktion nach Lungentransplantationen
Greek	Κυκλοσπορίνη (Χρήση δια εισπνοής)	Πρόληψη απόρριψης μοσχεύματος μετά από μεταμόσχευση πνεύμονα
Hungarian	Cyclosporin (inhalációs alkalmazásra)	Kilöködési reakció megelőzése tüdőtranszplantációt követően
Italian	Ciclosporina (uso inalatorio)	Prevenzione del rigetto dopo trapianto polmonare
Latvian	Ciklosporīns (inhalācijām)	Plaušu transplantāta atgrūšanas profilakse
Lithuanian	Ciklosporinas (inhaliacijoms)	Transplantanto atmetimo reakcijos prevencija po plaučių persodinimo
Maltese	Ciclosporin (inhalation use)	Prevention of graft rejection after lung transplantation
Polish	Cyklosporyna (inhalacja)	Zapobieganie odrzuceniu przeszczepu po transplantacji płuca
Portuguese	Ciclosporina (via inalatoria)	Prevenção da rejeição do enxerto após transplante do pulmão.
Slovak	Cyklosporín (inhalácia)	Prevenia odmietnutia štepú po transplantácii pľúc
Slovenian	Ciklosporin (za inhalacijo)	Preprečevanje zavrnitve presadka pri transplantaciji pljuč
Spanish	Ciclosporina (vía inhalatoria)	Prevención del rechazo del injerto tras el trasplante de pulmón
Swedish	Ciclosporin (användning för inhalation)	Förebyggande av transplantatavstötning efter lungtransplantation
Norwegian	Ciklosporin (til inhalasjon)	Profylakse mot rejeksjon etter lungetransplantasjon
Icelandic	Ciklósporín (til innöndunar)	Til að koma í veg fyrir höfnun eftir lungnaígræðslu

¹ At the time of designation