



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Dexamethasone phosphate (iontophoretic solution, ocular use) for the treatment of corneal graft rejection

On 15 April 2009, orphan designation (EU/3/09/636) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for dexamethasone phosphate (iontophoretic solution, ocular use) for the treatment of corneal graft rejection.

The sponsorship was transferred to Eyegate Pharma SAS, France, in September 2010 and to Interface International Consultancy Ltd, United Kingdom, in May 2012.

What is corneal graft rejection?

Corneal graft rejection is a problem that can occur after a cornea transplant, when the recipient's body rejects the transplanted cornea (the 'graft'). The cornea is the transparent surface at the front of the eye that covers the iris and the pupil. Corneal graft rejection is caused by the patient's immune system (the body's natural defences) recognising the transplanted cornea as 'foreign' and producing antibodies against it. This results in inflammation and damage to the graft.

Corneal graft rejection is a long-term debilitating disease because it can lead to loss of vision in the affected eye.

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

At the time of designation, corneal graft rejection affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 50,000 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 the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of submission of the application for orphan drug designation, corticosteroids (substances that reduce the activity of the immune system) were authorised in the EU to prevent or treat graft

*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. At the time of designation, this represented a population of 504,800,000 (Eurostat 2009).



rejection after cornea transplants. These medicines are available in various forms, such as eye drops, tablets and solutions for injection.

The sponsor has provided sufficient information to show that dexamethasone phosphate (iontophoretic solution, ocular use) might be of significant benefit for patients with corneal graft rejection because the medicine is given to patients directly into the eye using a particular device rather than as eye drops, as medicine taken by mouth or given by intravenous (into the vein) injection. This system may deliver higher amounts of the medicine into the eye and may lead to better outcomes for patients. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Dexamethasone phosphate is a corticosteroid that is already available in the EU as eye drops for the treatment of corneal graft rejection. It works by attaching to receptors on various types of immune cells in the eye fluid. This leads to a reduction in inflammation and damage caused to the transplanted cornea.

This medicine is a new formulation of dexamethasone phosphate that is given directly into the eye using an 'iontophoretic' device. The device is placed around the cornea and uses a small electrical current to move a dose of dexamethasone phosphate from a reservoir into the eye. In this way, a higher amount of corticosteroid is expected to penetrate into the anterior chamber (the fluid-filled space behind the cornea where the medicine works) than can be achieved with eye drops, oral or intravenous medicines.

What is the stage of development of this medicine?

The effects of dexamethasone phosphate (iontophoretic solution, ocular use) have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with corneal graft rejection were being designed.

At the time of submission, dexamethasone phosphate (iontophoretic solution, ocular use) was not authorised anywhere in the EU for the treatment of corneal graft rejection. Orphan designation of this medicine had been granted in the United States of America for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 2 April 2009 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	Dexamethasone phosphate (iontophoretic solution, ocular use)	Treatment of corneal graft rejection
Bulgarian	Дексаметазон фосфат (йонотопорезен разтвор, очно приложение)	Лечение при отхвърляне на присадка на роговица
Czech	Dexametazon fosfát (Iontoforézní roztok pro Oční podání)	Léčba odhojení (rejekce) korneálního transplantátu
Danish	Dexamethason-fosfat (Iontoforetisk opløsning, okulær brug)	Behandling af corneatransplantat-afstødning
Dutch	Dexamethasone-fosfaat (iontoforetische oplossing voor oculair gebruik)"	Behandeling van corneatransplantaat afstoting
Estonian	Deksametasoonfosfaat (iontoforeetilise lahuse, okulaarseks kasutamiseks)	Savkestasiiriku äratõuke raviks
Finnish	Deksametasonifosfaatti (Iiuos iontoforeesia varten, silmään käytettäväksi)	Sarveiskalvosiirännäisen hyljinnän hoito
French	Phosphate de dexamethasone (solution iontophorétique, voie ophtalmique)	Traitement du rejet de greffe cornéenne
German	Dexamethasonphosphat (iontophoretische Lösung, zur Anwendung am Auge)	Behandlung der Abstoßung von Hornhauttransplantaten
Greek	φωσφορική δεξαμεθαζόνη (Ιοντοφορετικό διάλυμα, οφθαλμική χρήση)	Θεραπεία απόρριψης μοσχεύματος κερατοειδούς
Hungarian	Dexametazon-foszfát (iontoforézis oldat, szemészeti alkalmazás)	Cornea transzplantátum kilökődésének kezelésére
Italian	Desametasone fosfato (Soluzione iontoforetica per uso oculare)	Terapia del rigetto nel trapianto di cornea
Latvian	Deksametazona fosfāts (jontoforēzes šķīdums, pilināšanai acīs)	Radzenes transplantāta atgrūšanas ārstēšana
Lithuanian	Deksametazono fosfatas (jontoforetinis tirpalas, vartoti akims)	Ragenos transplantato atmetimo reakcijos gydymas
Maltese	Dexamethasone phosphate (soluzjoni jontoforetika, użu għall-għajnejn)	Kura ta' riġettar ta' trapjant tal-kornea
Polish	Fosforan deksametazonu (Jontoforetyczny roztwór do oczu)	Leczenie odrzucenia przeszczepu rogówki
Portuguese	Fosfato de dexametasona (Solução iontoforética, uso ocular)	Tratamento da rejeição do enxerto da córnea
Romanian	Dexametazonă fosfat (soluție iontoforetică, uz oftalmic)	Tratamentul rejetului grefei de cornee
Slovak	Dexametazón fosfát (roztok na ionoforézu pre očné použitie)	Liečba rejekcie rohovkového štepu

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	Deksametazon fosfat (iontoforezna raztopina, okularna uporaba)	Zdravljenje zavrnitve presadka roženice
Spanish	Fosfato de dexametasona (solución iontoforética, vía oftálmica)	Tratamiento del rechazo del trasplante de córnea
Swedish	Dexametasonfosfat (jontoforetisk lösning, okulär användning)	Behandling av avstötning av hornhinnetransplantat
Norwegian	Deksametasonfosfat (iontoforetisk løsning, okulær bruk)	Behandling av avstøtning av corneatransplantat
Icelandic	Dexamethasón fosfat (fareindalækninga lausn, til notkunar í augu)	Meðferð við höfnun glæruígræðslu