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 antisense oligonucleotide (TATCCGGAGGGCTCGCCATGCTGCT) for the prevention of corneal graft rejection

On 17 April 2007, orphan designation (EU/3/07/445) was granted by the European Commission to Gene Signal SAS, France, for antisense oligonucleotide (TATCCGGAGGGCTCGCCATGCTGCT) for the prevention of corneal graft rejection.

What is corneal graft rejection?

After transplantation of the cornea (the round transparent part of the eye, external to the iris), there is a risk that the transplant (graft) will not be accepted by the patient's immune system, which would lead to a phenomenon called "rejection".
The cornea does not have blood vessels, so it is usually difficult for white blood cells and antibodies (both mediators of rejection) to reach it and activate rejection mechanisms. For this reason, rejection tends to occur less frequently in corneal transplants compared to other organs that do have blood vessels, such as the kidney, but it is still a feared complication as it can lead to loss of vision in the affected eye.
In some eye diseases, however, there can be formation of new blood vessels in the cornea, and this also may occur (or worsen) in the new transplanted cornea, thus allowing easier access for white blood cells and antibiotics, and an increased likelihood of rejection.

What are the methods of prevention available?

Currently, no satisfactory methods exist in the European Union that were authorised at the time of application, for the prevention of corneal graft rejection. However, eye drops containing corticosteroids (cortisone-like substances) are commonly prescribed after corneal transplantation to prevent rejection; other drugs that have been employed are cyclosporin and tacrolimus, both for the treatment and the prevention of corneal graft rejection.

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

According to the information provided by the sponsor, the population of patients eligible for prevention of corneal graft rejection was estimated to be approximately 46,000 persons in the European Union.

How is this medicinal product expected to act?

Antisense oligonucleotide (TATCCGGAGGGCTCGCCATGCTGCT) acts by blocking the production of a protein that is required for the formation and growth of new blood vessels. It does not act on already existing blood vessels. Since formation of new blood vessels in the cornea is believed to be one of the principal mechanisms by which the immune system may reject a corneal transplantation, the medicinal product is expected to reduce the likelihood of rejection itself.

[*] 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.

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What is the stage of development of this medicinal product?
The effects of antisense oligonucleotide (TATCCGGAGGGCTCGCCATGCTGCT) were evaluated in experimental models. At the time of submission of the application for orphan designation, no clinical trials in patients with corneal transplants were initiated.

Antisense oligonucleotide (TATCCGGAGGGCTCGCCATGCTGCT) was not authorised anywhere worldwide for the prevention of Corneal Graft Rejection, 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 8 March 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	Antisense oligonucleotide (TATCCGGAGGGCTCGCCATGCT GCT)	Prevention of corneal graft rejection
Bulgarian	Антисенс олигонуклеотид (TATCCGGAGGGCTCGCCATGCT GCT)	Профилактика на от отхвърляне на присадката на роговицата
Czech	Antisense oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Prevence odhojení (rejekce) korneálního transplantátu
Danish	Antisense oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Forebyggelse af afstødning af corneatransplantat
Dutch	Antisense-oligonucleotide (TATCCGGAGGGCTCGCCATGCT GCT)	Preventie van corneatransplantaat afstoting
Estonian	Antisense oligonukleotiid (TATCCGGAGGGCTCGCCATGCT GCT)	Savkestasiiriku äratõuke ennetamine
Finnish	Antisense-oligonukleotidi (TATCCGGAGGGCTCGCCATGCT GCT)	Sarveiskalvosiirteen hyljinnän ehkäisy
French	Oligonucléotide antisense (TATCCGGAGGGCTCGCCATGCT GCT)	Prévention du rejet de greffe de cornée
German	Antisense-Oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Prävention der Hornhauttransplantatabstoßung
Greek	Αντιπληροφοριακό Ολιγονουκλοτεϊδιο (TATCCGGAGGGCTCGCCATGCT GCT)	Πρόληψη απόρριψης μοσχεύματος κερατοειδούς
Hungarian	Antisens oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Cornea transzplantátum kilökődésének megelőzése
Italian	Oligonucleotide antisenso (TATCCGGAGGGCTCGCCATGCT GCT)	Prevenzione del rigetto nel trapianto di cornea
Latvian	Antisense oligonukleotīds (TATCCGGAGGGCTCGCCATGCT GCT)	Radzenes transplantātu atgrūšanas profilakse
Lithuanian	Priešprasmis oligonukleotidas (TATCCGGAGGGCTCGCCATGCT GCT)	Ragenos transplantato atmetimo reakcijos profilaktikai
Polish	Ooligonukleotyd antysensowy (TATCCGGAGGGCTCGCCATGCT GCT)	Zapobieganie odrzuceniu przeszczepu rogówki

Portuguese	Oligonucleótido anti-sentido (TATCCGGAGGGCTCGCCATGCT GCT)	Prevenção da rejeição do enxerto da córnea
Romanian	Oligonucleotid antisens (TATCCGGAGGGCTCGCCATGCT GCT)	Prevenirea rejetului grefei de cornee
Slovak	Antisense oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Prevencia odmietnutia štepu rohovky
Slovenian	Protismerni oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Preprečevanje zavrnitve presadka roženice
Spanish	Oligonucleótido antisentido (TATCCGGAGGGCTCGCCATGCT GCT)	Prevención del rechazo del injerto de córnea
Swedish	Antisens oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Förebyggande av avstötning av hornhinnetransplantat
Norwegian	Antisens oligonukleotid (TATCCGGAGGGCTCGCCATGCT GCT)	Forebygging av avstøtning av corneatransplantat
Icelandic	Antisense ólígónúkleótíð (TATCCGGAGGGCTCGCCATGCT GCT)	Að koma í veg fyrir höfnun hornhimnuígræðslu