

For the use of a Registered Medical Practitioner or Hospital only.

AUTOLOGOUS HUMAN LIMBAL EPITHELIAL CELLS CULTURED ON HUMAN AMNIOTIC MEMBRANE

ReliNethra®

(Autologous bio-engineered composite limbal epithelial graft)

DESCRIPTION

ReliNethra® is an autologous bio-engineered composite limbal epithelial graft for corneal disorders. It is prepared from the limbal biopsy excised from the healthy eye of the patient. It results in re-epithelialization of the damaged or diseased corneal surface. *ReliNethra*® transplant leads to renewal of ocular surface epithelial cells thereby replacing the damaged ocular surface with smooth and healthy cells. It is a 4 cm² denuded human amniotic membrane with autologous limbal epithelial cells expanded from limbal explants.

ReliNethra® is manufactured under aseptic conditions from human limbal biopsy (autologous). The donor of the biopsy is tested for antibodies to human immunodeficiency virus type 1 and type 2 (anti-HIV-1 and anti-HIV-2), hepatitis B surface antigen (HBsAg), antibodies to hepatitis C virus (HCV), CMV-IgM & IgG, and Syphilis-IgM & IgG. The cord blood of the placenta donor is tested and found to be negative for HIV-1, HIV-2, HBV, and HCV by PCR and CMV-IgM & IgG, and Syphilis-IgM/IgG by ELISA. Amniotic membrane is used as a substrate for culturing limbal epithelial cells. The limbal culture medium and the spent limbal culture medium are tested for sterility and endotoxins. The final product is tested for morphology before release.

MECHANISM OF ACTION

Limbal stem cell transplant results in re-epithelialization of the reconstructed corneal surface. Continuous centripetal movement of cultured corneal epithelium on the human amniotic membrane towards the visual axis supports the damaged ocular surface by smooth reconstruction.

CLINICAL STUDIES

The limitations of conventional treatment involving the repair of the damaged corneal surface with amniotic membrane alone are the risk of hemorrhage under the membrane, early disintegration of the membrane and suitability for use in only partial Limbal stem cell deficiency (LSCD). A serious limitation of transplantation of direct autologous limbal epithelial cells is that one or two limbal cell grafts spanning two or three clock hours of the limbus, have to be removed from the healthy contralateral eye. The approach of using autologous or allogenic bio-engineered composite graft for the treatment of damaged or diseased corneal epithelial surface is based on the tenet that a small population of Limbal stem cells (LSCs) may be expanded on the amniotic membrane for subsequent reconstruction of the ocular surface, without compromising the donor eye.

ReliNethra® is an autologous bio-engineered composite limbal epithelial graft comprising of limbal epithelial stem cells cultured ex-vivo on an extracellular carrier matrix, prepared by "Reliance Life Sciences Pvt. Ltd". An open labeled, prospective study to evaluate the efficacy and safety of *ReliNethra*® (an autologous bio-engineered composite limbal epithelial graft) was carried out on Indian patients. This study was aimed at assessing the safety and efficacy of *ReliNethra*®, for the treatment of a damaged or diseased corneal epithelial surface. Evaluation of Visual acuity (VA) was conducted on 25 evaluable patients.

The aim of cultivated limbal epithelium transplantation was to stabilize the ocular surface epithelium and improve vision. The functional ambulatory VA (< 6/60) could be improved from 1 pre-operative eye (4.17%) to 10 post-operative eyes (41.67%). Post-operative VA improved 2 or more grades in 52% cases (13/25) in worst case scenario and 56% cases (14/25) in best case scenario. Mean grade of improvement in VA (13 patients) = 5.7 and 1 patient had 12 grade improvement from HMCf to 6/9.

INDICATIONS

An autologous bio-engineered composite limbal epithelial graft is indicated in unilateral partial and total limbal stem cell deficiencies like chemical / thermal / mechanical and ionizing radiation injuries, multiple surgical procedures or cryotherapies affecting the limbal region and contact lens-induced keratopathy.

CONTRAINDICATIONS

- Bilaterally present limbal stem cell deficiency.
- Corneal thickness less than 0.4 mm.
- Co-existing conditions limiting the successful outcome of the transplant surgery like severe dry eye, lid margin keratinization, trichiasis, symblepharon etc.

WARNING

1. The container with the product should be opened only in the operation theatre under sterile conditions.
2. *ReliNethra*® has undergone clinical trials and the adverse effects observed were:
 - Pain in donor eye
 - Conjunctival congestion in donor eye
 - Pain in recipient eye
 - Lid edema in recipient eye
 - Discharge in recipient eye
 - Redness in recipient eye
 - Conjunctival congestion in recipient eye

PRECAUTIONS

1. Do not use *ReliNethra*® if the container is damaged, contaminated or any leakage noted.
2. The product should be washed four times with wash buffer with the help of sterile transfer pipette provided in the kit. For further details, please refer the user guidelines.
3. *ReliNethra*® i.e. the composite limbal epithelial graft should be placed on the cornea with the epithelial side facing upwards. For further details, please refer the user guidelines.
4. The composite graft should be transplanted into the recipient eye within 24 hours of dispatch from Reliance Life Sciences.

USE IN SPECIFIC POPULATIONS

PREGNANCY AND LACTATION

No studies have been performed till date in pregnant women; therefore transplant should be done in pregnant women only if clearly needed and as judged by the surgeon.

PEDIATRIC AND GERIATRIC POPULATION

No studies have been performed in children below the age of 6 years and in adults above 60 years, therefore transplant should be done in these cases only if clearly indicated and as judged by the surgeon.

DOSAGE

One graft of limbal epithelial stem cells (monolayer) cultured ex vivo on a 4cm² human amniotic membrane. For further details, please refer the usage guidelines.

STORAGE

ReliNethra® is to be stored in a cool dry place between 2°C and 8°C temperature. The graft should be utilized within 24 hours of packing.

CONTENTS OF THE KIT

Each *ReliNethra*® kit contains:

1. One sterile transport receptacle containing 4cm² denuded human amniotic membrane with cultured autologous limbal cells grown from limbal explants.
2. One sterile 3 ml transfer pipette.
3. One 90 mm sterile petridish.
4. Two tubes each containing 50 ml sterile wash buffer.

REFERENCES

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4. Tsai RJ, Li LM, Chen JK (2000). Reconstruction of damaged corneas by transplantation of autologous limbal epithelial cells. *N Engl J Med.* Jul 13;343(2):86-93.
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