

AUTOLOGOUS HUMAN CONJUNCTIVAL EPITHELIAL CELLS CULTURED ON HUMAN AMNIOTIC MEMBRANE

ReliNethra® C

(Autologous bio-engineered composite conjunctival epithelial cell graft)

DESCRIPTION

ReliNethra® C is an autologous bio-engineered composite conjunctival epithelial cell graft for treating conjunctival disorders. It is prepared from the conjunctival biopsy excised from the superior fornix preferably of contralateral healthy eye of the patient. It results in re-epithelialization of the damaged or diseased conjunctival surface. ReliNethra® C 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 conjunctival epithelial cells expanded from conjunctival explants.

ReliNethra® C is manufactured under aseptic conditions from human conjunctival 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, CMV-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, CMV-IgG and Syphilis-IgM/IgG by ELISA. Human amniotic membrane is used as a substrate for culturing conjunctival epithelial cells. The conjunctival culture media, the spent conjunctival biopsy collection media and the spent conjunctival culture media are tested for sterility and endotoxin. The product consisting of conjunctival epithelial cells expanded on denuded human amniotic membrane is checked for integrity and confluency under inverted, phase-contrast microscope before release.

COMPOSITION

ReliNethra® C is composed of conjunctival epithelial stem cells grown on a 4 cm² denuded human amniotic membrane with scattered explants.

MECHANISM OF ACTION

Conjunctival stem cell transplant results in restoration of physiological and functional conjunctival epithelium of the damaged or diseased eye.

CLINICAL STUDIES

The approach of using autologous or allogeneic bio-engineered composite graft for the treatment of damaged or diseased conjunctiva is based on the tenet that a small population of conjunctival epithelial stem cells may be expanded on the denuded human amniotic membrane for subsequent reconstruction of the ocular surface, without compromising the donor eye. Most studies of tissue equivalents have focused on the ability to reconstitute a tissue equivalent that bears the structural and functional characteristics of the tissue of origin. The use of bio-engineered conjunctival equivalents for the restoration of healthy conjunctiva may be important in a host of severe ocular surface disorders that involve the conjunctiva to restore the ocular surface equilibrium by tear film replacement, or after surgical excision of conjunctival lesions, thereby removing the need to harvest conjunctival autografts and cause iatrogenic injury to the ocular surface.

ReliNethra® C is an autologous bio-engineered composite conjunctival epithelial graft comprising of conjunctival 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® C was carried out in Indian patients. This study was aimed at assessing the safety and efficacy of ReliNethra® C, for restoration of physiological and functional conjunctival epithelium in 23 evaluable patients.

The aim of cultivated conjunctival epithelium transplantation was to stabilize the ocular surface epithelium. ReliNethra® C has demonstrated efficacy by restoring physiological and functional conjunctival epithelium when transplanted onto the diseased or damaged conjunctiva. Physiologically, there was adequate hydration with presence of tears, wet cornea with clear vision and clear fornix in all patients. The success rate of ReliNethra® C in 23 evaluable patients, based on the smooth and healthy appearance of the conjunctival surface was 82.6% at the end of six months.

INDICATIONS

ReliNethra® C, an autologous bio-engineered composite conjunctival epithelial cell graft is indicated in patients with damaged or diseased conjunctival surface requiring surgical correction of pterygium, symblepharon, chronic allergic conjunctivitis, toxic epidermal necrolysis, wide field excision of tumours, and/or chemical injuries.

CONTRAINDICATIONS

- Bilaterally present severe conjunctival disease or disorder.
- Previous conjunctival transplant surgery.
- Co-existing conditions limiting the successful outcome of the transplant surgery like severe dry eye (Schirmer's < 6), lid margin disorder or actively inflamed eye.

ADVERSE EVENTS

ReliNethra® C was transplanted in the defect caused by surgical excision of diseased or damaged conjunctiva. There were total 15 (60.00%) patients with at least one adverse event, of which 7 (28.00%) patients had at least one adverse event related to investigational product. There were no death or serious adverse event reported in the study. The most common adverse events (occurrence 5% patients) were ocular hyperaemia, pterygium, eye pain, corneal staining and headache.

WARNINGS AND PRECAUTIONS

1. The container with the product should be opened only in the operation theatre under sterile conditions.
2. Do not use ReliNethra® C if the container is opened, damaged, contaminated or any leakage noted.
3. 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.
4. ReliNethra® C should be placed on the diseased or damaged conjunctival surface with the epithelial side facing upwards. For further details, please refer the user guidelines.
5. ReliNethra® C should be transplanted into the recipient eye within 24 hours of packaging from Reliance Life Sciences.

DRUG INTERACTIONS

No evidence of interaction of ReliNethra® C with other drugs was observed in the course of clinical trial.

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 it is needed and judged by the surgeon.

PAEDIATRIC AND GERIATRIC POPULATION

ReliNethra® C clinical study could not identify enrolled patients below the age of 25 years and in adults above 67 years. Published literature mentions studies done in patients with age ranging from 10 to 72 years.

DOSAGE AND ADMINISTRATION

ReliNethra® C is a one time application of conjunctival epithelial stem cells (monolayer) cultured ex vivo on a 4cm² denuded human amniotic membrane. The graft should be washed four times with sterile wash buffer before transplantation. The conjunctival defect is covered with the graft and sutured with the adjacent conjunctiva. The remaining part of the graft should be trimmed and broad-spectrum ointment instilled before the eye is patched. For further details, please refer the user guidelines.

OVERDOSAGE

Not applicable, since this is one time stem cell transplant.

STORAGE

ReliNethra® C is to be stored in a cool dry place between 2°C and 8°C temperature.

SHELF LIFE

ReliNethra® C should be transplanted within 24 hours of packing the cultured graft.

CONTENTS OF THE KIT

Each ReliNethra® C kit contains:

1. One sterile transport receptacle containing 4cm² denuded human amniotic membrane with cultured autologous conjunctival cells grown from conjunctival 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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