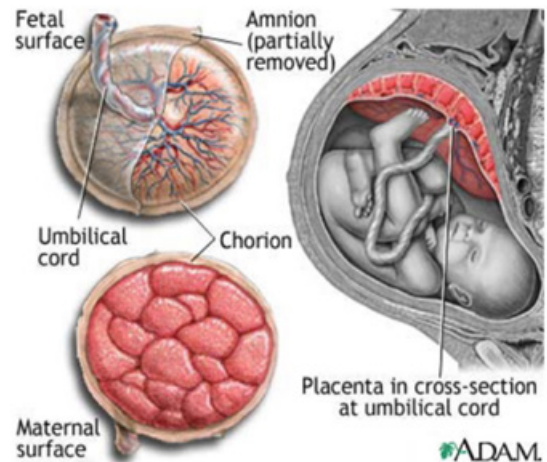


## Sources of AmnioMatrix

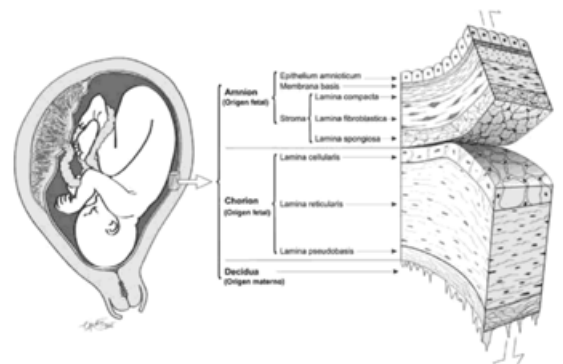
Amniotic membrane (AM) is obtained from donated placentas arranged through the Netcare Transplant Unit. Placentas are recovered with full consent from the donor.

All donors are screened for transmissible diseases such as HIV, Hepatitis B&C, CMV, HTLV I and II, Syphilis, HSV I and II. All amniotic membrane samples are tested during processing for bacterial and fungal contamination, to ensure sterility of the product.



## Anatomy of the AmnioMatrix

Amniotic membrane is the thin inner layer of the foetal membranes found on the inside the placenta. It is approximately 0.02 mm to 0.5 mm thick and consists of three different layers – single cuboidal epithelium layer, basement membrane and avascular stroma.



## Characteristics

Studies have found that the amniotic material has

### Anti-inflammatory effects

- Amniotic membrane suppresses the pro-inflammatory cytokines IL-1 $\alpha$  and IL-1 $\beta$ .<sup>1,2</sup>
- Amniotic membrane produces natural metalloprotease (MMP's) inhibitors.<sup>2,4</sup>

### Anti-microbial

- The amniotic membrane serves as a physical barrier against the external environment
- Close adherence of the membrane to the wound surface
- Amniotic membrane produces  $\beta$ -defensins, secretory leukocyte proteinase inhibitor (SLPI) and elafin.<sup>5,6</sup>



### Anti-scarring and Anti-adhesive activity

- Amniotic membrane also reduces protease activity via the secretion of TIMP's (tissue inhibitors of metalloproteinases) and therefore has an anti-fibrotic effect
- TGF- $\beta$  is down regulated which is responsible for the activation of fibroblasts and prevent the adhesion of injured surfaces to each other
- Amniotic membrane down regulates TGF- $\beta$  which activates fibroblasts, and its receptor expression by fibroblasts, reducing the risk of fibrosis<sup>7-10</sup>

### Non-immunogenic and low antigenicity

- Due to absence of viable epithelium cells
- Low or lack of expression of Histocompatibility (HLA) antigens A, B, C DR or beta 2 microglobulin
- The human placental membranes possess a unique molecular surface anatomy and biochemical properties and do not express MHC Class II antigens<sup>11-13</sup>

### Analgesic properties (absence of pain)

- Rapid Pain Relief<sup>11-15</sup>
- Due to efficient covering of the nerve endings

### Anti-angiogenic (Prevents the formation of new blood vessels)<sup>1</sup>

- Protection against loss of fluids and proteins
- Intact collagen matrix provides structure for cellular migration and proliferation
- Contains collagen types IV, V and VII which promote cellular differentiation and adhesion

### Promotion of Epithelialisation

- The basement membrane side of the amnion is used as support for epithelial cell growth and the maintenance of epithelial cell polarity<sup>4</sup>
- Amnion facilitate the migration of epithelial cells, promote their differentiation<sup>4</sup>
- Provide a new basement membrane
- Collagen-rich basement membrane is a good substrate for re-epithelialisation
- Expression of growth factors such as **KGF**, **b-FGF**, **HGF** and **TGF- $\beta$**  that promotes epithelialisation<sup>10</sup>

- 
- **KGF** = growth factor present in the epithelialisation-phase of wound healing in which the keratinocytes are covering the wound, forming the epithelium
  - **b-FGF** = growth factors involved in angiogenesis, wound healing, and embryonic development
  - **HGF** = regulates cell growth, cell motility, and morphogenesis
  - **TGF- $\beta$**  = controls proliferation, cellular differentiation

## Mode of Action

The amniotic membrane is used for its high concentration of cytokines and growth factors, and acts as a potent facilitator in wound healing. Generally the membrane is placed with the epithelial side down in contact with the wound surface in order to efficiently release the growth factors to the wound site. The use of the amniotic membrane to cover inflamed or exposed areas favourably influences the wound healing process, as well as, reducing the levels of pain and discomfort of the patient.

The amniotic membrane conforms easily to the wound surface and can be either glued or sutured to the wound surface. The membrane is hydrophilic and naturally absorbs the surrounding fluids. As part of the healing process the amnion resorbs into the wound. General literature suggests that the membranes completely resorb into the wound in about 4 - 6 weeks<sup>1</sup>.



# Amniotic membrane products

## 01. Dehydrated AmnioMatrix™

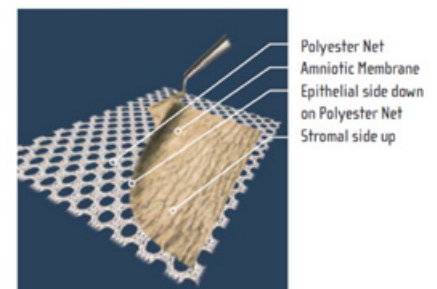
Dehydrated AmnioMatrix™, is a gamma-sterilized amniotic membrane tissue graft. It is denuded of the cuboidal epithelial layer, so no living cells are exposed to the patient. This membrane acts as a scaffold onto which new cells can grow once it has been placed on the wound. Dehydrated AmnioMatrix™ has a five year shelf life that can be stored at room temperature in a clean dry area. It is used in a surgical setting and is attached to the surgical site with sutures or tissue glue.

Dehydrated AmnioMatrix™ is packaged on a polyester net with the epithelial side orientated onto the net. The allografts are packaged aseptically in an inner polyethylene pouch and sealed with an outer peel pouch. The outer pouch can be peeled open using normal aseptic technique, introducing the inner-pouch onto the sterile field.

No special transport conditions are needed for dehydrated AmnioMatrix™. The tissue must be protected from excessive heat and moisture.

### Preferred storage conditions for dehydrated AmnioMatrix™

Location	Temperature	Use after Receipt
Unopened	Room Temperature (10 °C – 28 °C)	Within the expiration date printed on the product label. Usually 5 years since the day of production.



## 02. Frozen AmnioMatrix™

Frozen AmnioMatrix™ is a processed, frozen amniotic membrane tissue graft. The processing and preservation methods used by Next Biosciences retain the vital cytokines and growth factors of the amniotic membrane. This has been shown to be of particular value in ophthalmic surgery.

Current research shows that frozen human amniotic membrane has potential in orthopaedic wound covering, and soft tissue barrier to prevent adhesion after primary surgical repair. Frozen AmnioMatrix™ is used in a surgical setting and is attached to the surgical site with sutures or tissue glue.

Frozen AmnioMatrix™ is double packaged in an inner polyethylene pouch and an outer aluminium foil pouch. The packaged membrane is sealed and stored frozen at – 80°C.

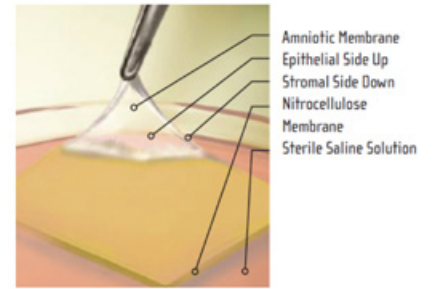
The outer pouch can be torn open across the tear notch, allowing the clear inner-pouch to be fished out with sterile forceps to be introduced to the sterile field. Using sterile scissors the pouch can be cut open just under the seal and the graft removed with sterile smooth forceps.

Frozen AmnioMatrix™ is distributed on dry ice (-80 °C). Samples can be used immediately after delivery or can be stored for up to 3 months in a standard home freezer (-20 °C). Once thawed this tissue product must be used immediately.



## Preferred storage conditions for Frozen AmnioMatrix™

Location	Temperature	Use after Receipt
Unopened Insulated Shipping Container(containing dry ice)	Frozen (-80 °C)	Within the expiration date, printed on the product packaging
Standard Freezer (home or general use)	Frozen (-20 °C)	Within 3 months of placing the product in the freezer or until expiration date printed on outer product packaging, whichever comes first
Ultra-low Temperature Freezer (-80°C Freezer)	Frozen (- 80 °C)	Until the expiration date printed on outer product packaging (shelf-life is 5 years from date of manufacture)



## Indications

### Indications of Corneal Surface Construction

- Persistent Epithelial Defects
- Anticipated delayed re-epithelialisation
- Non-healing Stromal Ulcers
- Partial Limbal Stem Cell Deficiency
- Bullous Keratopathy
- Band Keratopathy
- Mooren's ulcer

### Indications of Conjunctival Surface Reconstruction

- Chemical Burns
- Descemetocoele
- Cicatrizing Conjunctivitis
- Ocular Surface Squamous Neoplasia (OSSN)
- Leaking Blebs
- Filtering Surgery
- Symblepharon Release
- Fornix Reconstruction
- Socket Reconstruction
- Entropion Correction
- Scleral Melt
- Pterygium Surgery



## Orientation of the AmnioMatrix membrane

Patch or overlay technique	Graft or inlay technique	Multi-layer technique
<ul style="list-style-type: none"> <li>- AM is usually placed epithelial side down</li> <li>- Shallow corneal defects</li> <li>- Epithelium grows beneath the patch, which dissolves within a few weeks</li> <li>- Here the AM functions as a cover or a biological bandage 'contact lens' protecting the underlying healing epithelial surface</li> <li>- The intention is for the membrane to fall off or be removed over a period of time</li> </ul>	<ul style="list-style-type: none"> <li>- The AM is usually placed epithelial side up</li> <li>- Epithelium grows over the graft, securing itself to the basement membrane</li> <li>- The AM is intended to act as a substrate or scaffold for epithelial cells to grow and is therefore incorporated into the host tissue (cornea or conjunctiva)</li> </ul>	<ul style="list-style-type: none"> <li>- Support for deeper corneal ulcers</li> <li>- Fill the defect with layers of the AM, epithelial side up</li> <li>- Single sheet to secure the multiple layers over the top</li> <li>- Top layer can be epithelial side up or down</li> </ul>

## Amniotic Membrane Billing and Procedure Codes

Product code	Description	Size	Nappi code
LAM1515	Dehydrated Membrane	1.5cm x 1.5cm	493575001
LAM2020	Dehydrated Membrane	2.0cm x 2.0cm	493581001
LAM3030	Dehydrated Membrane	3.0cm x 3.0cm	493583001
LAM4040	Dehydrated Membrane	4.0cm x 4.0cm	493584001
CAM2020	Frozen Membrane	2.0cm x 2.0cm	651936001
CAM4040	Frozen Membrane	4.0cm x 4.0cm	651938001
CAM6060	Frozen Membrane	6.0cm x 6.0cm	165595001
CAM8080	Frozen Membrane	8.0cm x 8.0cm	569924001

Procedure codes	Description	ICD-10 Diagnosis code
3191	Blepharoplasty	H02.03
3161	Excision Papilloma	D23.1
3181, 0201	Ectropion/ Entropion repair	H02.1/0
3121, 0201	Corneal transplant	H18.6
3120, 3132, 3198, 3126, 0201	Lasik POI	H52.0/1/2
3125	Pterygium	H11.0
3134	Pterygium/Conjunctival cyst/Conjunctival tumour with graft used	H11.0



## Contra-indications

### AM should not be implanted into:

- Areas with an active or latent infection; particularly contra-indicated in the management of persistent epithelial defects with infectious corneal ulcers.
- Do not use on patients with a history of drug reactions to Ciprofloxacin or Amphotericin B.
- This product is intended for single patient use.

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Galaxy Building  
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T +27 (0) 11 697 2900  
F +27 (0) 11 697 2901  
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