Overview

ProKera™ consists of a piece of AmnioGraft® (cryopreserved human amniotic membrane) clipped into a dual PMMA symblepharon ring system (see sketch left). ProKera™ is used as a biologic bandage for suppressing inflammation and promoting corneal surface healing without sutures.

ProKera™ is assembled so that the stromal (sticky) side of the tissue is in contact with the corneal surface and fits snugly between the cornea and the eyelids by conforming to the corneal surface. ProKera™ also functions like a symblepharon ring while delivering the therapeutic benefits of a cryopreserved amnion graft including anti-inflammation, anti-scarring, anti-angiogenesis, promotion of healing and reduction of patient pain without sutures. After the biologic benefits of the tissue are delivered and healing is achieved, the ProKera™ ring set is removed.

ProKera™ is intended for use in eyes where the ocular surface cells have been damaged, or the underlying stroma is inflamed and scarred. It often eliminates the need for surgery and provides sight saving biologic actions. The most common indications for use are:

- Epithelial defects, erosion, or ulceration
- Chemical/thermal burns (acute stage)
- Following the removal of corneal lesions, e.g., band keratopathy
- Chronic recalcitrant keratitis from HZO, HSV, or vernal keratitis
- Stevens-Johnson syndrome (acute stage)
- In conjunction with socket or fornix reconstruction (to prevent lid/lash rubbing)

Supplies for Procedure

1. Sterile lid speculum
2. Sterile gloves
3. Anesthetic drops
4. Antibiotic drops
5. Sterile scissors (provided with the ProKera™ device)
6. Sterile forceps (provided with the ProKera™ device)
7. ProKera™ (by Bio-Tissue™) call for info: 1-888-296-8858

ProKera™ sizes:

<table>
<thead>
<tr>
<th>Catalog #</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>PK-15</td>
<td>15 mm</td>
</tr>
<tr>
<td>PK-16</td>
<td>16 mm</td>
</tr>
</tbody>
</table>

ProKera Usage by Application

<table>
<thead>
<tr>
<th></th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial Defect/Ulceration</td>
<td>52.1%</td>
</tr>
<tr>
<td>Chemical/Thermal Burn</td>
<td>11.6%</td>
</tr>
<tr>
<td>Together with PKP/LKP</td>
<td>9.3%</td>
</tr>
<tr>
<td>Lid Problems</td>
<td>4.7%</td>
</tr>
<tr>
<td>Removal of Lesions</td>
<td>3.7%</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>18.6%</td>
</tr>
</tbody>
</table>

Data provided by Bio-Tissue, Inc. from returned donor recipient information forms from transplanted devices (April 2005 - December 2005).
Pre-Insertion Tips:

• **Verify Eye Closure:** If there is an eye closure problem, ProKera™ should not be used. Exposure problems will diminish the effects of the membrane and should be treated prior to ProKera™ insertion or at the time of ProKera™ insertion with additional temporary tarsorrhaphy.

• **Consider Eye Opening for Sizing:** There are two different diameters of ProKera™ available: 15 mm and 16 mm. Most adult patients will tolerate a 16 mm ProKera™ device. ProKera™ should not be used for patients with unusually tight eyelids close to the eyeball making it difficult and/or painful to insert anything between the lid and the globe.

• **Handle Aseptically:** ProKera™ can be inserted in an office setting using aseptic technique; the supplies listed on page 1 assist with handling the device. ProKera™ is packaged in a dual pouch (as shown to the left). The outer aluminum foil pouch should not be placed in the sterile field, but the inner, clear pouch may be placed in a sterile field. The membrane in the device is slippery. Thus, carefully grab the ring with fingers using a sterile glove or with sterile, blunt instruments. Do not trim off the extra membrane hanging over the sides of the ring.

**Key Insertion Steps:**

- Use a lid speculum to open the eye
- Administer anesthetic drops
- Insert ProKera™ into the upper lid first, and then tuck it under the lower lid
- Administer prophylactic antibiotic drops after removing the speculum

**Using a tarsorrhaphy with ProKera™:**

After insertion, if there is no complaint of a foreign body sensation, and the patient seems to have reasonable blink and closure, then there is no need for a tarsorrhaphy. However, if the ProKera™ is a little too small for the eye, or the device does not center well on the corneal surface (e.g. with floppy lids or exophthalmos) or the eye does not blink/close well (e.g. neurotrophic), then add a temporary tarsorrhaphy (see illustration and photo below).
Post-Insertion Care:

- **Patient Instructions**: Patients should be instructed not to rub their eyes, excessively blink or move the ProKera™ insert with their fingers. Patients should not swim or soak their face in water without protective eyewear. The eye should be closed tightly during showering. As vision will be blurred by the opacity of the tissue, patients should not drive, operate heavy machinery or perform any other task that requires unobstructed vision or good depth perception.

- **Topical Medications**: Artificial tears or other eye drops should be used 3-4 times daily, especially if there is a concern about dry eye exposure. The cryopreserved amniotic membrane in ProKera™ does not interfere with antibiotics’ penetration. If desirable, ProKera™ can be soaked in antibiotic solution before placing it in the eye.

- **Routine Examination with ProKera™**: Without removing ProKera™, healing can be assessed using fluorescein staining (see photo to the right) and the IOP can be measured with a Tonopen. If temporary removal is required, then handle the ProKera™ device aseptically and store it in a sterile container with BSS before re-insertion.

- **Length of Wear**: The FDA approved ProKera™ can remain in the eye until the ocular surface has healed or the membrane has dissolved for up to 8 weeks after insertion. However, biologic actions are delivered and healing is complete within 1-2 weeks. For cases with severe inflammation (e.g. acute chemical burns), it is beneficial to insert a new ProKera™ device every 5 days to avoid PMN cells becoming trapped on the membrane which may lessen its therapeutic effect.

- **Membrane Dislodgment and Dissolution**: As the biologic actions of the cryopreserved amniotic membrane are delivered and the ocular surface heals, the membrane will thin and dissolve. If the membrane dissolves after adequate healing has taken place, then remove the device. However, the membrane should not dissolve in less than one week. If it does, this is most likely due to an exposure problem which should be corrected before the insertion of another ProKera™ and/or add a tarsorrhaphy.

**Removal Tips**:

ProKera™ can be removed using blunt, sterile forceps with or without the help of a lid speculum. The application of an eye ointment can facilitate the removal.

**Testimonials (from ProKera™ Users)**

**Neurotrophic Persistent and Non-healing Corneal Epithelial Defects/Ulcers**

Dr. Michael Ehrenhaus of NY, NY has used ProKera™ in patients with non-healing epithelial defects due to bacterial keratitis. The ProKera™ device stabilized their corneas and helped stop progression of the defects, some of which were deep, almost like a descemetocele. He can be reached for further comments or questions by phone at 718-780-2600.

Dr. Lisa Chriss of Orlando, FL was very impressed after using ProKera™ for a patient with a non-healing epithelial defect and scar due to HZO (under control) which failed to heal after using a bandage contact lens for 3 months. The defect healed 3 days after ProKera™ insertion. She can be reached for comments or questions by phone at 407-629-6646.

Dr. George Rosenwasser of Hershey, PA used ProKera™ after EDTA chelation in a one-eyed neurotrophic child with band keratopathy and vascularization. He noted a rapid and impressive improvement. He observed that “This device has fast-tracked the relief of damage from alkali burns to the ocular surface. I recommend it to anyone who sees a serious alkali injury, and the faster it is placed, the better.” He can be reached by phone at 717-533-5200.

**Reimbursement**: Medicare recommended that HCPCS Level II Supply Code V2790 (preserved amniotic membrane) should be expanded to cover ProKera™ during a May 11, 2006 public hearing. The effective date is pending. Coverage and payment for V2790 is at the discretion of Medicare local carriers. A copy of the invoice should be submitted with the claim form. Due to the complexities in coding and the evolving technology of amniotic membrane transplantation, it is highly recommended that you consult your coding expert with detailed questions. As a general rule, it is advisable to pre-qualify the patient’s insurance or use an Advanced Beneficiary Notice (ABN) to insure the Medicare patient is aware of responsibility for any costs not covered by the insurance carrier.
1. How often does ProKera™ fall out?
Due to the device construction and the placement of ProKera™ under the eyelids, ProKera™ will not fall out with normal wear or blink. However, the device may not be secured well in exophthalmos or severe floppy lid. A tarsorrhaphy can help to limit this.

2. If the sticky stromal side is down, when ProKera™ is removed, what keeps it from taking the epithelium with it?
ProKera™ acts as a biologic bandage and the epithelial healing takes place with the help of the biologic actions of the membrane underneath. Once the corneal surface inflammation reduces and the defect heals (visible by fluorescein staining), the amniotic membrane clipped into the PMMA rings will thin out or dissolve completely. The remaining PMMA ring will need to be removed after this has happened. No epithelium will be removed with the ring, even if the membrane is still intact.

3. What happens if the graft is sloughing off even with a tarsorrhaphy?
It is likely that there is an exposure problem if this happens. For example, in a recent case a patient suffering from the lack of Bell’s phenomenon (after HZO) the eye was not rotating during sleep. This created a severe exposure of the lower portion of the cornea as it is never covered by tear film. Amniotic membrane healed the defect, but broke down again for the very same reason. To overcome this issue, blood vessels will have to be brought to the peripheral cornea using a conjunctival flap and then covering it with ProKera™.

4. What if the membrane slips out of the ProKera™ ring? Should I try to clip it back in?
The amnion graft inserted in the ProKera™ ring will thin out as the healing of the corneal surface progresses. Occasionally this will cause the membrane to detach from the ring. If this occurs, remove the device. Do not try to reassemble it. Provided the healing is complete, another ProKera™ is unnecessary.

5. Why is there mucous debris with ProKera™ inserted?
The membrane may show some degradation during wear and thus generate some mucous debris. If this occurs simply rinse with non-preserved saline.