FLOSEAL Hemostatic Matrix, 5 mL

Intracardiac Use

DO NOT INFUSE INTRAVASCULARLY.

FLOSEAL Hemostatic Matrix, also referred to as an FLOSEAL Sponge, is not to be infused into blood vessels.

Description: Designation

The Gelatin Matrix component consists of a bovine-derived Gelatin Matrix component, a recombinant human Thrombin component, and purification processes and packaging during manufacture of the Gelatin Matrix component are non-pyrogenic.

FLOSEAL Thrombin Topical (recombinant), is a human coagulation protein produced via recombinant DNA technology that is genetically modified Chinese Hamster Ovary (CHO) cell line. FLOSEAL is identical in composition and structure to naturally occurring human thrombin.

The Thrombin component is obtained from a genetically modified Chinese Hamster Ovary (CHO) cell line. The Thrombin component may contain bovine or human thrombin.

Procedures:

- For surgical use only. Do not use orally.
- As with other hemostatic agents, do not apply FLOSEAL Matrix to sites where there is a negative pressure or a vacuum (e.g. due to patient positioning), as material may be drawn into the wound and be difficult to remove.
- Hemostatic effect is best achieved when FLOSEAL Matrix is applied as an aerosol or sprayed as a mist. Do not apply FLOSEAL Matrix to laser-irradiated wounds or to areas where laser or other heat is being applied - doing so could result in an uncontrolled life-threatening hemorrhage. The FLOSEAL Matrix is intended only for topical use.


does not attach a prosthetic device. Microfibrillar collagen or other acrylic adhesives, will be required to

- May not be used on bone surfaces
- Do not use FLOSEAL Matrix on bone surfaces where anesthetics, such as methylmethacrylate, have been used. Use of FLOSEAL Matrix may cause hemostatic failure to the adjacent prosthesis.

- If the use of FLOSEAL Matrix is stopped, the FLOSEAL Matrix should not be reapplied. Do not use FLOSEAL Matrix after protamine sulfate administration.

- Excess FLOSEAL Matrix (material not incorporated into the hemostatic clot) should always be removed by gentle irrigation from the site of application. Removal of excess is done to avoid excessive inflammatory response, adhesion, or reperfusion of the matrix.

- The compression of the brain and spinal cord resulting from the acceleration of the head is not the cause of any observed events. It was an expected outcome of the use of FLOSEAL Matrix in surgical procedures involving the central nervous system.

- Fibrillation Atrial 10 (6%) 8 (5%)
- Fibrillation Ventricular 4 (2%) 2 (1%)
- Hypertension 1 (0.5%) 2 (1%)
- Cardiac 94% (45/48) 60% (27/45)
- Drug Reaction 5 (3%) 3 (2%)
- Respiratory 3 (2%) 2 (1%)
- Urticaria 2 (1%) 1 (<1%)
- Vomiting 2 (1%) 1 (<1%)
- Hemorrhage 6 (4%) 6 (4%)
- Abdominal Pain 27 (17%) 21 (13%)
Secondary Endpoint: A secondary endpoint was time to hemostasis for the first treated bleeding site. The data for time to hemostasis are summarized in the table below.

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>FLOSEAL Matrix</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 1 minutes</td>
<td>41% (20/50)</td>
<td>21% (11/50)</td>
</tr>
<tr>
<td>1 – 2 minutes</td>
<td>69% (106/153)</td>
<td>32% (48/150)</td>
</tr>
<tr>
<td>2 – 3 minutes</td>
<td>85% (135/160)</td>
<td>71% (112/158)</td>
</tr>
<tr>
<td>3 – 5 minutes</td>
<td>83% (143/173)</td>
<td>68% (102/149)</td>
</tr>
<tr>
<td>5 – 10 minutes</td>
<td>87% (149/175)</td>
<td>77% (155/199)</td>
</tr>
</tbody>
</table>

*6 (± 2) patients in the FLOSEAL Matrix group and 3 in the Control group were excluded from all analyses. Patients were excluded if they exhibited excessive oozing in hemostasis for the first treated bleeding site.*

When the data were stratified by surgical specialty, the median times to hemostasis were shorter for the FLOSEAL Matrix group than for the Control group in all surgical categories, as shown in the table below.

<table>
<thead>
<tr>
<th>Time to Hemostasis</th>
<th>FLOSEAL Matrix</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>2.0 (1.5, 2.5)</td>
<td>6.0 (5.0, 6.0)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>2.8 (2.4, 3.0)</td>
<td>6.4 (6.0, 8.5)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>2.5 (2.6, 4.0)</td>
<td>6.5 (4.5, 8.0)</td>
</tr>
<tr>
<td>Spinal/Orthopedic</td>
<td>1.5 (1.5, 1.5)</td>
<td>3.0 (2.4, 4.5)</td>
</tr>
</tbody>
</table>

*Confidence interval using a Bonferroni correction.*

Use of FLOSEAL Matrix as a Hemostatic Agent for Nonsurgical Blood Loss

FLOSEAL Matrix® has been used as a hemostatic agent for the surgical control of arterial bleeding (e.g., post-mortem bleeding (ruptures) during autopsies in 15 patients, 30 applications, 6 deaths). Patients were followed for up to 24 hours following surgery and at all complications and outcomes that occurred during this period were reported in this study. No intraoperative complications were reported for Matrix application sites. No operative complications were reported in these patients.

The efficacy of FLOSEAL Matrix has been evaluated in a randomized controlled trial in 209 patients and 306 controls. The study endpoints included rate of successful hemostasis (defined as operative time comprised in the Control group, were excluded because of protocol deviations in measuring hemostasis for the first treated bleeding site. Furthermore, a decrease in transfusion overall postoperative bleeding, rate of transfusion hemostasis (defined as operative time comprised in the Control group, were excluded because of protocol deviations in measuring hemostasis for the first treated bleeding site. No intraoperative complications were reported for Matrix application sites. No operative complications were reported in these patients.

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