In a study evaluating sealing efficacy by the measurement of leak pressures, COSEAL achieved statistically significantly higher average leak pressures compared with controls as well as higher leak pressures compared with fibrin sealant. In a study evaluating sealing efficacy by the measurement of leak pressures, COSEAL achieved statistically significantly higher average leak pressures compared with controls as well as higher leak pressures compared with fibrin sealant.

**COSEAL: Sealing Efficacy**

<table>
<thead>
<tr>
<th></th>
<th>COSEAL</th>
<th>Fibrin Sealant</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressures in cm H2O</td>
<td>85</td>
<td>47</td>
<td>27</td>
</tr>
</tbody>
</table>

**COSEAL**
- Applicator designed for minimally-invasive surgery with flexible tip and dynamically vented regulator\(^1,4\)
- Indicated for sealing and adhesion prevention\(^1\)
- Fully synthetic, contains no human or animal proteins\(^1\)
- Contraindicated in individuals known to have anaphylactic or severe systemic reactions to human blood products\(^2,3\)

**EVICEL**
- Competitive Primer

**FOR INTERNAL USE ONLY**

**EVICEL is a fibrin sealant manufactured from pooled human source plasma. It consists of two packages: 1) one vial each of frozen sterile solutions of Biological Active Component 2 (BAC2) and thrombin and 2) a sterile spray device.**

**Adhesion Characteristics: COSEAL vs. EVICEL**

COSEAL forms a strong mechanical bond with synthetic grafts materials\(^1\) and also has the unique ability to chemically crosslink with itself and to tissue surfaces\(^6\).

COSEAL forms a cohesive anastomotic seal within seconds that adheres strongly, effectively providing a mechanical barrier to blood flow without the need to induce coagulation\(^5\). This contrasts with fibrin sealant, which has been reported to have rather poor adhesive qualities when applied to prosthetic grafts\(^7\).

**Applicators: COSEAL vs. EVICEL**

**COSEAL**
- DUPLOSPRAY Applicators\(^1,4\)
  - Metal cannula with curved, flexible tip
  - Tip can be bent with MIS grasper tool
  - Two convenient lengths: 20 cm, 30 cm

**EVICEL**
- Applicators\(^2,8\)
  - Unlike DUPLOSPRAY, EVICEL applicators/regulator do not have important safety features for endoscopic use
  - Sharp tip on metal cannula could potentially cause injury
  - Flexible devices may be difficult to control
**Product**

<table>
<thead>
<tr>
<th>Company</th>
<th>EVICEL</th>
<th>Johnson &amp; Johnson Wound Management (Ethicon, Inc.)</th>
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</table>

**Competitor's product messaging**
- FAST: Hemostasis can begin quickly with less preparation and minimal clogging.
- CLEAR: Designed to keep you focused on your procedure. Clear, stable clot.
- NOW: A safe and effective all-human fibrin sealant that doesn’t require an antifibrinolytic agent, while maintaining clot stability.

**Product Attributes**

| COSEAL
<table>
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<tbody>
<tr>
<td><strong>Effectiveness</strong></td>
</tr>
<tr>
<td>Time to polymerization</td>
</tr>
</tbody>
</table>
| Clinical efficacy | • 87% immediate hemostasis and 95% overall hemostasis (<5 minutes) achieved in aortic repair
| | • 47% immediate hemostasis and 86% overall hemostasis (<10 minutes) achieved in various peripheral vascular procedures using synthetic grafts |
| | • Thrombin enzymatically converts fibrinogen to fibrin
| | • Factor XIII activated by thrombin in the presence of calcium chloride, facilitating cross-linking and stabilization of fibrin clot
| | • Reduced amount of plasminogen

**EVICEL**

<table>
<thead>
<tr>
<th>Effectiveness</th>
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<tr>
<td>Within seconds</td>
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</table>

**Mechanism of action**

- Within the syringe, there are two types of chemically reactive PEGs (polyethylene glycol) that crosslink with each other to form a hydrogel barrier matrix that effectively reduces/reinforces adhesion formation.

**Product Information**

**Available application devices**
- EASY SPRAY System (Spray Applicator and Regulator)
- DUPLOSPRAY MIS System (20 and 30 cm Flexible Tip Applicator and Regulator)
- Standard applicator tips
- 22 cm extended applicator tips

**Active ingredients**

- Sprays with two polyethylene glycols (PEG), one is positively charged, the other negatively charged
- Dilute hydrogen chloride solution used to reconstitute PEGs
- Sodium phosphate/sodium carbonate solution to activate reconstituted PEGs causing them to cross-link with each other and covalently bond to tissue

**Kit contents**

- Liquid component in delivery device with transfer port for mixing of PEG powders
- PEG powder component syringe
- 2 standard applicator tips
- Drip or spray application device
- 45 cm flexible catheter
- 35 cm rigid tip

**Volumes/Size Available**

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<tr>
<th>Volumes Available</th>
<th>Volumes Available</th>
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</table>
| 2 mL | 2 mL (Thrombin/BAC2 vial sizes: 1.0 ea)
| 4 mL | 4 mL (Thrombin/BAC2 vial sizes: 2.0 ea)
| 8 mL | 8 mL (Thrombin/BAC2 vial sizes: 5.0 ea)

**Product use time limits**

- 2 hours after reconstitution
- 24 hours after thawing
- Immediately if drawn into syringes

**Bioabsorption time**

- Remains at the treated graft site for approximately 7 days, and is then completely eliminated from the body in 30 days

**Preparation time before use**

- Approximately 2 minutes

**Product is thawed in one of the following ways:**

**Contraindications**

- Do not use as a bronchial stump sealant, during bronchial sleeve resections, or for sealing dearterticated lung areas
- Do not use in procedures in which pleural adhesions are desired
- Must not be applied intraocularly
- For not use in patients with hypersensitivity to the active substances or to any of the excipients

**Indications**

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<th>COSEAL</th>
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| • Sealing suture lines along arterial and venous reconstructions.
| • Enforcement of suture and staple lines in lung resection procedures.
| • Patients undergoing cardiac surgery to prevent or reduce the incidence, severity and extent of post surgical adhesion formation.
| • Patients undergoing laparotomy or laparoscopic abdomino-pelvic surgery as an adjunct to good surgical technique intended to reduce the incidence, severity and extent of post surgical adhesion formation.

<table>
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<tr>
<th>EVICEL</th>
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| • Is used as supportive treatment in surgery where standard surgical techniques are insufficient, for improvement of hemostasis.
| • Also indicated as suture support for hemostasis in surgical vascular surgery.

**References**

4. DUPLOSPRAY [Instructions for Use-EU]. Deerfield, IL: PN21278 Rev. C.

**Probing Questions for Surgeons**

Are you aware that studies comparing COSEAL with fibrin sealant have indicated that COSEAL has higher average leak pressure than fibrin sealant? In a study evaluating sealing efficacy by the measurement of leak pressures after needle puncture, COSEAL achieved higher average leak pressures compared with fibrin sealant in an experimental amniotic membrane model. In another study COSEAL was found to seal leak pressures in the carotid artery of 660 +/- 120 mmHg (in vitro burst test for closure of puncture defects 0.6-0.9 mm in diameter in an animal model). COSEAL is therefore an acceptable choice for sealing high-pressure vessels such as the aorta.

Are you concerned that the spray applicators for EVICEL lack certain key safety features that are appropriate for minimally-invasive surgery (MIS) spray application? COSEAL DUPLOSPRAY was designed specifically for MIS procedures and enables a safe, aerosolized endoscopic spray application by reducing gas flow rate and dynamically venting gas throughout the spray application. The DUPLOSPRAY MIS regulator is also used exclusively with CO2 gas which is generally accepted as the safest gas to use in laparoscopic procedures. The COSEAL flexible tip applicator designed for use with the DUPLOSPRAY system comes in 20 cm or 30 cm sizes so you can choose the most appropriate size for the specific patient and procedure.

Are you concerned about the formation of postsurgical adhesions? COSEAL is indicated for both adjunctive sealing for arterial and venous reconstructions and to reduce the incidence, severity and extent of postsurgical adhesion formation.

**Handling Objections**

I use EVICEL because I prefer a sealant containing fibrin to a synthetic sealant. There are several advantages to using a synthetic product such as COSEAL. For example, EVICEL is contraindicated in individuals known to have anaphylactic or severe systemic reactions to human blood products. No such contraindications are indicated for COSEAL because it is fully synthetic. Studies also indicate that COSEAL is completely removed from the body in 30 days. There have been no such studies conducted reporting the bioabsorption rate of EVICEL.