SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

CoSeal®

Surgical Sealant

Caution: Federal law restricts this device to sale by or on the order of a physician (or properly licensed practitioner). [Rx ONLY]

INSTRUCTIONS FOR USE

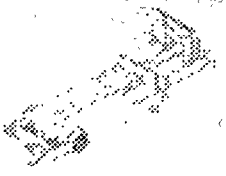
DEVICE DESCRIPTION

CoSeal Surgical Sealant (CoSeal) is composed of two synthetic polyethylene glycols (PEGs), a dilute hydrogen chloride solution and a sodium phosphate/sodium carbonate solution.

These components come in a kit that includes an applicator(s). At the time of administration, the mixed PEGs and solutions form a hydrogel that adheres to tissue.

The CoSeal kit includes:

LIQUID COMPONENTS POUCH: The Liquid Components Pouch consists of two syringes, containing solutions, which are pre-assembled into a housing. A transfer port closure is attached to the housing assembly to allow mixing of the PEG powders into the correct syringe. A clip is attached to the plunger rod of the syringe that does not require mixing with the PEG powders.



POWDER COMPONENT POUCH: The Powder Component Pouch consists of a syringe containing two PEG powders and a desiccant packet.

APPLICATOR POUCH: Each applicator pouch contains two applicators.

INDICATIONS

CoSeal is indicated for use in vascular reconstructions to achieve adjunctive hemostasis by mechanically sealing areas of leakage.

CONTRAINDICATIONS

There are no known contraindications for this device.

WARNINGS

Do not inject CoSeal into vessels.

CoSeal is intended for use as an adjunctive sealant and is not to be used in place of sutures, staples or mechanical closure.

CoSeal swells up to four times its volume within 24 hours of application and additional swelling may occur as the gel resorbs. Therefore, surgeons should consider the maximum swell volume and its possible effect on surrounding anatomic structures potentially sensitive to compression.

PRECAUTIONS

The safety and performance of CoSeal have not been established in children and pregnant women.

In vivo testing demonstrated a mild skin sensitization response in an animal model. Similar testing in humans has not been conducted.

During clinical investigations, the volume of CoSeal used per patient to effectively seal a typical vessel ranged from 2 mL to 16 mL. The maximum volume of CoSeal to be used per patient will be based upon the surgical procedure, such as the number and size of vessels to be treated. The safety of CoSeal has not been evaluated in patients receiving more than 16 mL.

ADVERSE EVENTS

In a prospective, randomized, controlled multicenter trial, 148 patients were treated with CoSeal or the control (absorbable gelatin sponge/thrombin hemostat). Table 1 shows the overall adverse events reported for CoSeal treated and control patients for the 10 most commonly reported events. The results are similar between the two treatment groups and are representative of events expected from patients undergoing vascular surgery for vascular access and occlusive vascular disease.

There were two deaths in the study. One control patient died during the study due to cardiopulmonary arrest. A second control patient died of sepsis and carbon dioxide narcosis with respiratory arrest. Five weeks post treatment, this patient had surgery for a duodenal ulcer with hemorrhage.

Table 1: Adverse Events

Adverse Event	CoSeal (n=74)	Control (n=74)
Edema	14 (18.9%)	11 (14.9%)
Elevated Temperature ≥101F*	10 (13.9%)	8 (11.1%)
Erythema	10 (13.5%)	7 (9.5%)
Infection	8 (10.8%)	6 (8.1%)
Thrombosis	6 (8.1%)	8 (10.8%)
Occlusion	6 (8.1%)	7 (9.5%)
Hematoma	5 (6.8%)	3 (4.1%)
Anemia	3 (4.1%)	4 (5.4%)
Non-Healing Wound**	4 (5.4%)	2 (2.7%)
Bleeding***	4 (5.4%)	1 (1.4%)

* Temperature data was collected on 72 patients from each treatment group.

** The non-healing wound was not at the treatment site for 3 of the 6 patients (1 control, 2 CoSeal patients).

*** Bleeding was not at the treatment site for 3 of the 5 patients (3 CoSeal patients).

When evaluating the total adverse events reported in the study, there were 185 events in CoSeal treated patients and 151 in Control patients. This is a difference of 34 more events in the CoSeal group. In evaluating this difference, it was found that one CoSeal treated patient contributed 35 adverse events which represents more than the total difference between treatment groups. From the total of 336 events only two (both controls) were attributed to the treatment material by the attending surgeon. The remaining 334 events are not related to the treatment material in the opinion of the treating physicians. It is concluded that there was not an unexpected adverse event finding, either by event type or number, attributed to the use of CoSeal. The safe use of CoSeal for sealing peripheral vascular reconstructions is supported by the findings of this randomized controlled clinical study.

CLINICAL STUDIES

U.S. Multicenter Study

Study Design and Objectives: A prospective, randomized, controlled multicenter trial was conducted to evaluate the safety and effectiveness of CoSeal versus an absorbable gelatin sponge/thrombin hemostat to seal anastomotic suture lines in patients undergoing placement of peripheral vascular grafts. An equivalence hypothesis was used. One hundred and forty eight (148) patients were treated with CoSeal or the control at nine centers. This study was designed to evaluate whether the CoSeal success rate was equivalent to the success rate for the control.

Table 2: Patient Accountability

	CoSeal	Control
Number Patients Treated	74	74
Number Patients with 1 Site Treated	12	20
Number Patients with 2 Sites Treated	62	54
Total Number of Sites Treated	136	128

Table 3: Patient Demographics by Age and Gender

	CoSeal (N=74)	Control (N=74)
Age (years)		
Mean ± s.d.	63 ± 13	61 ± 14
Median	64	63
Range	23 – 87	22 – 85
Males	41	37
Females	33	37
Surgical Procedure		
Bypass	29 (39%)	26 (35%)
AV-Shunt	43 (58%)	44 (59%)
Other	2 (3%)	4 (5%)

Primary Endpoint: The primary effectiveness outcome parameter measured was the cessation of bleeding (sealing) at a treatment site within 10 minutes.

Secondary Endpoint: The secondary measure of effectiveness was the *Time to Sealing* (the number of seconds from the time circulation is restored to the graft until the time bleeding has ceased at the site). Immediate sealing is defined as no bleeding when circulation was restored to the graft (immediate sealing = 0 seconds).

Table 4: Patients Achieving Complete Sealing
All Treated Patients [Success/Total] (%)

	CoSeal	Control
Immediate (0 seconds)	24/74 (32%)	12/74 (16%)
Within 10 Minutes (cumulative)	60/74 (81%)	58/74 (78%)

Table 5: Patients Achieving Complete Sealing by Surgical Group
All Treated Patients [Success/Total]* (%)

	CoSeal	Control
Bypass Grafts	20/29 (69%)	18/26 (69%)
AV-Shunts	40/43 (93%)	37/44 (84%)

* Patch grafts not reported.

Table 6: Sites Achieving Immediate Sealing by Degree of Pretreatment Bleeding, All Treated Sites

	CoSeal	Control
Oozing	50%	26%
Brisk	41%	3%

Table 7: Cumulative Number of Patients with Complete Sealing over 10 Minutes All Treated Patients (%)

	CoSeal (N=74)	Control (N=74)
Immediate (0 seconds)	24 (32%)	12 (16%)
0-1 Minute	34 (46%)	19 (26%)
0-3 Minutes	48 (65%)	29 (39%)
0-5 Minutes	55 (74%)	42 (57%)
0-10 Minutes	60 (81%)	58 (78%)

Multiple analyses were conducted to evaluate the effectiveness data by treatment site and by patient. These analyses demonstrated that the study objectives were met when the data was analyzed by patient as well as by site.

European Multicenter Study

A multi-center non-randomized clinical study was performed in Germany and The Netherlands with 131 patients treated in 10 centers. This trial was conducted to evaluate the safety and effectiveness of CoSeal to seal anastomotic suture lines in patients undergoing placement of peripheral vascular grafts using various types of graft materials.

Table 8: Patients Achieving Sealing within 10 Minutes by Surgical Group

	Success/Total (%)
Bypass Grafts	75/93 (81%)
AV-Shunts	25/27 (93%)
Arteriotomies	11/11 (100%)
Total	111/131 (85%)

Three different graft materials, PTFE, Dacron and autologous vein were used The primary performance outcome was to achieve successful sealing within 10 minutes.

Table 9: Patients Achieving Sealing by Graft Material Sealed within 10 Minutes Success/Total (%)

PTFE Grafts	48/65 (74%)
Dacron Grafts	19/20 (95%)
Autologous Grafts	44/46 (96%)

There were no significant adverse events related to product use reported in the European multi-center trial. The events reported were typical of patients with clinical conditions leading to vascular surgeries. One patient died during the study. The investigator indicated the myocardial infarction and death of this patient were "definitely not" sealant related.

DIRECTIONS FOR USE

HOW SUPPLIED

CoSeal and its accessories are **latex-free.**

CoSeal is supplied as a sterile single use only unit. Do not re-sterilize any components. Discard unused material.

CoSeal has a slight odor that does not affect its acceptability for use.

Additional applicators may be purchased separately.

Do not use if pouches, syringes or luer lock caps are damaged or opened.

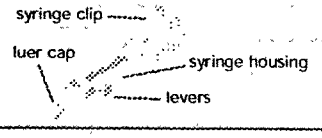
STORAGE CONDITIONS

Store CoSeal at room temperature (approximately 25°C).

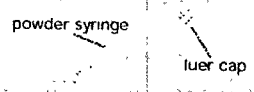
MIXING INSTRUCTIONS

- Use CoSeal within 2 hours of preparation.
- Using aseptic technique, open each pouch and transfer contents into the sterile field. In the sterile field, prepare the liquid and powder components as described below.

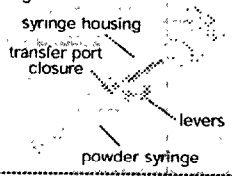
1. Remove the luer cap on the transfer port closure Do not remove the syringe clip.



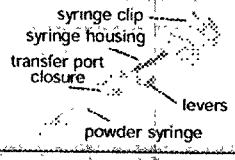
2. Remove the luer cap from the powder syringe.



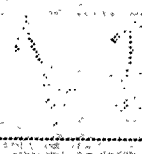
3. Connect the powder syringe to the opening on the transfer port closure. Transfer the liquid into powder by forcefully depressing the plunger. Mix contents back and forth between the syringes until the solid is completely dissolved (18-20 times). Push entire contents into the syringe contained in the syringe housing



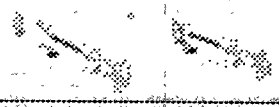
4. Disengage the powder syringe by detaching the transfer port closure as follows:
   - Grasp the powder syringe barrel
   - Press the levers on the syringe housing
   - Pull both the empty powder syringe and transfer port closure from the housing.



5. Holding the syringe tips up, level syringe plungers and rotate the syringe clip to connect to other plunger. Hold the syringe upright and expel all air.



6. Snap the applicator onto the end of the syringe housing. CoSeal is now ready to use. If a clear gel is desired, wait approximately 3 minutes after mixing.



APPLICATION

Note: For peripheral vascular graft procedures, restore blood circulation to the surgical site to expand the graft. Reclamp to stop circulation

1. Aspirate excess blood and blot or air dry all surfaces prior to application.
2. Hold the applicator approximately 3 cm from the site (touching the site or holding more than 6 cm from the site is not recommended). Apply sealant forcibly to enhance mixing, moving quickly along the anastomotic site.
3. If CoSeal is to be applied to another site several minutes after first application, immediately wipe the applicator tip with gauze and set device upright to prevent clogging.
4. Apply a uniform layer of sealant to the treatment site. If necessary, rotate the site and bend the applicator to facilitate exposure of all surfaces. Overlap the application slightly to ensure complete coverage of the treatment site. Following application wait at least 60 seconds before restoring circulation, applying irrigation, blotting with gauze, or touching the sealant.
5. If the material remains "watery" and does not gel within approximately 30 seconds, flush the site with saline, and aspirate the material.
6. If the treated site fails to seal, blot the surface dry. Reclamping the vessel may be required to dry the field for reapplication of CoSeal. Reapply sealant. Do not disturb the sealant. If the sealant does not seal, flush the site with saline, aspirate and use standard treatment
7. If the applicator becomes clogged, replace it with a new applicator as follows: Press the ribbed surface of levers on the syringe housing and remove the clogged applicator Attach the new applicator.

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