CoSeal Surgical Sealant
INSTRUCTIONS FOR USE

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

DEVICE DESCRIPTION AND ACTION

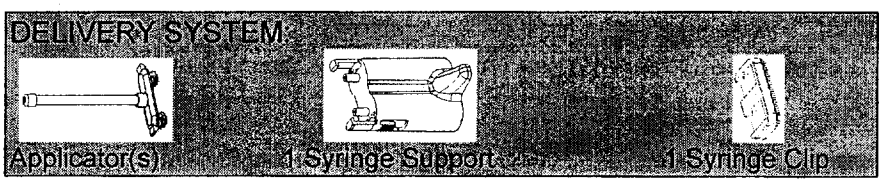
CoSeal Surgical Sealant (CoSeal) is a synthetic hydrogel indicated for use in vascular reconstructions to achieve adjunctive hemostasis by mechanically sealing areas of leakage. The hydrogel is formed at the time of administration when Component A and Component B are mixed together.

The CoSeal kit includes:

1. COMPONENT A POUCH: Component A consists of two syringes connected by a stopcock, one containing polyethylene glycol (PEG) powder and the other a liquid sodium phosphate buffer, and a desiccant packet.

2. COMPONENT B POUCH: Component B consists of two syringes connected by a stopcock, one containing PEG powder and the other a liquid sodium phosphate/sodium carbonate buffer, and a desiccant packet.

3. DELIVERY SYSTEM POUCH: The CoSeal kit contains the following:



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.

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 of sealant.

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 (Success/Total)		
	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 with 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.

HOW SUPPLIED

CoSeal is supplied as a sterile single use only unit. Discard unused material.

Do not re-sterilize any components. CoSeal has a slight odor that does not affect its acceptability for use.

In addition to the applicator(s) provided, additional applicators may be purchased separately.

Do not use if pouches are damaged or opened, or if the stopcock is in the open position upon receipt.

STORAGE CONDITIONS

Store CoSeal at 2-8° C.

See Directions for Use.

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