The Medicines Company

PreveLeak™ Surgical Sealant

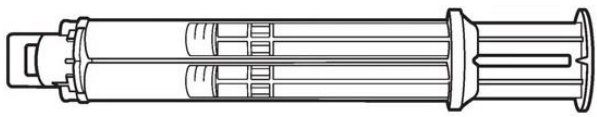
Rx only

Instructions for Use

DEVICE DESCRIPTION

PreveLeak Surgical Sealant (PreveLeak) is a sealant developed to seal suture holes formed during surgical repair of the circulatory system and to reinforce sutured anastomoses. When applied, PreveLeak creates an elastic biocompatible gel that seals suture holes or gaps formed between synthetic grafts or patches and native vessel anastomosis. PreveLeak adheres to the native tissues as well as synthetic materials, including PTFE and Dacron grafts, and facilitates sealing along anastomotic closure lines. After application, PreveLeak is a natural golden color and stays soft and flexible. Animal studies showed significant absorption by 12 months with biodegradation that continues beyond 24 months.

PreveLeak is provided in a double-barreled syringe assembly containing equal volumes of purified bovine serum albumin (BSA) and polyaldehyde. PreveLeak is supplied in a double pouch, with two delivery tips and terminally sterilized.



PreveLeak is ready to use once the pouch is opened, the syringe cap removed, the delivery tip is attached and the tip is primed. When the plunger is depressed, the two components are thoroughly mixed as they pass through the delivery tip. After application, the sealant is allowed to remain undisturbed for at least 60 seconds before unclamping and exposing the anastomosis to arterial pressure. PreveLeak is applied as a viscous liquid that gels within approximately 10-15 seconds. PreveLeak is terminally sterilized by e-beam irradiation and is provided in a double pouch with two delivery tips. Additional sterile delivery tips are available separately. PreveLeak is provided for single-use only.

INDICATIONS

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

CONTRAINDICATIONS

- Not for use in patients with known allergies to materials of bovine or shellfish origin.
- Not for intravascular use.
- Not for cerebrovascular repair or cerebrospinal leak repair.

WARNINGS

- Do not use as a substitute for sutures or staples.
- Avoid exposure to nerves.
- Do not use in the presence of obvious infection and use with caution in contaminated areas of the body.
- Do not allow either the uncured or polymerized form to contact circulating blood.
- PreveLeak contains a material of animal origin that may be capable of transmitting infectious agents.
- Repeated use of PreveLeak in subsequent surgeries has not been studied. Hypersensitivity reactions were not seen using PreveLeak, but hypersensitivity of BSA has been reported.

PRECAUTIONS

- Avoid contact with skin or other tissue not intended for application.
- Safety and effectiveness of PreveLeak in minimally invasive procedures have not been established.
- Safety and effectiveness of PreveLeak in coronary artery bypass grafting (CABG) have not been established.
- Do not use blood saving devices when suctioning excess PreveLeak from the surgical field.
- PreveLeak syringe and delivery tips are for single patient use only. Do not re-sterilize.
- Do not use if packages have been opened or damaged.
- Take care not to spill contents of syringe. Avoid tissue contact with material expelled from delivery tip during priming.
- Avoid pausing more than 10-15 seconds between priming and application to prevent polymerization within the delivery tip.
- Use of PreveLeak in pediatric or pregnant patients has not been studied.
- Minimize use in patients with abnormal calcium metabolism (e.g. chronic renal failure, hyperparathyroidism). Polyaldehyde treated tissue can have an enhanced propensity for mineralization.
- Evidence of cytotoxicity was observed during cell culture-based laboratory assays and is believed to be due to the polyaldehyde component of the product. No evidence of cytotoxicity was observed in animal or clinical studies.

CLINICAL STUDIES

The applicant performed a pivotal clinical study to establish a reasonable assurance of safety and effectiveness of the PreveLeak Surgical Sealant when used during vascular surgical procedures to provide adjunctive hemostasis. This study was a prospective, randomized, controlled trial conducted in the United States under IDE #G070211. Data from this clinical study were the primary basis for the PMA approval decision. In addition, data collected from a multi-center, non-randomized clinical study in Europe were also provided and considered in support of this PMA. A summary of the pivotal clinical study is presented below.

A. Study Design

Patients were treated between October 2008 and December 2009. The database for this PMA reflected data collected through March 2010 and included 217 patients. There were 11 investigational sites. A maximum of 12 ml PreveLeak was studied in a single patient.

The study was a prospective, multi-center, two-arm, randomized clinical study conducted to evaluate the safety and effectiveness of the PreveLeak Surgical Sealant versus a control in sealing suture lines at the anastomosis between native vessels and synthetic (e.g. PTFE/Dacron) vascular grafts or patches used during open vascular reconstruction, vascular repair or hemodialysis access. Subjects were randomly assigned 1:1 to either receive PreveLeak or the control device (Gelfoam Plus [Gelfoam/thrombin], a legally marketed alternative with a similar intended use), just prior to the time it was administered, for all treatment sites during the surgical procedure. All subjects were followed for 3 months following treatment.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the study was limited to patients who met the following key inclusion criteria:
   a. The subject must be ≥ 18 years old.
   b. The subject must be scheduled for the surgical placement of a PTFE or Dacron vascular graft or patch for large vessel repair/arterial reconstruction or hemodialysis access or arteriotomy.
   c. The subject has no child bearing potential or has a negative serum or urine pregnancy test within 7 days of the index procedure.
   d. The subject is willing and able to be contacted for the follow up visits at 6 weeks (± 7 days) and 3 months (± 7 days).
   e. The subject or guardian must provide written informed consent using a form that is reviewed and approved by the Institutional Review Board.

   Patients were not permitted to enroll in the study if they met any of the following key exclusion criteria:
   a. The subject has a known hypersensitivity or contraindication to heparin, bovine or seafood products.
   b. The subject has a history of bleeding diathesis or coagulopathy, or will refuse blood transfusions.
   c. The subject is currently enrolled in this, or another investigational device or drug trial that has not completed the required follow-up period.

2. Follow-Up Schedule

   All patients were examined during their hospital stay, and were scheduled to return for follow-up examinations at 6 weeks (±7 days) and at 3 months (±7 days) post-operatively. Adverse events and complications were recorded at all visits.

3. Clinical Endpoints

   With regards to safety, the primary endpoint was the cumulative incidence of significant bleeding, infection, neurological deficit or immune/inflammatory allergic response observed within 6 weeks post treatment. Additional safety endpoints included adverse event assessment at the following time points: in-hospital, 6 weeks and 3 months post-surgery.

   With regards to effectiveness, the primary endpoint was immediate sealing, as evidenced by no bleeding after clamp release during the surgical procedure. Additional effectiveness endpoints included sealing at intervals of 1, 3, 5 and 10 minutes after clamp release, measured as both bleeding status and time to sealing; device malfunctions and ability to deliver the sealant; and type and quantity of additional hemostatic agents used during the procedure.

B. Accountability of PMA Cohort

At the time of database lock, of the 217 patients enrolled in PMA study, 91% (197/217) were available for analysis at the completion of the study, the 3-month post-operative visit. The subject accountability is provided in **Table 1**.

Table 1: Subject Accountability

	PreveLeak Surgical Sealant (n = 110)	Control (n = 107)
Randomized	110 (100%)	107 (100%)
Treated	110 (100%)	107 (100%)
Discharged	110 (100%)	107 (100%)
Completed 6-Week Follow-Up	102 (92.7%)	100 (93.5%)
Completed 3-Month Follow-Up	100 (90.9%)	97 (90.7%)

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a peripheral vascular sealant study performed in the US. **Table 2** depicts the key patient demographics.

Table 2: Patient Demographics

	PreveLeak Surgical Sealant (n = 110)	Control (n = 107)	P value
Age (Years)			0.7415
Mean ± SD (N)	66.2 ± 12.3	65.7 ± 12.3	
Range	20.8 – 86.6	26.2 – 95.1	
Gender			
Male	37.3%	34.6%	0.6793
Female	62.7%	65.4%	
Race/Ethnicity			
White	68.9%	69.2%	0.3053
Black	30.2%	27.9%	
Hawaiian/Pacific Islander	0.9%	0.0%	
Asian	0.0%	2.9%	
Hispanic/Latino	11.0%	10.3%	0.8622*
Body Mass Index (kg/m^2)			
Mean ± SD (N)	28.8 ± 6.5	28.1 ± 7.2	0.4874
Range	14.5 – 49.3	17.9 – 59.3	

*Hispanic/Latino v. Non-Hispanic/Latino

The surgical procedures during which the PreveLeak product was used are described in **Table 3**.

Table 3: Surgical Procedure Characteristics

	PreveLeak Group (N=110 subjects, 167 sites)	Control Group (N=107 subjects, 164 sites)	Difference (95% C.I.)	p-value
Type of Surgical Procedure				
Aortic Procedures	10.9% (12/110)	14.0% (15/107)	-3.1% (-11.9, 5.7)	0.7156
Extremity Bypass Procedures	18.2% (20/110)	17.8% (19/107)	0.4% (-9.8, 10.6)	
Carotid Procedures	27.3% (30/110)	19.6% (21/107)	7.7% (-3.6, 18.9)	
Hemodialysis Access Grafting	22.7% (25/110)	24.3% (26/107)	-1.6% (-12.9, 9.7)	
Other	20.9% (23/110)	24.3% (26/107)	-3.4% (-14.5, 7.7)	
Type of Graft				
PTFE	67.7% (113/167)	62.8% (103/164)	4.9% (-5.4, 15.1)	0.3532
Dacron	32.3% (54/167)	37.2% (61/164)	-4.9% (-15.1, 5.4)	
Diameter of Graft (mm)				
Mean ± SD (N)	8.2 ± 4.0 (128)	8.6 ± 4.9 (131)		
Range (min, max)	(4.0, 28.0)	(3.0, 34.0)		
% of Grafts = Patch	23.4% (39/167)	19.5% (32/164)		
Number of anatomical sites treated				
One	53.6% (59/110)	54.2% (58/107)		
Two	40.9% (45/110)	38.3% (41/107)		
Three	5.5% (6/110)	7.5% (8/107)		

There were no statistically significant differences between the two randomized treatment groups with respect to basic demographics, surgical procedure performed or the type of graft utilized.

D. Safety and Effectiveness Results

1. Safety Results

The primary analysis of safety was based on the total cohort of 217 subjects who were evaluated at six weeks post-procedure. As indicated in **Table 4**, there were no statistically significant differences between the treatment and control groups with regards any of the primary safety endpoints treated individually, as listed in **Table 4**. The difference between the two groups with respect to the cumulative incidence of safety measures, i.e., the incidence of subjects having one or more safety endpoints occurring within 6 weeks, was statistically significant (46.4% PreveLeak compared to 59.8% control, $p < 0.05$).

Table 4: Primary Safety Endpoint Events through 6 Weeks

Safety Measure within 6 Weeks Post Treatment	PreveLeak Group (N=110)	Control Group (N=107)	Difference (95% C.I.)	p-value
Significant Bleeding	35.5% (39/110)	45.8% (49/107)	-10.3% (-23.3, 2.7)	0.1209
Infection	14.8% (16/108)	23.6% (25/106)	-8.8% (-19.3, 1.7)	0.1031
Neurological Deficit	5.6% (6/108)	3.8% (4/105)	1.8% (-3.9, 7.4)	0.7482
Immune/Inflammatory Allergic Response	0% (0/108)	0.9% (1/106)	-0.9% (-2.8, 0.9)	0.4953
Cumulative Incidence of Safety Measures	46.4% (51/110)	59.8% (64/107)	-13.5% (-26.6, -0.3)	0.0472

The incidence of infections occurring within 6 weeks post-treatment was 14.8% for the PreveLeak group compared to 23.6% for the Control group (p=0.1031). Based on the protocol definition, infections include all instances where the subject's white blood cell count was 20% elevated from baseline, or where there was a positive blood or wound culture sufficient to cause the clinical investigator to take action. Therefore, all instances where antibiotics were required to treat an adverse event were included in this classification. The incidence of infections classified as serious adverse events occurring within 6 weeks post-treatment was 6.5% (7/108) for the PreveLeak group compared to 16.0% (17/106) for the Control group. This difference was statistically significant (p=0.0268).

Adverse effects that occurred in the pivotal study:

The serious adverse events that occurred in this study are presented in **Table 5** and **6**. There were no significant differences between the two randomized groups with respect to the prevalence of other serious adverse events potentially associated with vascular procedures occurring within 6 weeks or between 6 weeks and 3 months post-treatment.

Table 5: Serious Adverse Events through 6 Weeks

Serious Adverse Event	PreveLeak Group (N=110)	Control Group (N=107)	Difference (95% C.I.)	p-value
Death	3.6% (4)	0.9% (1)	2.7% (-1.2, 6.7)	0.3694
Hypotension	2.7% (3)	0.0% (0)	2.7% (-0.3, 5.8)	0.2467
Thrombosis/ Thromboembolism	1.8% (2)	0.0% (0)	1.8% (-0.7, 4.3)	0.4978
Ischemia	1.8% (2)	0.9% (1)	0.9% (-2.2, 4.0)	1.0000
Respiratory Failure/ Dysfunction	1.8% (2)	0.9% (1)	0.9% (-2.2, 4.0)	1.0000
Steal Syndrome	1.8% (2)	0.0% (0)	1.8% (-0.7, 4.3)	0.4978
Myocardial Infarction	0.9% (1)	0.0% (0)	0.9% (-0.9, 2.7)	1.0000
Pleural Effusion	0.0% (0)	0.9% (1)	-0.9% (-2.8, 0.9)	0.4931

A total of seven deaths were reported with six deemed related to the subjects' underlying condition and one due to natural causes.

Table 6: Serious Adverse Events - 6 Weeks through 3 Months

Serious Adverse Event	PreveLeak Group (N=110)	Control Group (N=107)	Difference (95% C.I.)	p-value
Infection	2.7% (3)	1.9% (2)	0.9% (-3.1, 4.8)	1.0000
Thrombosis/ Thromboembolism	0.9% (1)	0.9% (1)	0.0% (-2.6, 2.5)	1.0000
Death	0.9% (1)	0.9% (1)	0.0% (-2.6, 2.5)	1.0000

2. Effectiveness Results

The primary analysis of effectiveness, a comparison of immediate suture line sealing, was conducted on the 331 anatomic sites treated as part of the study. As indicated in **Table 7**, the difference in suture line sealing between the two groups was statistically significant, indicating superior sealing in the PreveLeak group. This effectiveness analysis was also conducted on a per-patient basis, with no change in the results or conclusions.

Table 7: Primary Effectiveness Analysis: Immediate Suture Line Sealing

Parameter	PreveLeak Group	Control Group	Difference (95% C.I.)	Conclusion
Immediate Suture Line Sealing	60.5% (101/167)	39.6% (65/164)	20.8% (10.3, 31.4)	PreveLeak is Superior to Control

A significantly higher percentage of PreveLeak sites achieved immediate sealing compared to the control group when PTFE grafts were used for the bypass procedure, while no such difference was observed for Dacron grafts **(Table 8)**. In addition, no statistically significant difference in immediate sealing between the PreveLeak and control groups was observed during aortic or carotid procedures, while immediate sealing was significantly higher for the PreveLeak sites in extremity bypass, hemodialysis access grafting procedures, and all other types of vascular procedures, as seen in **Table 9**. It is important to note that the study was not designed to be powered for these types of comparisons.

Table 8: Primary Effectiveness by Type of Graft

	% of Sites with No Bleeding on Clamp Release			
Type of Graft	PreveLeak Group (N=167)	Control Group (N=164)	Difference (95% C.I.)	p-value
PTFE	62.8% (71/113)	34.0% (35/103)	28.9% (16.1, 41.6)	<0.0001
Dacron	55.6% (30/54)	49.2% (30/61)	6.4% (-11.9, 24.6)	0.4946

Table 9: Primary Effectiveness by Surgical Procedure

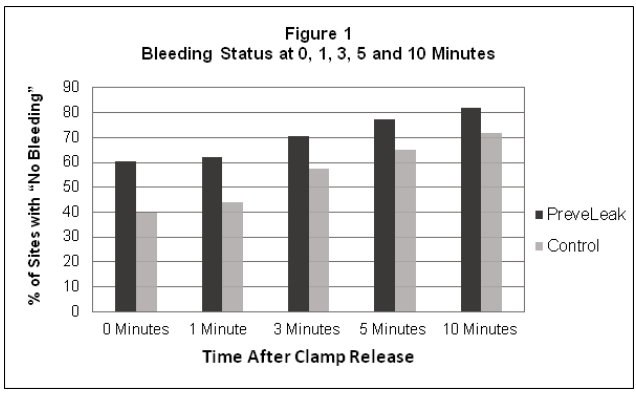
	% of Sites with No Bleeding on Clamp Release			
Surgical Procedure	PreveLeak Group (N=167)	Control Group (N=164)	Difference (95% C.I.)	p-value
Aortic Procedures	77.3% (17/22)	70.0% (21/30)	7.3% (-16.7, 31.3)	0.5591
Extremity Bypass Procedures	62.5% (20/32)	26.7% (8/30)	35.8% (12.8, 58.9)	0.0046
Carotid Procedures	30.0% (9/30)	38.1% (8/21)	-8.1% (-34.6, 18.4)	0.5461
Hemodialysis Access Grafting	69.6% (32/46)	32.6% (14/43)	37.0% (17.7, 56.3)	0.0005
Other Vascular Procedures	62.2% (23/37)	35.0% (14/40)	27.2% (5.7, 48.7)	0.0172

a. Bleeding Status through 10 Minutes

As a secondary endpoint, bleeding status was recorded for each treatment site immediately following clamp release, and at 1, 3, 5 and 10 minute intervals following clamp release. At each time point, the clinical investigator recorded either "Bleeding" or "No Bleeding." The percent of treated sites achieving hemostasis at each time point is presented in **Table 10** and **Figure 1**.

Table 10: Bleeding Status at 0, 1, 3, 5 and 10 Minutes

	% of Sites with "No Bleeding"		
Time After Clamp Release	**PreveLeak Group (N=167)**	**Control Group (N=164)**	**Difference (95% C.I.)**
Immediate (0 Minutes)	60.5% (101/167)	39.6% (65/164)	20.8% (10.3, 31.4)
1 Minute	62.3% (104/167)	43.9% (72/164)	18.4% (7.8, 28.9)
3 Minutes	70.7% (118/167)	57.3% (94/164)	13.3% (3.1, 23.6)
5 Minutes	77.2% (129/167)	65.2% (107/164)	12.0% (2.3, 21.7)
10 Minutes	82.0% (137/167)	72.0% (118/164)	10.1% (1.1, 19.1)



At ten minutes, there was no statistically significant difference in bleeding between the PreveLeak control groups with respect to the type of graft used or the type of procedure performed, as seen in **Tables 11** and **12.**

Table 11: Bleeding Status at 10 Minutes by Type of Graft

Type of Graft	**% of Sites with "No Bleeding" at 10 Minutes**			
	PreveLeak Group (N=167)	**Control Group (N=164)**	**Difference (95% C.I.)**	**p-value**
PTFE	83.2% (94/113)	72.8% (75/103)	10.4% (-0.7, 21.4)	0.0650
Dacron	79.6% (43/54)	70.5% (43/61)	9.1% (-6.6, 24.8)	0.2601

Table 12: Bleeding Status at 10 Minutes by Surgical Procedure

Surgical Procedure	**% of Sites with "No Bleeding" at 10 Minutes**			
	PreveLeak Group (N=167)	**Control Group (N=164)**	**Difference (95% C.I.)**	**p-value**
Aortic Procedures	95.5% (21/22)	80.0% (24/30)	15.5% (-1.3, 32.2)	0.2165
Bypass-Extremities	71.9% (23/32)	63.3% (19/30)	8.5% (-14.7, 31.8)	0.4721
Carotid Procedures	70.0% (21/30)	57.1% (12/21)	12.9% (-13.9, 39.6)	0.3444
Hemodialysis Access Grafting	93.5% (43/46)	83.7% (36/43)	9.8% (-3.4, 22.9)	0.1876
Other	78.4% (29/37)	67.5% (27/40)	10.9% (-8.8, 30.5)	0.2842

b. Time to Sealing through 10 Minutes

Time to sealing refers to the time the incision site was completely sealed, i.e., the last time point in which bleeding status equaled "No Bleeding" for each treatment site.

Kaplan-Meier methods were employed to summarize the cumulative time to sealing for all treated sites and compare the results between treatment groups. Censored observations include treatment sites where the clinical investigator intervened and used additional methods to achieve hemostasis prior to 10 minutes after clamp release. Among the 167 sites treated in the PreveLeak group, 56.6% were sealed at 0 minutes, 62.7% at 1 minute, 71.3% at 3 minutes, 78.7% at 5 minutes, and 85.5% at 10 minutes after clamp release. Among the 164 sites treated in the Control group, 36.6% were sealed at 0 minutes, 44.1% at 1 minute, 58.2% at 3 minutes, 68.1% at 5 minutes, and 76.5% at 10 minutes after clamp release. Time to sealing was significantly better for PreveLeak compared to the Control group ($p < 0.0005$) (**Figure 2** and **Table 13**).

Figure 2: Cumulative Time to Sealing – Kaplan Meier Results

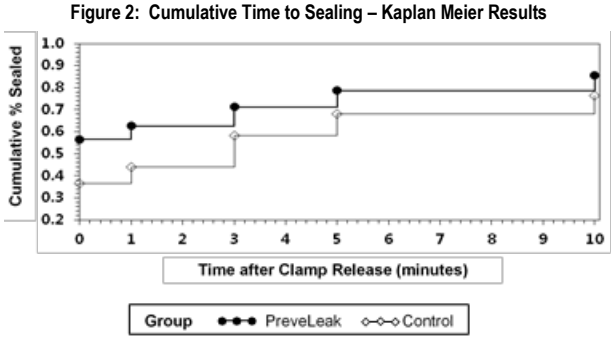


Table 13: Cumulative Time to Sealing – Kaplan Meier Results

	Time Period after Clamp Release				
	0 minutes	1 minute	3 minutes	5 minutes	10 minutes
PreveLeak Group					
# Sites at beginning of Interval	167	72	62	43	32
# Censored Prior to Interval	1	0	6	0	4
# at Risk	166	72	56	43	28
# sealed	94	10	13	11	9
% Sealed	56.6	62.7	71.3	78.7	85.5
Standard error (%)	3.9	3.8	3.6	3.3	2.9
Control Group					
# Sites at beginning of Interval	164	104	90	62	45
# Censored Prior to Interval	0	2	7	3	3
# at Risk	164	102	83	59	42
# sealed	60	12	21	14	11
% Sealed	36.6	44.1	58.2	68.1	76.5
Standard error (%)	3.8	3.9	3.9	3.8	3.5

Wilcoxon Test between Groups, p-value = 0.0004

c. Surgery and Hospitalization Data

The total surgery time was defined as the time the initial incision was made to the time the dressings were placed. The average surgery time was 3.2 ± 1.4 hours for the PreveLeak group, which was statistically significantly less than the 3.8 ± 2.2 hours for the Control group ($p \leq 0.01$). The total hospitalization time was defined as the number of days between the initial study procedure and the date of hospital discharge. The average hospitalization time was 4.1 ± 5.5 days for the PreveLeak group and 5.4 ± 7.0 days for the Control group, which does not represent a statistically significant difference (**Table 14**).

Table 14: Procedural Data for all Treated Sites

Procedural Data	PreveLeak (N=110 pts / 167 sites)	Control (N=107 pts / 164 sites)	Difference (95% C.I.)	p-value
Time between Clamp release and Bleeding Stopped (min)				
Mean ± SD (N)	5.1 ± 15.1 (166)	5.3 ± 7.6 (164)	---	0.0008[1]
Median	0.0	3.0		
Range (min, max)	(0, 132)	(0, 40)		
Total Surgery Time (hrs)				
Mean ± SD (N)	3.2 ± 1.4 (110)	3.8 ± 2.2 (106)	-0.7 (-1.2, -0.2)	0.0085
Range (min, max)	(1.0, 7.7)	(1.0, 11.1)		
Total Hospitalization Time (days)				
Mean ± SD (N)	4.1 ± 5.5 (110)	5.4 ± 7.0 (107)	-1.3 (-3.0, 0.4)	0.1273
Range (min, max)	(0, 42)	(0, 43)		

[1]Wilcoxon, 2 sample test.

POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of this class of surgical sealants:

- Application of the sealant to tissue not targeted for the procedure
- Failure of the sealant to adhere to the tissue
- Hypersensitivity reaction such as swelling or edema at the application site
- Possible transmission of infectious agents from materials of animal origin
- Thrombosis and thromboembolism

Below is a list of the potential adverse effects (e.g., complications) associated with cardiac and vascular procedures:

• Adhesions	• Ischemia
• Anastomotic pseudoaneurysm	• Lymphocele/lymph fistula
• Aortic insufficiency	• Myocardial infarction
• Cardiac tamponade	• Neurological deficits
• Cerebral emboli	• Organ system dysfunction/failure
• Coagulopathy	• Pain
• Death or irreversible morbidity	• Paraplegia
• Dissection	• Pleural effusion
• Edema	• Pulmonary emboli
• Erythema	• Renal dysfunction/failure
• Hematoma	• Stroke or cerebral infarction
• Hemorrhage	• Thrombosis
• Infection	• Vasospasm
• Injury to normal vessels or tissue	• Vessel rupture and hemorrhage

For the specific adverse events that occurred in the clinical studies, please see the Clinical Study section above.

Directions for Use

HOW SUPPLIED

Packaging contains one double-barreled syringe and two delivery tips.

Additional delivery tips may be purchased separately.

PreveLeak and its accessories are not made with natural rubber latex.

PreveLeak is supplied sterile for single use only.

Do not re-sterilize or reuse any components.

Discard unused material.

Do not use if package is opened or damaged.

STORAGE

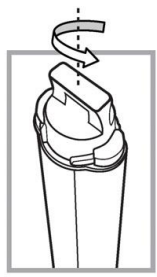
Store at 2-8°C.

NOTES:

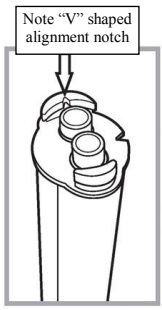
- In case of contact with eyes, flush with plenty of water and seek medical attention.
- Take special care when assembling and handling the device to prevent accidental discharge from the syringe.
- PreveLeak polymerizes rapidly. Use sealant immediately after priming the delivery tip to avoid the tip becoming blocked and requiring replacement.

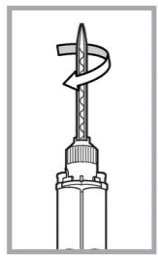
PREPARATION

1. Remove from box and allow PreveLeak to reach room temperature prior to use.
2. Open the outer pouch and place the inner sterile pouch onto the sterile field.
3. Open the inner pouch and remove the double-barrel syringe and the delivery tips.
4. Hold the syringe by the barrel, cap-end upwards.



5. Remove the cap by turning 90˚ counterclockwise and pulling upwards, using a slight side to side rocking motion. Note how the cap attaches and detaches since the delivery tip is attached in the same manner.





6. Attach the delivery tip to the syringe as follows: Locate the small alignment tab on the hub-end of the delivery tip. Locate the corresponding v-shaped alignment notch in one of the two upper locking wings at the open end of the syringe. Align the tab in the notch and push delivery tip into place. Turn delivery tip 90˚ clockwise to lock the tip to the syringe.

Application Procedure:

7. Ensure that the application site is clamped and there is no active bleeding.
8. Prime the syringe by discarding the first 0.25 ml of sealant immediately prior to use. This ensures that fully mixed product in the proper proportions is delivered to the application site. PreveLeak is now ready to be applied to the surgical site. Apply the sealant in a slow and steady manner over the top of the suture line with the delivery tip approximating the sutures.
9. After the application is complete, leave the clamps in place for at least 60 seconds before restoring circulation, applying irrigation, blotting with gauze or touching the sealant.
10. Prior to restoring circulation, carefully use blunt dissection to ease away any sealant attached to the clamps. Gently remove the clamps without disturbing the sealant at the application site.
11. Do not manipulate the synthetic graft or patch.

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