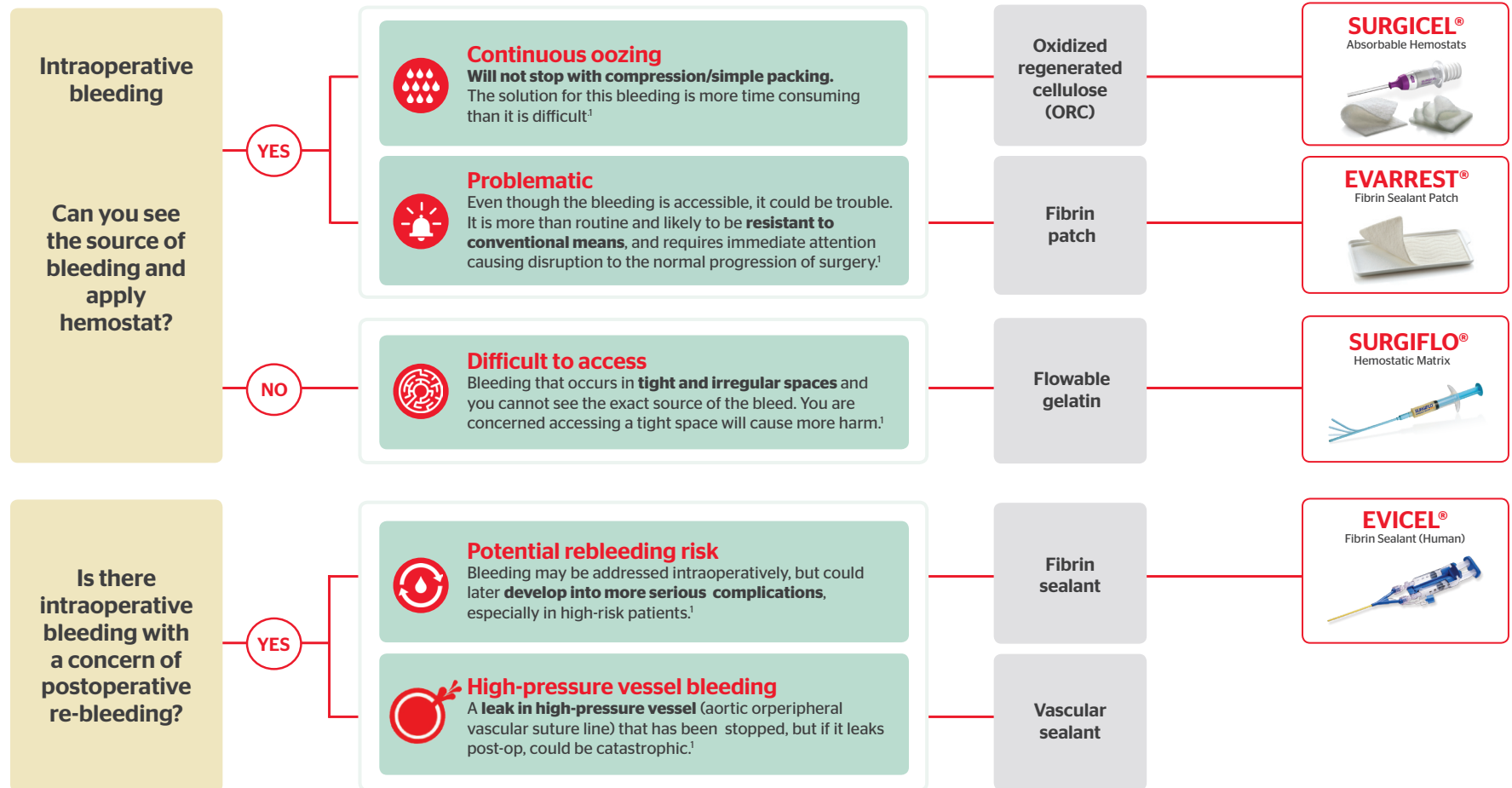


Addressing Surgical Bleeding Situations With Adjunctive Hemostats*



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BLEEDING SITUATIONS



Continuous oozing

Will not stop with compression/ simple packing. The solution for this bleeding is more time consuming than it is difficult.¹



Problematic

Even though the bleeding is accessible, it could be trouble. It is more than routine and likely to be **resistant to conventional means** and requires immediate attention causing disruption to the normal progression of surgery.¹



Difficult to access

Bleeding that **occurs in tight and irregular spaces** and you cannot see the exact source of the bleed. You are concerned accessing a tight space will cause more harm.¹



Potential re-bleeding risk

Bleeding may be addressed intraoperatively, but could later **develop into more serious complications**, especially in high-risk patients.¹



High-pressure vessel bleeding

A **leak in a high-pressure vessel** (aortic or peripheral vascular suture line) that has been stopped but could be catastrophic if it leaks post-op.¹

CATEGORY SOLUTIONS

Oxidized regenerated cellulose (ORC)

An absorbable plant-based biomaterial that expedites the hemostasis process by serving as a scaffold for platelet adhesion and aggregation that leads to quick clot formation.²

Fibrin patch

Fibrinogen/thrombin patch provides mechanical integrity and supports clot formation independently of the patient coagulation profile in indicated patients.³

Flowable gelatin

A gelatin-based foam that flows into the bleeding area and serves as a scaffold for platelet adhesion and can be combined with thrombin to expedite clot formation.⁴

Fibrin sealant

Fibrinogen and thrombin, when mixed, create a fibrin clot independent of the patient coagulation profile.⁵

Vascular sealant

A surgical adhesive that secures suture lines and provides a mechanical seal.

SURGICEL®

Absorbable Hemostats



EVARREST®

Fibrin Sealant Patch



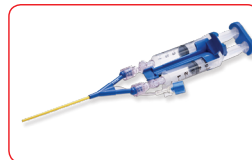
SURGIFLO®

Hemostatic Matrix



EVICEL®

Fibrin Sealant (Human)



*The bleeding situations identified reflect customer insights/market research on optimal adjunctive hemostat utilization. The product solutions should only be used in accordance with their instructions for use. Product recommendations should not supplant medical judgment. Surgeon preference, experience, and patient needs may dictate alternate technique. Review all relevant precautions, especially the indications, contraindications, warnings, and information for use. Please see package inserts for Full Prescribing Information. The visual does not reflect any sequential order in use.

The Hemostatic Cascade

Understanding the steps of hemostasis is important in achieving the right solution.

Antithrombotic medications disrupt the body's ability to form a clot

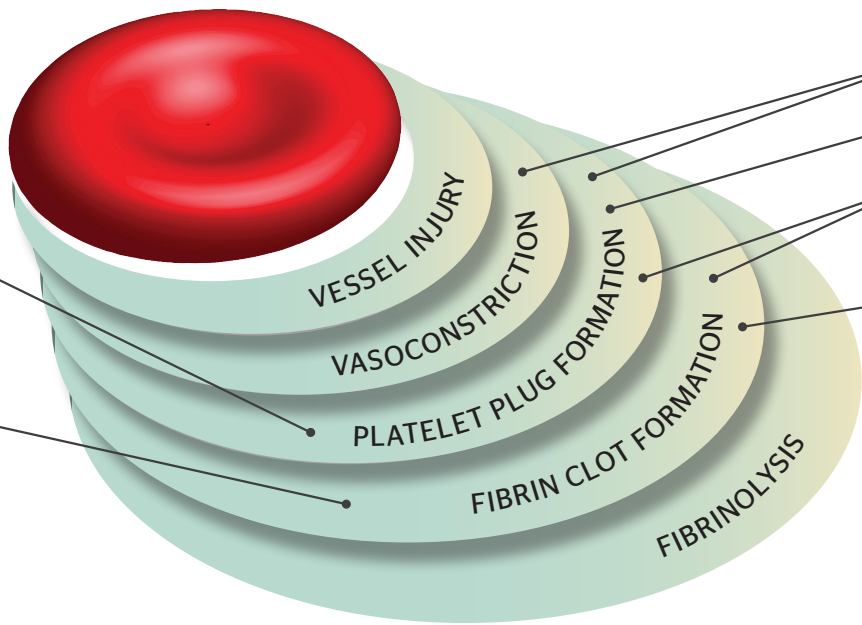
PLAVIX®

ASPIRIN

HEPARIN

WARFARIN

XARELTO®



Adjunctive hemostats have different mechanisms of action to stop bleeding

The third-party trademarks used herein are trademarks of their respective owners.

Different bleeding situations require different solutions

| Primary Methods | | Adjunctive Methods |
|---|--|--|
| Mechanical | Energy | Hemostats and Sealants |
| <ul style="list-style-type: none">• Clamps• Ligating clips• Staples• Sutures• Bone wax• Digital pressure• External bandages | <ul style="list-style-type: none">• Monopolar and Bipolar Electrosurgery• Ultrasonic• Advanced Bipolar | <ul style="list-style-type: none">• Oxidized Regenerated Cellulose• Flowable Gelatin• Fibrin Sealants• Fibrin Patches• Vascular Sealants |

Important Risk Information: Adjunctive hemostats are not intended for use on nonbleeding tissue or for prophylactic use. The bleeding situations identified reflect customer insights/market research on optimal adjunctive hemostat utilization. The product solutions should only be used in accordance with their instructions for use. Product recommendations should not supplant medical judgment. Surgeon preference, experience, and patient needs may dictate alternate technique. Review all relevant precautions, especially the indications, contraindications, warnings, and information for use. Please see package inserts for Full Prescribing Information.

SURGICEL® Powder Absorbable Hemostat Essential Product Information

INDICATIONS

SURGICEL® Powder (oxidized regenerated cellulose) is used adjunctively in surgical procedures to assist in the control of capillary, venous, and small arterial hemorrhage when ligation or other conventional methods of control are impractical or ineffective.

CONTRAINDICATIONS

- Do not inject or place SURGICEL® Powder into an open blood vessel.
- SURGICEL® Powder should not be used to control hemorrhage from large arteries.
- SURGICEL® Powder is used to help achieve hemostasis in, around, or in proximity to foramina in bone, areas of bony confine, the spinal cord, or the optic nerve and chiasm, it must always be removed after hemostasis is achieved since it will swell and could exert unwanted pressure.
- SURGICEL® Powder should not be used for implantation in bone defects, such as fractures, since there is a possibility of interference with callus formation and a theoretical chance of cyst formation.

WARNINGS

- Closing with SURGICEL® Powder in a contaminated wound without drainage may lead to complications and should be avoided.
- SURGICEL® Powder should not be impregnated with anti-infective agents or with other materials such as buffering or hemostatic substances.
- SURGICEL® Powder is dry and there may be difficulties in precise delivery under certain circumstances. Unintentional device placement may result in powder scattering and device migration that may increase the risk of adhesion formation.
- Although SURGICEL® Powder is bactericidal against a wide range of pathogenic microorganisms, it is not intended as a substitute for systemically administered therapeutic or prophylactic antimicrobial agents to control or to prevent postoperative infections.
- Do not attempt to trim the applicator tip.

PRECAUTIONS

- SURGICEL® Powder should not be used in conjunction with autologous blood salvage circuits, because its fragments may pass through the transfusion filters of blood-scavenging systems.
- Use only as much SURGICEL® Powder (oxidized regenerated cellulose) as is necessary and apply only where needed for hemostasis. Remove any excess before surgical closure in order to facilitate absorption and to minimize the possibility of foreign body reaction.
- In urological procedures, minimal amounts of SURGICEL® Powder should be used and care must be exercised to prevent plugging of the urethra, ureter, or a catheter by dislodged portions of the product.
- Since absorption of SURGICEL® Powder could be prevented in chemically cauterized areas, its use should not be preceded by application of silver nitrate or any other escharotic chemicals.
- If SURGICEL® Powder is used temporarily to line the cavity of open wounds, it should be removed by irrigation with sterile water or saline solution after bleeding has stopped.
- Precautions should be taken in otorhinolaryngologic surgery to ensure that none of the material is aspirated by the patient (e.g., controlling hemorrhage after tonsillectomy and controlling epistaxis).
- This applicator tip is not intended for laparoscopic or other endoscopic use.

ADVERSE EVENTS

- Paralysis and nerve damage have been reported when other SURGICEL® products were used around, in, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm.
- Blindness has been reported in connection with surgical repair of a lacerated left frontal lobe when other SURGICEL® products were placed in the anterior cranial fossa (see WARNINGS and PRECAUTIONS).
- Foreign body reactions have been reported with other products from the SURGICEL® Family of Absorbable Hemostats.
- Burning has been reported when other SURGICEL® products were applied after nasal polyp removal. Headache, burning, stinging, and sneezing in epistaxis and other rhinological procedures, and stinging when SURGICEL® product was applied on surface wounds (varicose ulcerations, dermabrasions, and donor sites) have also been reported.

For more information and technical questions, call 1-800-795-0012.

071582-170602

SURGICEL Essential Product Information

INDICATIONS

SURGICEL® Absorbable Hemostat (oxidized regenerated cellulose) is used adjunctively in surgical procedures to assist in the control of capillary, venous, and small arterial hemorrhage when ligation or other conventional methods of control are impractical or ineffective. SURGICEL® ORIGINAL, SURGICEL® FIBRILLAR™ and SURGICEL® NU-KNIT® Hemostats can be cut to size for use in endoscopic procedures.

PRECAUTIONS

- Use only as much SURGICEL® Absorbable Hemostat as is necessary for hemostasis, holding it firmly in place until bleeding stops. Remove any excess before surgical closure in order to facilitate absorption and minimize the possibility of foreign body reaction.
- In urological procedures, minimal amounts of SURGICEL® Absorbable Hemostat should be used and care must be exercised to prevent plugging of the urethra, ureter, or a catheter by dislodged portions of the product.
- Since absorption of SURGICEL® Absorbable Hemostat could be prevented in chemically cauterized areas, its use should not be preceded by application of silver nitrate or any other escharotic chemicals.
- If SURGICEL® Absorbable Hemostat is used temporarily to line the cavity of large open wounds, it should be placed so as not to overlap the skin edges. It should also be removed from open wounds by forceps or by irrigation with sterile water or saline solution after bleeding has stopped.
- Precautions should be taken in otorhinolaryngologic surgery to assure that none of the material is aspirated by the patient. (Examples: controlling hemorrhage after tonsillectomy and controlling epistaxis.)
- Care should be taken not to apply SURGICEL® Absorbable Hemostat too tightly when it is used as a wrap during vascular surgery (see Adverse Reactions).

ADVERSE EVENTS

- "Encapsulation" of fluid and foreign body reactions have been reported.
- There have been reports of stenotic effect when SURGICEL® Absorbable Hemostat has been applied as a wrap during vascular surgery.
- Paralysis and nerve damage have been reported when SURGICEL® Absorbable Hemostat was used around, in, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm.
- Blindness has been reported in connection with surgical repair of a lacerated left frontal lobe when SURGICEL® Absorbable Hemostat was placed in the anterior cranial fossa.
- Possible prolongation of drainage in cholecystectomies and difficulty passing urine per urethra after prostatectomy have been reported.

For more information, please consult your doctor or for product quality and technical questions, call 1-800-795-0012.

063768-161128

EVARREST® Fibrin Sealant Patch

Important Safety Information

Indications and Usage

EVARREST® is a fibrin sealant patch indicated for use with manual compression as an adjunct to hemostasis in adult patients undergoing surgery, when control of bleeding by conventional surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical.

Limitations for Use

- Cannot be used in place of sutures or other forms of mechanical ligation in the treatment of major arterial or venous bleeding.
- Not for use in children under one month of age
- Laparoscopic and other minimally invasive surgeries where manual compression would be difficult to achieve.

Important Safety Information

For topical use only. Apply immediate manual compression over the entire surface of the patch and maintain contact pressure for 3 minutes to control the bleeding.

Do not apply intravascularly. This can result in life threatening thromboembolic events.

Do not use to treat bleeding from large defects in arteries or veins where the injured vascular wall requires conventional surgical repair and maintenance of vessel patency or where there would be persistent exposure of EVARREST® to blood flow and/or pressure during absorption of the product. Thrombosis can occur if absorbed systemically.

Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products. EVARREST ® can cause hypersensitivity reactions including anaphylaxis.

Avoid application to contaminated areas of the body or in the presence of active infection. Infection can occur.

EVARREST contains oxidized regenerated cellulose which adheres to bleeding surfaces. Inadvertent adhesions can occur.

Avoid use in, around, or in proximity to, foramina in bone or areas of bony confines where swelling may cause compression.

Use the least number of patches required to cover the entire bleeding area. Portions of excess patch material can become dislodged and migrate to other areas of the body.

Do not use more than eight 2x4 inch (5.1 x 10.2 cm) or more than four 4x4 inch (10.2 x 10.2 cm) patches.

Use in patients who have been previously exposed to EVARREST® has not been studied.

May carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

The adverse reactions reported during clinical trials occurred in less than 1% of all cases and included deep venous thrombosis, pulmonary embolism, blood fibrinogen increase, anastomotic hemorrhage, post procedural and intra-abdominal hemorrhage, abdominal distension, anemia, gastrointestinal hemorrhage, thoracic cavity drainage, pleural effusion, abdominal abscess, ascites, localized intra-abdominal fluid collection, cardiac failure, operative hemorrhage, and ischemic bowel.

Pediatrics: Safety and effectiveness in pediatric patients have not been established. Use in children under the age of one month may be unsafe or ineffective due to small size and limited ability to apply the patch as recommended.

Please see package insert for EVARREST® Full Prescribing Information.

To report SUSPECTED ADVERSE REACTIONS, contact ETHICON Customer Support Center at 1-877-384-4266 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

SURGIFLO® Hemostatic Matrix Kit Essential Product Information (Made from Absorbable Gelatin Sponge, USP) with Thrombin

DESCRIPTION

SURGIFLO® with Thrombin (SURGIFLO® Hemostatic Matrix Kit) is intended for hemostatic use by applying to a bleeding surface.

ACTIONS

When used in appropriate amounts SURGIFLO® is absorbed completely within 4 to 6 weeks.

INTENDED USE/INDICATIONS

SURGIFLO®, mixed with thrombin solution, is indicated in surgical procedures (other than ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or other conventional methods is ineffective or impractical.

CONTRAINDICATIONS

- Do not use SURGIFLO® in intravascular compartments because of the risk of embolization.
- Do not use SURGIFLO® in patients with known allergies to porcine gelatin.
- Do not use SURGIFLO® in closure of skin incisions because it may interfere with the healing of skin edges. This interference is due to mechanical interposition of gelatin and is not secondary to intrinsic interference with wound healing.

WARNINGS

- SURGIFLO® should not be used in the presence of infection and should be used with caution in contaminated areas of the body.
- SURGIFLO® should not be used in instances of pumping arterial hemorrhage. SURGIFLO® will not act as a tampon or plug in a bleeding site.
- SURGIFLO® should be removed from the site of application when used in, around, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm because it may swell resulting in nerve damage.
- Excess SURGIFLO® should be removed once hemostasis has been achieved.
- The safety and effectiveness of SURGIFLO® for use in ophthalmic procedures has not been established.
- SURGIFLO® should not be used for controlling post-partum intrauterine bleeding or menorrhagia.
- The safety and effectiveness of SURGIFLO® has not been established in children and pregnant women.
- The blue flexible applicator tip should not be trimmed to avoid exposing internal guidewire.
- The white straight applicator tip should be trimmed away from the surgical area. Cut a square angle to avoid creating a sharp tip.

PRECAUTIONS

- Safe and effective use of SURGIFOAM® Sponge has been reported in a published neurologic retrospective study involving 1700 cases in Europe. Safe and effective use in neurosurgery has not been proven through randomized, controlled clinical studies in the United States.
- SURGIFLO® is supplied as a sterile product and cannot be resterilized.
- SURGIFLO® should not be used for packing unless excess product that is not needed to maintain hemostasis is removed. SURGIFLO® may swell up to 20% upon contact with additional fluid.
- SURGIFLO® should not be used in conjunction with autologous blood salvage circuits.
- SURGIFLO® should not be used in conjunction with methylmethacrylate adhesives.
- In urological procedures, SURGIFLO® should not be left in the renal pelvis or ureters to eliminate the potential foci for calculus formation.

ADVERSE EVENTS

A total of 142 patients received SURGIFOAM® Sponge during a clinical trial comparing SURGIFOAM® Sponge to another absorbable gelatin sponge. In general, the following adverse events have been reported with the use of absorbable porcine gelatin-based hemostatic agents:

- Gelatin-based hemostatic agents may serve as a nidus for infection and abscess formation and have been reported to potentiate bacterial growth.
- Giant cell granulomas have been observed at implant sites when used in the brain.
- Compression of the brain and spinal cord resulting from the accumulation of sterile fluid have been observed.
- Multiple neurologic events were reported when absorbable gelatin-based hemostatic agents were used in laminectomy operations, including cauda equina syndrome, spinal stenosis, meningitis, arachnoiditis, headaches, paresthesias, pain, bladder and bowel dysfunction, and impotence.
- The use of absorbable gelatin-based hemostatic agents during the repair of dural defects associated with laminectomy and craniotomy operations, has been associated with fever, infection, leg paresthesias, neck and back pain, bladder and bowel incontinence, cauda equina syndrome, neurogenic bladder, impotence, and paresis.
- The use of absorbable gelatin-based hemostatic agents has been associated with paralysis, due to device migration into foramina in the bone around the spinal cord, and blindness, due to device migration in the orbit of the eye, during lobectomy, laminectomy, and repair of a frontal skull fracture and lacerated lobe.
- Foreign body reactions, "encapsulation" of fluid, and hematoma have been observed at implant sites.
- Excessive fibrosis and prolonged fixation of a tendon have been reported when absorbable gelatin-based sponges were used in severed tendon repair.
- Toxic shock syndrome was reported in association with the use of absorbable gelatin-based hemostats in nasal surgery.
- Fever, failure of absorption, and hearing loss have been observed when absorbable hemostatic agents were used during tympanoplasty.

EVICEL® Fibrin Sealant (Human)

IMPORTANT SAFETY INFORMATION

Indication

EVICEL® Fibrin Sealant (Human) is indicated as an adjunct to hemostasis for use in patients undergoing surgery, when control of bleeding by standard surgical techniques (such as suture, ligature, or cautery) is ineffective or impractical.

Contraindications

- Do not inject directly into the circulatory system. Intravascular application of EVICEL® may result in life-threatening thromboembolic events.
- Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products.
- Do not use for the treatment of severe or brisk arterial bleeding.
- Do not use EVICEL® for spraying in endoscopic or laparoscopic procedures where the minimum recommended distance from the applicator tip to the target site cannot be ensured.

Warnings and Precautions

- Life-threatening air or gas embolism has occurred with the use of spray devices employing a pressure regulator to administer EVICEL®. This event appears to be related to the use of the spray device at pressures higher than recommended and/or at distances closer than recommended to the surface of the tissue.
- Monitor changes in blood pressure, pulse, oxygen saturation, and end-tidal CO2 when spraying EVICEL® because of the possibility of gas embolism.
- To reduce the risk of potentially life-threatening gas embolism, spray EVICEL® using only pressurized CO2 gas at the pressures and distances recommended for the specific tips.
- Use EVICEL® spray application only if it is possible to accurately judge the spray distance, especially during endoscopic or laparoscopic procedures.
- Prior to applying EVICEL®, dry surface areas of the wound by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices). Prepare and administer EVICEL® according to the instructions and with only devices recommended for this product.
- May carry a risk of transmitting infectious agents, e.g. viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

The most common adverse reactions reported in clinical trials are peripheral edema, abdominal abscess, infection, hematoma, incision site hemorrhage, vascular graft occlusion, postoperative wound complication and decreased hemoglobin.

For complete indications, contraindications, warnings, precautions, and adverse reactions, please reference full package insert.

021323-170803

EVITHROM® Thrombin, Topical (Human) for Topical Use Only
Lyophilized Powder for Solution

EVITHROM® is a topical thrombin indicated as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible and control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical.

EVITHROM® may be used in conjunction with an Absorbable Gelatin Sponge, USP.

Important Safety Information

- For topical use only.
- Do not inject.
- Apply EVITHROM® on the surface of bleeding tissue only.
- The amount of EVITHROM® required depends upon the area of tissue to be treated and the method of application. In clinical studies, volumes up to 10 ml were used in conjunction with Absorbable Gelatin Sponge.
- Do not use for the treatment of severe or brisk arterial bleeding.
- Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products. Hypersensitivity reactions, including anaphylaxis, may occur.
- There is a potential risk of thrombosis if absorbed systemically.
- May carry a risk of transmitting infectious agents such as viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite manufacturing steps designed to reduce the risk of viral transmission.
- The most common adverse reactions during clinical trial (reported in at least 2% of subjects treated with EVITHROM®) were prolonged activated partial thromboplastin time, increased INR, decreased lymphocyte count, prolonged prothrombin time and increased neutrophil count.
- None of the patients treated with EVITHROM developed antibodies to human thrombin or to human Factor V/Va. The clinical significance of these findings is unknown.

For complete indications, contraindications, warnings, precautions, and adverse reactions, please reference full package insert.

021328-140912