Floseal Hemostatic Matrix 5 mL/10 mL

ENG

Instructions for Use

DO NOT INJECT INTRAVASCULARLY.

FLOSEAL Hemostatic Matrix ("FLOSEAL") must not be injected into blood vessels.

Short Instruction:

1. **Apply FLOSEAL directly to the source of bleeding.**
2. **Maintain FLOSEAL at the site (source of bleeding) for 2 minutes with gentle approximation.**
3. **Use adequate amounts of FLOSEAL to completely cover the tissue defect.**
4. **Work quickly.**
5. **Always irrigate excess FLOSEAL away. Use gentle irrigation.**

Device Description

The FLOSEAL kit consists of a bovine-derived Gelatin Matrix, a human derived Thrombin Component, Applicator tips, and several mixing accessories. The mixing accessories include a syringe, a pre-filled Sodium Chloride Solution ampoule, and a vial adapter for needle-free reconstitution. The accessories are included to facilitate the reconstitution and mixing of the Thrombin into the Gelatin Matrix. Applicator tips are included to facilitate the delivery of FLOSEAL to the site to be treated. (For specific kit contents, see Table in "How Supplied" section.)

The Gelatin Matrix, manufactured by Baxter Healthcare Corporation, consists of crosslinked gelatin granules and is provided sterile and non-pyrogenic in a standard disposable syringe.

The Thrombin (Human) is a sterile, non-pyrogenic, freeze-dried, vapor-heated and solvent detergent-treated powder preparation made from pooled human plasma. The Sodium Chloride Solution is a sterile, non-pyrogenic solution. After reconstitution of the lyophilized Thrombin in Sodium Chloride Solution, the resulting thrombin solution contains 500 IU/mL Thrombin (Human).

FLOSEAL is a combination of the Gelatin Matrix and the Thrombin Component. Thrombin must be added to the Gelatin Matrix prior to use. FLOSEAL is biocompatible and resorbed within 6 to 8 weeks, consistent with normal wound healing.

How Supplied

FLOSEAL is provided in the configuration shown in the table below.

The Gelatin Matrix component of FLOSEAL is sterilized by irradiation.

FLOSEAL Hemostatic Matrix Kit Configuration		
Gelatin Matrix	**Thrombin Component**	**Ampoule Component**
5 mL Configuration		
• 1 x 5 mL syringe with Gelatin Matrix • 1 x 5 mL syringe for Matrix Preparation with integral female Luer connector • 2 x Applicator tips • 1 x Malleable tip	• 1 x vial Thrombin (Human), Vapor Heated, Solvent/ Detergent treated, 2500 IU • 1 x Needle-free vial adaptor	• 1 x 0.9% Sodium Chloride Solution Ampoule, 5 mL

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FLOSEAL Hemostatic Matrix Kit Configuration		
Gelatin Matrix	**Thrombin Component**	**Ampoule Component**
10 mL Configuration		
• 1 x 10 mL syringe with Gelatin Matrix • 1 x 10 mL syringe for Matrix Preparation • 1 x Luer Connector • 2 x Applicator tips • 1 x Malleable tip	• 1 x vial Thrombin (Human), Vapor Heated, Solvent/ Detergent treated, 5000 IU • 1 x Needle-free vial adaptor	• 1 x 0.9% Sodium Chloride Solution Ampoule, 10 mL

The Thrombin is processed using aseptic technique. The contents of the thrombin component are then sealed in a double pouch and treated with ethylene oxide to render the external component surfaces suitable for use in the sterile field. The Ampoule component is provided terminally sterilized.

Indications

FLOSEAL is indicated in surgical procedures as an adjunct to hemostasis when control of bleeding, ranging from oozing to spurting, by ligature or conventional procedures is ineffective or impractical.

Contraindications

Do not use FLOSEAL in patients with known allergies to materials of bovine origin.

Warnings

Do not inject or compress FLOSEAL into blood vessels.

Do not apply FLOSEAL in the absence of active blood flow, e.g., while the vessel is clamped or bypassed. Extensive intravascular clotting and even death may result.

FLOSEAL is not intended as a substitute for meticulous surgical technique and the proper application of ligatures or other conventional procedures for hemostasis.

FLOSEAL is not intended to be used as a prophylactic hemostatic agent to prevent postoperative bleeding.

Excess FLOSEAL Matrix (material not incorporated in the hemostatic clot) should always be removed by gentle irrigation from the site of application. Meticulous irrigation is required when used in, around, or in proximity to foramina in bone, areas of bony confine, the spinal cord, the brain and/or cranial nerves.

As with any implantable material, the use of FLOSEAL is not recommended in the presence of an active infection.

FLOSEAL should be used with caution in contaminated areas of the body. If signs of infection or abscess develop where FLOSEAL has been applied, re-operation may be necessary in order to remove the infected material and allow drainage.

Regardless of the type of surgical procedure, surgeons should consider the maximum swell volume of FLOSEAL, which is between 10 – 20%, after product is applied to source of bleeding and its potential effect on the surrounding anatomic areas. Maximum swell volume is achieved within about 10 minutes.

The safety and effectiveness of FLOSEAL for use in ophthalmic procedures has not been established.

FLOSEAL should not be used for controlling intrauterine post-partum bleeding or menorrhagia.

The safety and effectiveness of FLOSEAL has not been established in children and pregnant women.

FLOSEAL contains Gelatin of bovine origin. The risk with respect to Transmissible Spongiform Encephalopathies (TSE) has been minimized in accordance with regulatory guidelines by a manufacturing process with demonstrated TSE inactivation capacity.

FLOSEAL also contains Thrombin made from human plasma. When medicines are made from human blood and plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections. The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A and parvovirus B19V viruses.

Do not use air to remove residual FLOSEAL from the accompanying applicator tips.

The applicator tips should not be cut.

All infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Baxter Healthcare Corporation. The physician should discuss the risks and benefits of this product with the patient.

Precautions

For single use only. Do not resterilize.

As with other hemostatic agents, circumstances that result in a negative peripheral venous pressure (e.g. patient positioning) may draw material into the vascular system, potentially resulting in life-threatening thromboembolic events.

As with other hemostatic agents, do not allow FLOSEAL to enter into cell saver equipment, extracorporeal cardiopulmonary bypass circuits or autologous blood salvage circuits. It has been demonstrated that fragments of collagen-based hemostatic agents may pass through 40 µm transfusion filters of blood scavenging systems.

Do not use FLOSEAL on bone surfaces where adhesives, such as methylmethacrylate or other acrylic adhesives, will be required to attach a prosthetic device. Microfibrillar collagen has been reported to reduce the strength of methylmethacrylate adhesives used to attach prosthetic devices to bone surfaces.

Do not use FLOSEAL in the closure of skin incisions because it may interfere with the healing of the skin edges due to mechanical interposition of gelatin. The safety and effectiveness of the use of FLOSEAL Matrix as a carrier for antibiotic solutions or powders has not been established.

The Thrombin Solution can be denatured by contact with solutions containing alcohol, iodine, or heavy metal ions. If antiseptics containing such substances have been used near the site of bleeding, FLOSEAL Matrix should not be applied until after the application site is cleaned to remove any such substances.

Adverse Events

In a randomized prospective, concurrently controlled clinical trial using a formulation of FLOSEAL Gelatin Matrix containing bovine thrombin, (FLOSEAL), a total of 309 patients received FLOSEAL or the Control (Gelatin Sponge + Thrombin).

The most common adverse events recorded during and after the application of the hemostatic agents were anemia, atrial fibrillation, infection, and hemorrhage. The following is a complete list of adverse events reported in greater than 1% of patients that were observed in the pivotal clinical trial for the FLOSEAL group. The corresponding adverse events for the Control group are listed for comparison. None of the adverse events that occurred were judged by the surgeon to be "Probably Related" to the use of FLOSEAL.

Adverse Events Reported in Greater than 1% of Patients in the FLOSEAL Clinical Trial Patients		
Adverse Event	**FLOSEAL**	**Control (Gelatin Sponge + Thrombin)**
Anemia	12 (8%)	7 (4%)
Fibrillation Atrial	10 (6%)	8 (5%)
Infection	10 (6%)	11 (7%)
Hemorrhage	6 (4%)	6 (4%)
Pneumonia	6 (4%)	2 (1%)
Urinary Tract Infection	6 (4%)	3 (2%)
Rash	5 (3%)	3 (2%)
Edema	5 (3%)	1 (<1%)
Hypotension	4 (3%)	2 (1%)
Respiratory Distress	4 (3%)	3 (2%)
Confusion	4 (3%)	0 (0%)
Dural Tear	4 (3%)	4 (3%)
Fibrillation Ventricular	4 (3%)	3 (2%)
Arrhythmia	4 (3%)	0 (0%)
Heart Failure Right	3 (2%)	2 (1%)
Thrombosis Arterial	3 (2%)	8 (5%)
Fever	3 (2%)	2 (1%)
Atelectasis	3 (2%)	1 (<1%)
Pleural Effusion	3 (2%)	5 (3%)
Counts reflect number of patients in each treatment group reporting one or more adverse events that map to a Modified COSTART 5th edition body system. At each level of summarization (Adverse Event), patients are only counted once.		

Other adverse events observed in 1% or less of the FLOSEAL clinical trial patients were myocardial infarction, cellulitis, pneumothorax, pain, cerebrovascular accident, hallucination, paraesthesia, bradycardia, abscess, diarrhea, urinary retention, dehiscence, skin ulcer, transfusion reaction, dyspnea, heart arrest, lung edema, back pain, ventricular tachycardia, neuropathy, acute kidney failure, kidney tubule necrosis, gastritis, nausea, nausea and vomiting, skin rash, hyperglycemia, and heel ulcer.

The following adverse events, all rated "mild", were deemed by the surgeon to be "Possibly Related" to the use of FLOSEAL: anemia (2 patients, 1%), mild post-operative bleeding (1 patient, <1%), and local inflammation (1 patient, <1%). No other adverse events were deemed by the surgeon to be related to the use of FLOSEAL.

Allergic reactions may be encountered in people sensitive to bovine materials. The following medical complaints, whether deemed associated with the use of FLOSEAL or not, have been reported with frequency of “very rare” (less than .01% of kits sold):

– Allergic Response
– Post operative bleeding
– Lack of efficacy
– Embolism
– Nerve Compression
– Adhesion formation
– Respiratory Distress
– Hydrocephaly
– Jaundice
– Death
– Inflammation
– Infection
– Pneumoperitoneum

Directions for Use

Thrombin must be added to the Gelatin Matrix prior to use.

1. FLOSEAL Preparation

Inspect the integrity of the contents of the FLOSEAL Kit. If the packaging or vial has been damaged or opened, do not use.

2. Opening the kit

Open the package containing the ampoule and deliver the ampoule to the sterile field.

Open the outer pouch of the thrombin component and deliver the inner pouch to the sterile field. Items in this package will be used to reconstitute the Thrombin prior to mixing with the Gelatin Matrix. Once placed in the sterile field, the inner package may be opened at any time.

Open the outer pouch of the gelatin matrix component and deliver the inner pouch to the sterile field. Once placed in the sterile field, the inner package may be opened at any time.

3. Preparing the Thrombin solution

First, remove the Tyvek lid from the vial adapter packaging. Remove twist-off cap from the Sodium Chloride ampoule. While gripping the vial adapter packaging, attach the pre-filled Sodium Chloride ampoule to the Luer connector of the vial adapter and remove from remaining packaging.

Remove the plastic flip-off cap from the Thrombin vial. While holding the vial adapter, pierce the rubber stopper of the Thrombin vial. Transfer the entire contents of the Sodium Chloride ampoule into the Thrombin vial. Gently swirl the Thrombin vial with vial adapter and ampoule attached until the Thrombin is completely dissolved. Once reconstituted, the Thrombin Solution should be used promptly. However, the solution may be stored at 2 – 25 °C, in the vial up to four hours.

4. Mixing the Thrombin Solution into the Gelatin Matrix

5 mL Configuration: Remove ampoule, attach empty 5 mL syringe with female luer connector to the vial adapter and draw the thrombin solution from the vial to the indicated mark (4 mL). Discard the empty Thrombin vial and the vial adapter appropriately.

10 mL Configuration: Remove ampoule, attach the Luer connector to the empty 10 mL syringe. Attach 10 mL syringe with Luer connector, to the vial adapter and draw the thrombin solution from the vial to the indicated mark (8 mL). Discard the empty Thrombin vial and the vial adapter appropriately.

The following is applicable to both 5 mL and 10 mL Configurations

Remove the Luer cap from the Gelatin Matrix Syringe carefully to avoid spilling the Gelatin Matrix granules. Connect this syringe to the syringe containing the Thrombin solution.

Push the plunger of the Thrombin solution syringe to quickly pass the solution into the syringe containing the Gelatin Matrix. This constitutes “one pass.” It may take several passes for all the Gelatin Matrix granules to hydrate. Do not use excessive force to push the dry granules through the Luer connector during the first few passes as it may clog.

Transfer the Gelatin Matrix-Thrombin solution mixture back and forth between the syringes for a total of 10 passes back and forth.

Ensure the syringe labeled FLOSEAL contains the FLOSEAL Matrix.

If desired, connect an Applicator tip to the FLOSEAL syringe. The Malleable Tip can be identified by the dark blue luer.

FLOSEAL may also be extruded directly from the syringe.

If the Malleable Tip is selected, attach the Tip to the FLOSEAL syringe and form the Tip as necessary to access the surgical site.

As necessary, flush the Malleable tip with an equivalent amount of saline to expel any residual FLOSEAL that may remain in the tip.

Baxter has no control over variability, tolerances, mechanical strength or changes in products (e.g. Applicator Tips) from other manufacturers. Therefore Baxter cannot ensure that products of other manufacturers will function in a satisfactory manner, when used with FLOSEAL.

FLOSEAL may be used up to eight (8) hours after mixing with the Thrombin solution.

Allow 30 seconds after preparation before product is applied to ensure optimal product consistency and performance.

A small amount of clear liquid may be expressed initially from the FLOSEAL syringe.

After use, properly dispose of the FLOSEAL device with tip attached.

5. FLOSEAL Placement/Application

Do not inject FLOSEAL into blood vessels. See the Contraindications, Warnings, Precautions, and Adverse Events sections contained in these Instructions for Use.

For best results, FLOSEAL should be in complete contact with the actively bleeding tissue surface.

6. Application Technique

Identify the source of bleeding at the tissue surface. This is the target site for FLOSEAL application.

Manually approximate a gauze sponge moistened with sterile (non-heparinized) saline against the bleeding surface and use the Applicator tip (or syringe tip) to dispense FLOSEAL between the sponge and the bleeding surface. The gauze sponge will hold FLOSEAL in place against the bleeding surface in the presence of active bleeding. Apply enough FLOSEAL to create a small “mound” of material at the source of bleeding. FLOSEAL may also be applied first onto a moist gauze or cottonoid which is then used to deliver and approximate the material to the source of bleeding.

For tissue defects (“divots” or “craters”), begin applying FLOSEAL at the deepest part of the lesion, and continue applying material as the syringe (or Applicator tip, if used) is withdrawn from the lesion. This “back-filling” action will ensure that FLOSEAL comes into contact with the entire bleeding surface at the tissue defect.

Apply a gauze sponge to approximate the FLOSEAL against the bleeding surface, conforming it to the lesion.

After approximately two minutes, lift the gauze sponge and inspect the wound site. If bleeding has ceased, excess FLOSEAL (not incorporated in the hemostatic clot) should always be removed by gentle irrigation and suctioned from the application site.

To minimize disruption of the clot, remove gauze sponges after hemostasis has been achieved. If the gauze sponge adheres to the newly-formed clot, irrigate the sponge with non-heparinized saline and carefully remove it from the treated site.

In cases of persistent bleeding, indicated by saturation and bleeding through the granules, insert the Applicator tip through the center of the mass of previously placed FLOSEAL to deliver fresh FLOSEAL as close as possible to the tissue surface. After re-application of FLOSEAL, resume approximation with a gauze sponge for up to another two minutes, and then inspect the site again. Repeat re-application if necessary.

Once bleeding has ceased, excess FLOSEAL material not incorporated in the hemostatic clot should always be removed by gentle irrigation and suctioned from the application site. (see “Warnings” section)

Do not disrupt the FLOSEAL-clot complex by physical manipulation. FLOSEAL incorporated in the hemostatic clot should be left *in situ.*

Storage Conditions

The FLOSEAL Kit should be stored at 2 – 25°C.

Do not freeze.

Definition of Symbols

Latex-free

Do not use if package is damaged

Do not inject into blood vessels

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