

Floseal® Hemostatic Matrix

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. Irrigate excess Floseal away gently, so as not to disturb the new clot.

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 with an integral female Luer connector attached, a small bowl, and a 5 mL syringe with needle attached. The mixing 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 Calcium Chloride Solution is a sterile, non-pyrogenic solution. After reconstitution of the lyophilized Thrombin in Calcium 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.

Floseal Hemostatic Matrix Kit Configuration	
Gelatin Matrix Component	Thrombin Component
<ul style="list-style-type: none">• 1 x 5 mL syringe with Gelatin Matrix• 1 x 5 mL syringe with female Luer connector• 1 x bowl for Thrombin solution• Applicator tips (2)	<ul style="list-style-type: none">• 1 x 2,500 IU/vial Human Thrombin VH S/D• 1 x 5 mL vial Calcium Chloride solution<ul style="list-style-type: none">o 200 µmol CaCl₂• 1 x 5 mL syringe with needle attached

The Gelatin Matrix component of Floseal is sterilized by irradiation.

The Thrombin and its Calcium Chloride diluent are processed using aseptic technique, which includes a sterilizing filtration. The thrombin components 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.

Indications

Floseal is indicated in invasive¹ or surgically invasive² procedures as an adjunct to hemostasis when control of bleeding by ligature or conventional procedures is ineffective or impractical.

¹ Invasive means penetration inside the body through a body orifice

² Surgically invasive means penetration inside the body through the surface of the body, with the aid or in the context of a surgical operation.

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.

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 effective on surgical bleeding, from oozing to active.

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

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.

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 approximately 20% of Floseal after product is applied 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 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.

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.

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

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.

When placed into cavities or closed tissue spaces, gentle approximation is advised. When applied to a bleeding site, the particles of Floseal Matrix swell approximately 20% upon contact with blood or other fluids. Maximum swell volume is achieved within about 10 minutes.

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.

Floseal should not be used in conjunction with methylmethacrylate or other acrylic adhesives. Microfibrillar collagen has been reported to reduce the strength of methylmethacrylate adhesives used to attach prosthetic devices to bone surfaces. Do not use Floseal on bone surfaces where adhesives will be required to attach a prosthetic device.

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.

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 vials have been damaged or opened, do not use.

2. Opening the kit

Open the outer package containing the Thrombin component and deliver the sterile inner package 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. Alternatively, the Thrombin solution may be prepared and transferred to the sterile field using aseptic technique.

Open the outer package containing the Gelatin Matrix Component and deliver the sterile inner package to the sterile field. Once placed in the sterile field, the inner package may be opened at any time.

3. Preparing the Thrombin solution

Remove the plastic flip-off cap from the Calcium Chloride diluent vial. Remove the plastic flip-off cap from the Thrombin vial. Using the 5 mL syringe with needle attached, provided in the Thrombin Component package, transfer the 5 mL of Calcium Chloride diluent to the vial containing the Thrombin. Keep the 5 mL syringe with needle attached in the Thrombin vial. Discard the empty Calcium Chloride Solution vial appropriately.

Gently swirl the vial 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 for up to four hours.

Using the syringe, transfer the Thrombin solution from the Thrombin vial to the small bowl provided in the Gelatin Matrix Component package.

4. Mixing the Thrombin Solution into the Gelatin Matrix

An empty 5 mL syringe with a female Luer connector is provided with the Gelatin Matrix Component. Using this syringe, aspirate the Thrombin solution from the small bowl into the syringe to the indicated mark (4 mL).

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 fully 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 **at least 20 passes**.

Ensure the syringe labeled Floseal contains the Floseal Matrix. If desired, connect an Applicator tip to the Floseal syringe. Floseal may also be extruded directly from the syringe.

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 two (2) hours after mixing with the Thrombin solution.

Product consistency may not be optimal if used prior to 30 seconds after preparation. A small amount of clear liquid may be expressed initially from the Floseal syringe.

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.

The particles of Floseal swell approximately 20% upon contact with blood or other fluids. Maximum swell volume is achieved within about 10 minutes.

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.

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.

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. (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.



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Definition of Symbols



Latex-free



Do not use if package is damaged



Do not inject into blood vessels

Floseal is a trademark of Baxter International Inc. Portions of this kit are covered by US Patents #5,209,776, #5,292,362, #6,063,061 and #6,066,325, European Patent #EP0542880B1, and by pending patent applications.

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