

Gelfoam®

(absorbable gelatin sponge, USP)
Gelfoam® Plus Hemostasis Kit

DESCRIPTION

GELFOAM® PLUS is supplied as a ready to use medical device kit containing GELFOAM® Sterile Sponge, Thrombin (Human) dried powder, Saline Solution (0.9% Sodium Chloride Injection USP) and a sterile 10 mL syringe with needle.

GELFOAM Sterile Sponge is a medical device intended for application to bleeding surfaces as a hemostatic agent. It is a water-insoluble, off-white, nonelastic, porous, pliable product prepared from purified porcine skin, Gelatin USP Granules and Water for Injection, USP. It may be cut without fraying and is able to absorb and hold within its interstices many times its weight of blood and other fluids.

Thrombin (Human) is a sterile, non-pyrogenic, freeze-dried, vapor-heated, solvent/detergent-treated powder preparation made from pooled human plasma. The lyophilized Thrombin (Human) is reconstituted with Saline Solution. GELFOAM Sterile Sponge is wetted with a thrombin solution containing **125** units/mL Thrombin (Human) prior to application. *The potency of Thrombin expressed in units is determined using a clotting assay against an internal reference standard for potency that has been calibrated against the World Health Organization (WHO) Second International Standard for Thrombin, 01/580. Therefore, a unit used herein is equivalent to an International Unit.*

Thrombin (Human) is manufactured from pooled Source Plasma obtained from US licensed plasma collection centers. A two-step vapor heating process and an additional solvent/detergent treatment is included in the manufacture of Thrombin. The virus reduction factors (expressed as log₁₀) for Thrombin are presented in Table 1 below. No procedure, however, has been shown to be completely effective in removing viral infectivity from derivatives of human plasma (see WARNINGS).

Table 1: Reduction Factors for Virus Removal and/or Inactivation during the Manufacture of Thrombin (Human)

Manufacturing Step	Mean Reduction Factors [log ₁₀] of Virus Tested				
	Virus Reduction Factor of Virus Tested				
	HIV-1	HAV	BVDV	PRV	MMV
Thrombin Precursor mass capture	3.2	1.5	1.8	2.5	1.2
Vapor Heat Treatment	>5.5	>4.9	>5.3	>6.7	1.0
Solvent/Detergent Treatment	>5.3	n.d.	>5.5	>6.4	n.d.
Ion Exchange Chromatography	n.d.	n.d.	n.d.	n.d.	3.6
Overall Reduction Factor (ORF)	>14.0	>6.4	>12.6	>15.6	5.8

n. d. not determined

ACTION

GELFOAM Sterile Sponge has hemostatic properties. While its mode of action is not fully understood, its effect appears to be more physical than the result of altering the blood clotting mechanism. Collagen hemostatic devices have been used in combination with thrombin to achieve hemostasis. Thrombin (Human) has been shown to enhance the hemostatic properties of Gelfoam Sterile Sponge compared to saline diluent. Thrombin is an enzyme of the blood coagulation system that functions to convert fibrinogen (present in the patient's blood) into an insoluble fibrin clot. Additionally, thrombin promotes clot formation by activating platelets, leading to fibrin binding and aggregation of these cells.

When not used in excessive amounts, GELFOAM Sterile Sponge is absorbed completely, with little tissue reaction. This absorption is dependent on several factors, including the amount used, degree of saturation with blood or other fluids, and the site of use. When placed in soft tissues, GELFOAM Sterile Sponge is usually absorbed completely within four to six weeks, without inducing excessive scar tissue. When applied to bleeding nasal, rectal or vaginal mucosa, it liquefies within two to five days.

INDICATIONS

HEMOSTASIS: GELFOAM PLUS is intended as a hemostatic device for surgical procedures when control of capillary, venous, and arteriolar bleeding by pressure, ligature, and other conventional procedures is either ineffective or impractical.

Thrombin (Human) used without the GELFOAM Sterile Sponge is not indicated for hemostasis.

CONTRAINDICATIONS

GELFOAM PLUS should not be used in closure of skin incisions because it may interfere with healing of the skin edges. This is due to mechanical interposition of gelatin and is not secondary to intrinsic interference with wound healing. GELFOAM PLUS should not be placed in intravascular compartments, because of the risk of embolization.

WARNINGS

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

GELFOAM PLUS contains Thrombin, which is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain virus infections, and by inactivating and removing certain viruses (refer to DESCRIPTION). Despite these measures, such products can still potentially transmit disease. Because this product is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent. ALL infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider. The physician should discuss the risks and benefits of this product with the patient.

The components of GELFOAM PLUS are supplied as a sterile product and cannot be resterilized. If the vials and GELFOAM Sterile Sponge packaging have been opened or damaged, do not use.

The safety and efficacy of GELFOAM PLUS has not been evaluated in controlled clinical trials. The hemostatic properties of GELFOAM PLUS have been evaluated in a swine animal model study. See CLINICAL STUDIES.

The use of GELFOAM PLUS is not recommended in the presence of infection. GELFOAM PLUS should be used with caution in contaminated areas of the body. If signs of infection or abscess develop where Gelfoam Sterile Sponge has been positioned, reoperation may be necessary in order to remove the infected material and allow drainage.

Only the minimum amount of GELFOAM Sterile Sponge necessary to achieve hemostasis should be used. Once hemostasis is attained, excess GELFOAM Sterile Sponge should be carefully removed.

While packing a cavity for hemostasis is sometimes surgically indicated, GELFOAM Sterile Sponge should not be used in this manner unless excess product not needed to maintain hemostasis is removed.

Whenever possible, GELFOAM Sterile Sponge should be removed after use in laminectomy procedures and from foramina in bone, once hemostasis is achieved. This is because GELFOAM Sterile Sponge may swell to its original size on absorbing fluids, and produce nerve damage by pressure within confined bony spaces.

The packing or wadding of GELFOAM Sterile Sponge, particularly within bony cavities, should be avoided, since swelling to original size may interfere with normal function and/or possibly result in compression necrosis of surrounding tissues.

PRECAUTIONS

Use only the minimum amount of GELFOAM Sterile Sponge needed for hemostasis, holding it at the site until bleeding stops, then removing the excess.

Since thrombin can be denatured by contact with solutions containing alcohol, iodine or heavy metal ions, GELFOAM PLUS should not be applied before the wound surface is cleaned to remove any antiseptics that may contain such substances.

GELFOAM PLUS should **not** be used for controlling postpartum hemorrhage or menorrhagia. It has been demonstrated that fragments of another hemostatic agent, microfibrillar collagen, pass through the 40µ transfusion filters of blood scavenging systems.

GELFOAM PLUS should not be used in conjunction with autologous blood salvage circuits since the safety of this use has not been evaluated in controlled clinical trials.

Microfibrillar collagen has been reported to reduce the strength of methylmethacrylate adhesives used to attach prosthetic devices to bone surfaces. As a precaution, GELFOAM PLUS should not be used in conjunction with such adhesives.

GELFOAM PLUS is not recommended for the primary treatment of coagulation disorders.

It is not recommended that GELFOAM PLUS be saturated with an antibiotic solution or dusted with antibiotic powder.

GELFOAM PLUS contains Thrombin made from human plasma. Some viruses, such as parvovirus B19, are particularly difficult to remove or inactivate at this time. Parvovirus B19 most seriously affects pregnant women, or immune-compromised individuals. Symptoms of parvovirus B19 infection include fever, drowsiness, chills, and runny nose followed about two weeks later by a rash, and joint pain. Patients should be encouraged to consult their physician if such symptoms appear.

ADVERSE REACTIONS

GELFOAM SPONGE: Adverse Reactions

There have been reports of fever associated with the use of GELFOAM Sterile Sponge, without demonstrable infection. GELFOAM Sterile Sponge may serve as a nidus for infection and abscess formation¹, and has been reported to potentiate bacterial growth. Giantcell granuloma has been reported at the implantation site of absorbable gelatin product in the brain², as has compression of the brain and spinal cord resulting from the accumulation of sterile fluid.³ Foreign body reactions, "encapsulation" of fluid and hematoma have also been reported.

When GELFOAM Sterile Sponge was used in laminectomy operations, multiple neurologic events were reported, including but not limited to cauda equina syndrome, spinal stenosis, meningitis, arachnoiditis, headaches, paresthesias, pain, bladder and bowel dysfunction, and impotence.

Excessive fibrosis and prolonged fixation of a tendon have been reported when absorbable gelatin products were used in severed tendon repair. Toxic shock syndrome has been reported in association with the use of GELFOAM Sterile Sponge in nasal surgery. Fever, failure of absorption, and hearing loss have been reported in association with the use of GELFOAM Sterile Sponge during tympanoplasty.

Thrombin: Adverse Reactions

As with any other plasma derivatives, anaphylactoid or anaphylactic reactions may occur in rare cases. No adverse events of this type were reported during the course of clinical trials using fibrin sealant containing the same human thrombin component. Mild reactions can be managed with antihistamines; severe hypotensive reactions require immediate intervention using current principles of shock therapy.

ADVERSE REACTIONS REPORTED FROM UNAPPROVED USES

GELFOAM PLUS is not recommended for use other than as an adjunct for hemostasis. While some adverse medical events following the unapproved use of GELFOAM have been reported (see ADVERSE REACTIONS), other hazards associated with such use may not have been reported. When GELFOAM has been used during intravascular catheterization for the purpose of producing vessel occlusion, the following adverse events have been reported; fever, duodenal and pancreatic infarct, embolization of lower extremity vessels, pulmonary embolization, splenic abscess, necrosis of specific anatomic areas, asterixis, and death. These adverse medical events have been associated with the use of GELFOAM Sterile Sponge for repair of dural defects encountered during laminectomy and craniotomy operations: fever, infection, leg paresthesias, neck and back pain, bladder and bowel incontinence, cauda equina syndrome, neurogenic bladder, impotence, and paresis.

CLINICAL STUDIES

GELFOAM Sterile Sponge is a water-insoluble, hemostatic device prepared from purified porcine skin gelatin, and capable of absorbing up to 45 times its weight of whole blood.⁴

The absorptive capacity of GELFOAM is a function of its physical size, increasing as the size of the gelatin sponge increases.⁵ The mechanism of action of surface-mediated hemostatic devices is supportive and mechanical.⁵ Surface-acting devices, when applied directly to bleeding surfaces, arrest bleeding by the formation of an artificial clot and by producing a mechanical matrix that facilitates clotting.⁶ Jenkins et al⁷ have theorized that the clotting effect of GELFOAM may be due to release of thromboplastin from platelets, occurring when platelets entering the sponge become damaged by contact with the walls of its myriad of interstices. Thromboplastin interacts with prothrombin and calcium to produce thrombin, and this sequence of events initiates the clotting reaction. The authors suggest that the physiologic formation of thrombin in the sponge is sufficient to produce formation of a clot, by its action on the fibrinogen in blood.⁷ The sponge's physical properties of the gelatin sponge hasten clot formation and provide structural support for the forming clot.⁸ Several investigators have claimed that GELFOAM becomes liquefied within a week or less and is completely absorbed in four to six weeks, without inducing excessive scar formation.^{9,10,11} Barnes⁹ reviewed experiences with GELFOAM in gynecologic surgery. No excessive scar tissue, attributable to the absorption of GELFOAM, could be palpated at postoperative examination.

ANIMAL PHARMACOLOGY

Surface-acting hemostatic devices, when applied directly to bleeding surfaces, arrest bleeding by providing a mechanical matrix that facilitates clotting.^{6,8,13,14} Due to their bulk, surface-acting hemostatic agents slow the flow of blood, protect the forming clot, and offer a framework for deposition of the cellular elements of blood.^{6,7,8,13} MacDonald and Mathews¹⁵ studied GELFOAM implants in canine kidneys and reported that it assisted in healing, with no marked inflammatory or foreign-body reactions. Jenkins and Janda¹³ studied the use of GELFOAM in canine liver resections and noted that the gelatin sponge appeared to offer a protective cover and provide structural support for the reparative process. Correll et al¹⁴ studied the histology of GELFOAM Sterile Sponge when implanted in rat muscle and reported no significant tissue reaction.

ANIMAL STUDY

An animal study was performed to evaluate the efficacy of Gelfoam Plus containing vapor heated and solvent/detergent treated (VH S/D) human thrombin compared to Gelfoam and saline using the porcine liver abrasion model (data provided in Table 2 below). Treatment effect was evaluated using multiple logistic regression models based on percent success on bleeding scores where success was a bleeding score less than 3 (Scores of 0, 1, 2, 3, 4, and 5 were assigned to no bleeding, ooze, very mild, mild, moderate, and severe; respectively¹⁶). Based on these results, the confidence intervals of human thrombin VH S/D versus Saline odds ratios at 9 and 12 minutes post treatment were greater than 1.0, showing human thrombin VH S/D as superior to Saline at 9 and 12 minutes. Based on the results of the bleeding score model, the confidence intervals of human thrombin VH S/D versus Saline odds ratios at 3, 6, 9, and 12 minutes post treatment were greater than 1.0, showing human thrombin VH S/D as more effective than Saline.

Table 2: Results of 2x2 Frequencies at Each Time Point Post-treatment for Each Gelfoam Preparation (n=40 per group)

Minute	Treatment	Success (Score<=2) Frequency	Failure (Score>2) Frequency	Success %
3	Gelfoam + Saline	39	1	97.5
	Gelfoam + Human Thrombin VH S/D in Saline	39	1	97.5
6	Gelfoam + Saline	33	7	82.5
	Gelfoam + Human Thrombin VH S/D in Saline	38	2	95.0
9	Gelfoam + Saline	25	15	62.5
	Gelfoam + Human Thrombin VH S/D in Saline	39	1	97.5
12	Gelfoam + Saline	21	19	52.5
	Gelfoam + Human Thrombin VH S/D in Saline	39	1	97.5

Thrombin has been demonstrated to have a significant effect on time to hemostasis at identical time points relative to saline in a separate model.¹⁶

Gelfoam with human thrombin was shown to be more effective than Gelfoam and saline.

DOSAGE AND ADMINISTRATION

Sterile technique should always be used in removing the inner envelope containing the GELFOAM Sterile Sponge from the outer printed sealed envelope and during reconstitution of the Thrombin (Human). The minimum amount of GELFOAM PLUS of appropriate size and shape should be applied to the bleeding site and held firmly in place until hemostasis is observed. Opened envelopes of unused GELFOAM Sterile Sponge should always be discarded.

DIRECTIONS FOR USE GELFOAM PLUS Preparation:

1. Open the GELFOAM PLUS kit box outside the sterile field.
2. Inspect the integrity of the contents of the Gelfoam Sponge package. If the packaging, Gelfoam, vials or packaged syringe with needle have been damaged or opened, do not use.
3. Open the outer GELFOAM Sponge package and deliver the sterile inner package to the sterile field. Once placed on the operating field, the inner package may be opened at any time.
4. Reconstitute the Thrombin with Saline Solution aseptically as described below prior to transferring the solution to the sterile field.

GELFOAM PLUS

Preparing the Thrombin Solution

5. Remove the plastic flip-off caps from the sodium chloride solution vials. Remove the plastic flip-off cap from the Thrombin (Human) vial. Disinfect the rubber stoppers of all vials with a germicidal solution and allow to dry. Do not use iodine-containing preparations such as betadine for disinfection.
6. Using the 10 mL syringe with needle attached, withdraw contents of the 1st sodium chloride vial and gently transfer 5 mL of solution into the thrombin vial by dispensing into a small dish. Transfer the remaining 5 mL into the vial containing the lyophilized thrombin. Keep the 10 mL syringe with needle attached in the thrombin vial. Discard the empty sodium chloride solution vial appropriately.
7. Gently swirl the Thrombin (Human) vials until the Thrombin is completely dissolved. Once reconstituted, the Thrombin solution is ready for use. The solution may be used up to 4 hours after reconstitution.
8. Aspirate the Thrombin solution into the syringe. Transfer the Thrombin solution into the sterile field by dispensing into the same dish. Using the 10 mL syringe with needle attached, withdraw contents of 2nd sodium chloride vial and gently transfer all 10 mL of solution into the sterile field by dispensing it into the dish. Discard the empty thrombin vial, sodium chloride vial and 10 mL syringe with needle attached appropriately.

GELFOAM Sterile Sponge Wetting and Application Technique:

Note: Sterile technique should always be used to remove GELFOAM Sterile Sponge from its packaging.

9. Cut sponge to the desired size.
10. Immerse cut sponge in the Thrombin solution and then withdraw, squeeze between gloved fingers to expel air bubbles, and then replace in the thrombin solution until needed. The GELFOAM Sponge should promptly return to its original size and shape in the solution. If it does not, it should be removed again and kneaded vigorously until all air is expelled and it does expand to its original size and shape when returned to the Thrombin solution.
11. Use GELFOAM PLUS wet or blotted to dampness on gauze before application to the bleeding site.

Note: The GELFOAM PLUS should be held in place with moderate pressure, using a pledget of cotton or small gauze sponge which will absorb any excess. Removal of the pledget or gauze is made easier by wetting it with a few drops of sterile saline, to prevent pulling up the GELFOAM PLUS which by then should enclose a firm clot.

Use of suction applied over the pledget of cotton or gauze to draw blood into the GELFOAM PLUS is unnecessary, as the GELFOAM PLUS will draw up sufficient blood by capillary action.

The first application of GELFOAM PLUS will usually control bleeding, but if not, additional applications may be made using fresh pieces, prepared as described above.

Use only the minimum amount of GELFOAM PLUS, cut to appropriate size, necessary to produce hemostasis. The GELFOAM PLUS may be left in place at the bleeding site, when necessary.

Since GELFOAM Sponge causes little more cellular reaction than does the blood clot, the wound may be closed over it. GELFOAM PLUS may be left in place when applied to mucosal surfaces until it liquefies.

HOW SUPPLIED

GELFOAM PLUS is supplied as follows:

- 1 x sterile sponge size 100, enclosed in an outer peelable envelope
- 1 x vial, Thrombin (Human), Vapor Heated, Solvent/Detergent Treated, 2500 units
- 2 x vials, 0.9% Sodium Chloride Injection USP (Preservative free) - 10 mL each
- 1 x 10 mL sterile syringe with needle attached

STORAGE AND HANDLING

Store GELFOAM PLUS at 15-25°C (59-77°F). If individual components of the GELFOAM PLUS are removed from the packaging prior to use, store components according to individual conditions specified on the label.

Individual components of the GELFOAM PLUS are sterile. Inspect contents of the GELFOAM PLUS prior to use. If the GELFOAM Sponge packaging or vials have been damaged or opened, do not use. Sterility of the sponge is assured unless the outer envelope has been damaged or opened.

Caution: Federal law restricts this device to sale by or on the order of a physician.

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