GEL-FLOW™ KIT 6 mL

GEL-FLOW™ NT Absorbable Gelatin Powder and Thrombin, Topical (Bovine) U.S.P., Thrombin-JMI®, 5,000 International Units Syringe Spray Kit

GEL-FLOW™ NT 6 mL

Absorbable Gelatin Powder
Hemostatic Matrix for Flowable Applications

A hemostatic standard of care,[1-7] in a flowable

GEL-FLOW is a topical hemostat in a versatile, flowable configuration, giving the flexibility needed in purchasing, preparation, and delivery.[1,3,5,8]

This image illustrates GEL-FLOW NT, which was prepared following the preparation instructions per label, using 5 mL of either thrombin solution or a sterile diluent. Thrombin and/or sterile saline solution is not included with GEL-FLOW NT.[8]

Image does *not* represent the actual size of product.

INDICATION FOR GEL-FLOW NT

GEL-FLOW NT is indicated in surgical procedures, including those involving cancellous bone bleeding, as a hemostatic device, when control of capillary, venous, and arteriolar bleeding by pressure, ligature, and other conventional procedures is either ineffective or impractical. Although not necessary, GEL-FLOW NT can be used either with or without thrombin to obtain hemostasis.

SELECTED SAFETY INFORMATION FOR GEL-FLOW NT

GEL-FLOW NT 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.

GEL-FLOW NT must not be placed in intravascular compartments because of the risk of embolization.

(continued on page 2)

INDICATION FOR THROMBIN-JMI

THROMBIN-JMI is topical bovine thrombin indicated to aid 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.

In various types of surgeries, solutions of THROMBIN-JMI may be used in conjunction with an Absorbable Gelatin Sponge, USP for hemostasis.

SELECTED SAFETY INFORMATION FOR THROMBIN-JMI

WARNING: SEVERE BLEEDING AND THROMBOSIS COMPLICATIONS

- **THROMBIN-JMI can cause fatal severe bleeding or thrombosis. Thrombosis may result from the development of antibodies against bovine thrombin. Bleeding may result from the development of antibodies against factor V. These may cross-react with human factor V and lead to its deficiency.**
- **Do not re-expose patients to THROMBIN-JMI if there are known or suspected antibodies to bovine thrombin and/or factor V.**
- **Monitor patients for abnormal coagulation laboratory values, bleeding, or thrombosis.**

- Do not inject directly into the circulatory system. Because of its action in the clotting mechanism, THROMBIN-JMI can cause extensive intravascular clotting or death.
- Do not re-expose patients to THROMBIN-JMI if there are known or suspected antibodies to bovine thrombin and/or factor V.
- Do not administer to patients with a history of hypersensitivity to THROMBIN-JMI, its components and/or to material of bovine origin.
- Do not use for treatment of severe or brisk arterial bleeding.

(continued on page 2)

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT. Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

Pfizer

GEL-FLOW™ KIT 6 mL

GEL-FLOW™ NT Absorbable Gelatin Powder and Thrombin, Topical (Bovine) U.S.P., Thrombin-JMI®, 5,000 International Units Syringe Spray Kit

Next generation of GELFOAM® (absorbable gelatin powder from absorbable gelatin sponge, USP) and THROMBIN-JMI

This image illustrates GEL-FLOW NT, which was prepared following the preparation instructions per label, using 5 mL of either thrombin solution or a sterile diluent. Thrombin and/or sterile saline solution is not included with GEL-FLOW NT.[8]

Provides variable viscosity levels based on surgical need[8]

Delivers 5,000 IU of thrombin in final, flowable mixture[9]

Allows complete sterile field preparation[8,9]

GEL-FLOW™ NT 6 mL

Absorbable Gelatin Powder
Hemostatic Matrix for Flowable Applications

GEL-FLOW NT is a prefilled sterile syringe containing 550 mg of absorbable gelatin powder that is specifically designed[8]:

- To form a **versatile flowable** for use in surgical procedures, including those involving cancellous bone bleeding, as a hemostatic device, when control of capillary, venous, and arteriolar bleeding by pressure, ligature, and other conventional procedures is either ineffective or impractical[8]
- To be **prepared directly within the syringe** by mixing with thrombin solution or sterile saline from another syringe[8]
- With **two attached applicator tips for delivery to deep and narrow administration sites**[8]
- For single use only[8]

SELECTED SAFETY INFORMATION FOR GEL-FLOW NT (continued)

Do not use GEL-FLOW NT in patients with known allergies to porcine collagen.

Life-threatening anaphylactic reactions, including death, have been reported after exposure to absorbable gelatin. Patients with history of allergies to porcine products may be at risk of serious acute hypersensitivity reactions, including anaphylaxis. If an anaphylactic reaction is observed, absorbable gelatin administration should be immediately discontinued and any applied product removed.

SELECTED SAFETY INFORMATION FOR THROMBIN-JMI (continued)

- Allergic reactions, including anaphylactic/anaphylactoid reactions, have been reported following administration of THROMBIN-JMI.
- Institute intensive supportive measures and treat individual symptoms. Secure the airway and establish adequate respiratory exchange.

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

Safety and immunogenicity

THROMBIN-JMI is a biologically active hemostatic agent that works directly at the end of the coagulation cascade[9-11]

- Studies comparing THROMBIN-JMI with human thrombin and recombinant human thrombin (rhThrombin) demonstrated similar safety profiles regarding treatment-related adverse events. Increased development of antibodies to bovine thrombin and bovine factor V did occur in patients treated with THROMBIN-JMI[1,3,5]
- GEL-FLOW™ Kit (GEL-FLOW™ NT Absorbable Gelatin Powder and Thrombin, Topical [Bovine] U.S.P., Thrombin -JMI®, 5,000 International Units Syringe Spray Kit) contains a 5,000 IU THROMBIN-JMI vial, a 5 mL vial of diluent, a sterile transfer device, a sterile disposable luer-lock syringe, and a spray tip in a sterile inner tray[9]

THROMBIN-JMI safety

The safety of THROMBIN-JMI was evaluated in multiple clinical trials[1,3,5,9,12]

- The most common adverse reactions (incidence ≥2%) were hypersensitivity, bleeding, anemia, postoperative wound infection, thromboembolic events, hypotension, pyrexia, tachycardia, and thrombocytopenia[9]
- In the 2006 study, no serious adverse reactions related to the gel treatment were reported[9,12]
- In the 2007 study, the reported adverse reactions in the THROMBIN-JMI treatment group were: cardiac events (18%), hypersensitivity (17%), other infections (15%), bleeding (11%), postoperative wound infection (10%), and thromboembolic events (5%). The safety profiles for rhThrombin and bovine thrombin were similar[3,9]
- In the 2008 study, serious adverse reactions (pyrexia and post-procedural hematoma) were reported in 2 patients receiving THROMBIN-JMI. The safety profiles for human thrombin and bovine thrombin were comparable[1,9]
- In the 2019 study, the most common treatment-emergent adverse reactions (experienced by >5% of patients within a treatment group) were procedural pain, nausea, constipation, pruritus, muscle spasms, insomnia, pyrexia, and vomiting. No substantial differences in treatment-emergent adverse events incidences were noted between treatment groups[5,9]

The effect of repeat exposure was evaluated in a 2006 multicenter, prospective, randomized, double-blinded, controlled trial on 72 patients with diabetic foot ulcers, using a gel prepared with THROMBIN-JMI and autologous platelet rich plasma that was applied weekly for 12 weeks. There were 40 patients treated with the gel at 14 sites. Safety parameters were evaluated during the 12 weeks of treatment and the 3-month follow-up period.[9,12]

In the 2007 randomized, double-blind, controlled trial that compared rhThrombin to THROMBIN-JMI, 206 patients received THROMBIN-JMI and 205 patients received rhThrombin as adjuncts to hemostasis in liver resection, spine, peripheral arterial bypass, and dialysis access surgeries. There were 401 patients who completed the trial.[3,9]

In the 2008 multicenter, prospective, randomized, double-blinded, controlled trial that compared plasma-derived human thrombin to THROMBIN-JMI, 152 patients received THROMBIN-JMI and 153 patients received human thrombin applied topically to the target bleeding site with a gelatin sponge.[1,9]

In a 2019 prospective, randomized, phase 2, noninferiority study, topical human thrombin was compared with THROMBIN-JMI during vascular, hepatic, soft tissue, and spinal open surgery procedures. A total of 205 patients were randomized in a 2:1 ratio to receive human thrombin (n=137) or THROMBIN-JMI (n=68).[5,9]

SELECTED SAFETY INFORMATION FOR GEL-FLOW NT (continued)

GEL-FLOW NT is not intended as a substitute for meticulous surgical technique and the proper application of ligatures, or other conventional procedures for hemostasis.

Unused, opened GEL-FLOW NT syringes or packs must be discarded. GEL-FLOW NT must not be resterilized.

SELECTED SAFETY INFORMATION FOR THROMBIN-JMI (continued)

- THROMBIN-JMI causes thrombosis if it enters the circulatory system. Apply topically. DO NOT INJECT.
- Inhibitory antibodies may develop in patients and interfere with hemostasis. Monitor patients for abnormal coagulation laboratory values, bleeding, or thrombosis.

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

THROMBIN-JMI®
Thrombin, Topical (Bovine) U.S.P.

Immunogenicity

Inhibitory antibodies may develop in patients and interfere with hemostasis. Monitor patients for abnormal coagulation laboratory values, bleeding, or thrombosis[9]

2007 STUDY — In the 2007 study, 5% of patients (10 out of 200) who received THROMBIN-JMI were positive at baseline for the presence of antibodies and 21.5% (43 out of 200) were positive after treatment[3,9]

2008 STUDY — In the 2008 study, 12.7% of patients (16 out of 126) who received THROMBIN-JMI demonstrated seroconversion for at least one of the four antibodies assayed[1,9]

2019 STUDY — In the 2019 study, 3.2% of patients (2 out of 61) who received THROMBIN-JMI showed low-level titers of antibodies to bovine factor V with no clinical relevance[5,9]

The percentages above are incomparable due to differences in study data.

The THROMBIN-JMI® (Thrombin, Topical [Bovine] U.S.P.) manufacturing process

THROMBIN-JMI has been chromatographically purified and further processed by ultrafiltration.[9]

THROMBIN-JMI undergoes multistep chromatographic purification and ultrafiltration. The manufacturing process for THROMBIN-JMI has been further improved by the addition of viral filtration and impurity reduction processes. Analytical studies demonstrate the capability of the current manufacturing process to remove significant amounts of extraneous proteins, and result in a reduction of factor Va light chain content to levels below the limit of detection of semi-quantitative Western Blot assay (<92 ng/mL, when reconstituted as directed). The clinical relevance of these findings is unknown.[9]

SELECTED SAFETY INFORMATION FOR GEL-FLOW NT (Absorbable Gelatin Powder) (continued)

Only the minimum amount of GEL-FLOW NT mixture necessary to achieve hemostasis should be used and applied to the bleeding site with pressure until bleeding stops. Once hemostasis is attained, excess GEL-FLOW NT mixture should be carefully removed.

The use of GEL-FLOW NT is not recommended in the presence of infection. GEL-FLOW NT should be used with caution in contaminated areas of the body.

SELECTED SAFETY INFORMATION FOR THROMBIN-JMI (continued)

Most common adverse reactions (incidence greater than or equal to 2%) are hypersensitivity, bleeding, anemia, post-operative wound infection, thromboembolic events, hypotension, pyrexia, tachycardia and thrombocytopenia. Advise patients to consult their physician if they experience leg tenderness or swelling, chest pain, shortness of breath, or difficulty speaking or swallowing.

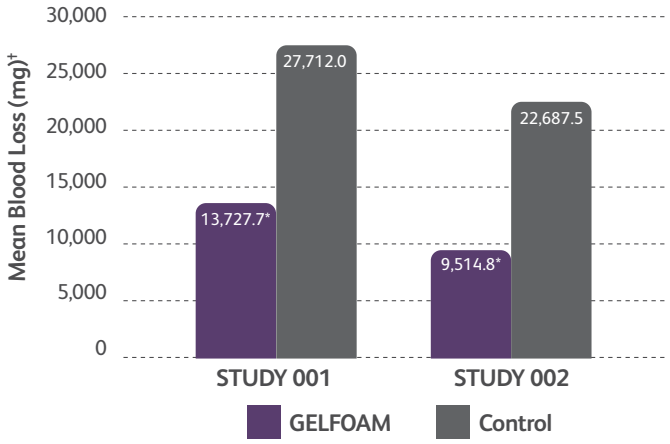
Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

Studies have shown that absorbable gelatin powder is an effective hemostatic agent[8]

Clinical studies have shown the efficacy of GELFOAM® Sterile Powder (absorbable gelatin powder), the absorbable gelatin powder contained in GEL-FLOW NT, as a hemostatic agent for intraoperative sternal bone bleeding in cardiopulmonary bypass surgery.[8]

- **The most frequently reported events during the study with GELFOAM Sterile Powder versus the control group were atrial fibrillation (13% vs 11% of all patients), wound infection (6% vs 1% of all patients), and perioperative event (4% vs 5% of all patients)[8]**
- **Normal bone healing was similar (97% of all patients) for GELFOAM and control groups at hospital discharge; at the 3-month follow-up, 95% of all patients in the GELFOAM group and 93% of all patients in the control group were healed[8]**

GELFOAM has shown superior hemostasis vs saline treatment to the cut sternal bone surface of evaluable patients[8]



*P-value <0.001, which demonstrates statistical significance.
†Total (during and after surgery) blood loss over 72 hours.

ADVERSE EVENTS[8]	GELFOAM (n=108)	CONTROL (n=107)
Atrial fibrillation	14 (13%)	12 (11%)
Wound infection	6 (6%)	1 (1%)
Perioperative event	4 (4%)	5 (5%)

Data from two open-label, controlled clinical studies conducted at separate investigation sites in patients 18 to 74 years of age who were undergoing cardiopulmonary bypass surgery and receiving the absorbable gelatin powder application (n=108, all patients) or no treatment (n=107, all patients) to the cut sternal surface immediately following sternotomy. Study objectives were to evaluate the effectiveness of GELFOAM Sterile Powder to help control sternal bone bleeding during cardiopulmonary bypass surgery, determine whether GELFOAM Sterile Powder interfered with bone healing, and identify any systemic or local wound side effects from leaving GELFOAM Sterile Powder *in situ*. Blood loss was monitored during and 72 hours after surgery.[8]

SELECTED SAFETY INFORMATION FOR GEL-FLOW NT (continued)

The packing of GEL-FLOW NT, particularly within bony cavities, should be avoided, since swelling may interfere with normal function and/or possibly result in compression necrosis of surrounding tissues.

SELECTED SAFETY INFORMATION FOR THROMBIN-JMI® (Thrombin, Topical [Bovine] U.S.P.) (continued)

There is no human or animal data regarding use during pregnancy. It is also not known whether THROMBIN-JMI can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. THROMBIN-JMI should be given to a pregnant woman only if clearly needed.

Safety and effectiveness in children have not been established.

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

In preclinical study data, using higher concentrations of thrombin with absorbable gelatin powder yielded improved hemostasis[13]

In a randomized, controlled, blinded, *in vivo*, preclinical study conducted on a liver lesion model in swine, an inverse dose-related response was observed between the thrombin concentration within the GEL-FLOW™ NT (Absorbable Gelatin Powder) syringe and the visual bleeding scores. GEL-FLOW NT was reconstituted to a flowable mixture of 7 mL of total volume by mixing the GEL-FLOW NT powder with 5 mL of one of three solutions of varying thrombin concentrations to result in final thrombin concentrations of 250 IU/mL, 375 IU/mL, and 770 IU/mL in the flowable.[8,13]

Correlations cannot be made to clinical outcomes

THROMBIN-JMI® (Thrombin, Topical [Bovine] U.S.P.) was used for all thrombin concentrations tested in this study[8,9,13]

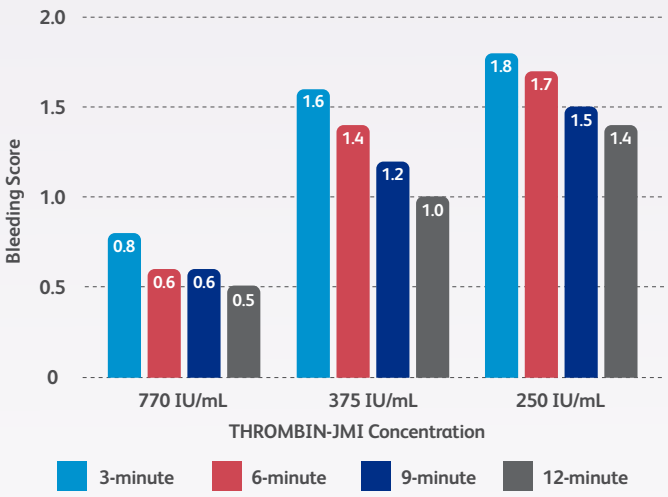
The 770 IU/mL thrombin concentration provided statistically lower bleeding scores than either 375 IU/mL or 250 IU/mL thrombin concentrations.[8,13,*]

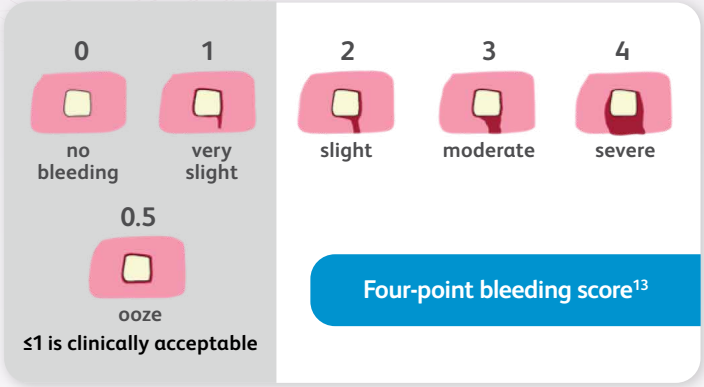
At least 770 IU/mL thrombin concentration is obtained when GEL-FLOW NT is prepared with THROMBIN-JMI following the instructions in the GEL-FLOW NT package insert; 375 IU/mL and 250 IU/mL concentrations for thrombin are lower than the recommended doses for THROMBIN-JMI. For recommended doses for THROMBIN-JMI, please consult the complete Prescribing Information.[8,9]

In another preclinical study using absorbable gelatin along with thrombin, there was a significant difference in bleeding scores at both the 3- and 6-minute mark (P<0.001 for both), compared with just using absorbable gelatin alone.[14]

*Per the THROMBIN-JMI Prescribing Information, for routine use, THROMBIN-JMI is reconstituted with sterile isotonic saline at a recommended concentration of 1,000 to 2,000 international units per mL.[8,9]

An inverse dose-related clinical response was observed with different concentrations of THROMBIN-JMI in GEL-FLOW NT[13]





Bleeding scores were measured at 3, 6, 9, and 12 minutes according to a visual scale (see table above), with scores of 0 (no bleeding), 0.5 (ooze), 1 (very slight), 2 (slight), 3 (moderate), and 4 (severe). Scores of ≤1 were considered clinically acceptable.[8,9,13]

SELECTED SAFETY INFORMATION FOR GEL-FLOW NT (continued)

Whenever possible, GEL-FLOW NT should be removed after use in laminectomy procedures and from foramina in bone, once hemostasis is achieved. This is because GEL-FLOW NT may swell on absorbing fluids and produce nerve damage by pressure within confined bony spaces.

SELECTED SAFETY INFORMATION FOR THROMBIN-JMI

WARNING: SEVERE BLEEDING AND THROMBOSIS COMPLICATIONS

- **THROMBIN-JMI can cause fatal severe bleeding or thrombosis. Thrombosis may result from the development of antibodies against bovine thrombin. Bleeding may result from the development of antibodies against factor V. These may cross-react with human factor V and lead to its deficiency.**
- **Do not re-expose patients to THROMBIN-JMI if there are known or suspected antibodies to bovine thrombin and/or factor V.**
- **Monitor patients for abnormal coagulation laboratory values, bleeding, or thrombosis.**

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

Correlations cannot be made to clinical outcomes

In a preclinical study, the addition of thrombin to absorbable gelatin powder provided superior control of bleeding versus absorbable gelatin powder alone[14]

In a randomized, controlled, preclinical study, four swine underwent open laparotomy after receiving unfractionated heparin. Twenty biopsies were performed on each swine; 10 biopsies treated with GELFOAM® (absorbable gelatin powder) + human thrombin solution, and 10 biopsies treated with GELFOAM + saline solution. Bleeding was objectively scored by using a four-point model at the 3-, 6-, 9-, and 12-minute mark.[14]

- **The control group (absorbable gelatin powder + 0.9% saline solution) was compared with the treatment group (absorbable gelatin powder + 125 IU/mL human thrombin solution)[14]**
- **At the 3-minute mark, 52.5% of the control group vs 92.5% of the treatment group were able to maintain hemostasis; 52.5% of the control group vs 95% of the treatment group were able to maintain hemostasis at the 6-minute mark[14]**
- **By minute 12, 97.5% of the treatment group were able to maintain hemostasis versus 72.5% in the control group[14]**

SELECTED SAFETY INFORMATION FOR GEL-FLOW NT™ (Absorbable Gelatin Powder) (continued)

GELFOAM should not be placed in the vicinity of the cerebral ventricular space or where there is a possibility of a cerebrospinal fluid fistula to the target bleeding site. GELFOAM should also not be used as a tissue substitute to repair tissue defects of the dura or the cranium. GELFOAM may migrate from central nervous system cerebrospinal fluid surgical sites into the cerebral ventricular space and compromise the cerebrospinal fluid circulation. Hydrocephalus and cerebrospinal fluid retention, requiring a re-intervention to remove GELFOAM residue, have been reported in adult and pediatric patients. In some cases, these complications occurred several months after use of GELFOAM.

SELECTED SAFETY INFORMATION FOR THROMBIN-JMI® (Thrombin, Topical [Bovine] U.S.P.) (continued)

- Do not inject directly into the circulatory system. Because of its action in the clotting mechanism, THROMBIN-JMI can cause extensive intravascular clotting or death.
- Do not re-expose patients to THROMBIN-JMI if there are known or suspected antibodies to bovine thrombin and/or factor V.
- Do not administer to patients with a history of hypersensitivity to THROMBIN-JMI, its components and/or to material of bovine origin.
- Do not use for treatment of severe or brisk arterial bleeding.

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

Product preparation[9]

5,000 IU SYRINGE SPRAY KIT *WITH GEL-FLOW™ NT (Absorbable Gelatin Powder)*

For preparation entirely within the sterile field.

For Topical use on the surface of bleeding tissue only.

- Do not inject directly into the circulatory system. Because of its action in the clotting mechanism, THROMBIN-JMI can cause extensive intravascular clotting or death.
- Do not re-expose patients to THROMBIN-JMI if there are known or suspected antibodies to bovine thrombin and/or factor V.
- Do not administer to patients with a history of hypersensitivity to THROMBIN-JMI, its components and/or to material of bovine origin.
- Do not use for treatment of severe or brisk arterial bleeding.

1. Remove the outer lid by pulling up at the indicated edge. The inner tray is sterile and suitable for introduction into any operating field.

2. Remove the cover on the inner tray to expose the sterile contents.

3. Using the sterile syringe equipped with a transfer device, draw all of the 5 mL of the saline diluent from the vial into the syringe.

4. Inject the saline diluent into the THROMBIN-JMI thrombin vial from the syringe to reconstitute the THROMBIN-JMI thrombin powder.
5. When the THROMBIN-JMI thrombin powder is completely dissolved, draw the THROMBIN-JMI thrombin solution into the syringe.

TIP: Place the thrombin vial on a flat surface, and inject the diluent straight down into the thrombin vial.

6. Remove the syringe from the transfer device by turning syringe counterclockwise.
7. DISCARD the SPRAY TIP.

8. Use the THROMBIN-JMI thrombin solution syringe according to the directions for use in the GEL-FLOW NT package insert.

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

Product preparation[8]

Directions for use

GEL-FLOW NT **must be saturated** with sterile saline or thrombin* solution before use as an adjunct to hemostasis. Prior to GEL-FLOW NT application, the target bleeding site should be visualized if feasible. GEL-FLOW NT is provided as 550 mg GELFOAM® Sterile Powder (absorbable gelatin powder) pre-packaged in a 10 mL syringe for hydration. Use only the minimum amount of GEL-FLOW NT mixture necessary to produce hemostasis.

Always use sterile technique when handling GEL-FLOW NT.

Before Use: Inspect the GEL-FLOW NT package for signs of damage. DO NOT use if the package is damaged. Open the package and remove the GEL-FLOW NT syringe.

Preparing GEL-FLOW NT: GEL-FLOW NT may be prepared to desired consistency (by adjusting the volume of saline or thrombin solution used for hydration) up to 3 hours prior to application using standard sterile technique. Following the instructions below will yield an average of 7 mL of uniform mixture within the syringe, with a measured minimum delivery volume of 6 mL.

1-2

1. Draw up 5 mL of sterile saline or thrombin† solution into an empty 10 mL sterile syringe with luer lock (diluent and syringe not included).
2. Connect the GEL-FLOW NT syringe to the sterile saline or thrombin solution syringe via the pre-attached connecting luer.

3-4

3. To begin mixing, swiftly push at once the entire volume of the sterile saline or thrombin solution into the GEL-FLOW NT syringe.
4. Wait 10-15 seconds to allow the gelatin powder to become saturated with the sterile saline or thrombin solution.

5-6

5. Push the saturated gelatin powder back into the sterile saline or thrombin solution syringe.
6. Continue exchanging the solution between syringes until all components are thoroughly mixed (approximately 10 complete two-way exchanges) and the consistency is even. If at any point the mixture does not appear uniform, perform additional exchanges between syringes to ensure contents are adequately mixed and the resulting mixture looks homogenous.

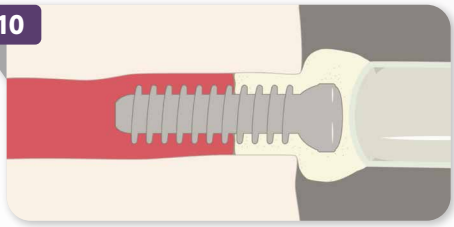
7-8

7. Disconnect the mixing syringe containing the GEL-FLOW NT mixture and remove connecting luer.
8. GEL-FLOW NT may be dispensed directly from the syringe.

9

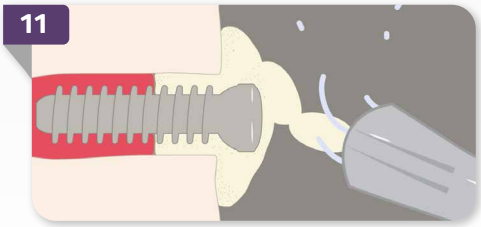
9. If desired, attach an applicator tip.
   - Two applicator tips (one white malleable and one clear trimmable) with retainer clip are provided.
   - The clear trimmable applicator tip can be used as provided or trimmed to the desired length. If trimmed, cut at a square angle to avoid creating a sharp tip.

10



10. Smear, fill, or press the mixture against the bleeding surface.

11



11. Remove the excess GEL-FLOW NT mixture once hemostasis is achieved.

Notes: Once hemostasis is achieved, GEL-FLOW NT mixture may be left at the bleeding site when necessary. GEL-FLOW NT mixture may be left in place when applied to mucosal surfaces until it liquefies. Since GEL-FLOW NT causes little more cellular reaction than does the blood clot, the wound may be closed over it. **For use with thrombin, consult the thrombin insert for complete prescribing information and proper sample preparation.[8]**

*Prepared as per thrombin label instructions.
†GEL-FLOW NT does not include thrombin or sterile saline diluent. Consult the relevant thrombin insert for complete prescribing information and proper sample preparation.[8]

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

INDICATION FOR GEL-FLOW NT™ (Absorbable Gelatin Powder)

GEL-FLOW NT is indicated in surgical procedures, including those involving cancellous bone bleeding, as a hemostatic device, when control of capillary, venous, and arteriolar bleeding by pressure, ligature, and other conventional procedures is either ineffective or impractical. Although not necessary, GEL-FLOW NT can be used either with or without thrombin to obtain hemostasis.

IMPORTANT SAFETY INFORMATION FOR GEL-FLOW NT

GEL-FLOW NT 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.

GEL-FLOW NT must not be placed in intravascular compartments because of the risk of embolization.

Do not use GEL-FLOW NT in patients with known allergies to porcine collagen.

Life-threatening anaphylactic reactions, including death, have been reported after exposure to absorbable gelatin. Patients with history of allergies to porcine products may be at risk of serious acute hypersensitivity reactions, including anaphylaxis. If an anaphylactic reaction is observed, absorbable gelatin administration should be immediately discontinued and any applied product removed.

GEL-FLOW NT is not intended as a substitute for meticulous surgical technique and the proper application of ligatures, or other conventional procedures for hemostasis.

Unused, opened GEL-FLOW NT syringes or packs must be discarded. GEL-FLOW NT must not be resterilized.

Only the minimum amount of GEL-FLOW NT mixture necessary to achieve hemostasis should be used and applied to the bleeding site with pressure until bleeding stops. Once hemostasis is attained, excess GEL-FLOW NT mixture should be carefully removed.

The use of GEL-FLOW NT is not recommended in the presence of infection. GEL-FLOW NT should be used with caution in contaminated areas of the body.

The packing of GEL-FLOW NT, particularly within bony cavities, should be avoided, since swelling may interfere with normal function and/or possibly result in compression necrosis of surrounding tissues.

Whenever possible, GEL-FLOW NT should be removed after use in laminectomy procedures and from foramina in bone, once hemostasis is achieved. This is because GEL-FLOW NT may swell on absorbing fluids and produce nerve damage by pressure within confined bony spaces.

GELFOAM should not be placed in the vicinity of the cerebral ventricular space or where there is a possibility of a cerebrospinal fluid fistula to the target bleeding site. GELFOAM should also not be used as a tissue substitute to repair tissue defects of the dura or the cranium. GELFOAM may migrate from central nervous system cerebrospinal fluid surgical sites into the cerebral ventricular space and compromise the cerebrospinal fluid circulation. Hydrocephalus and cerebrospinal fluid retention, requiring a re-intervention to remove GELFOAM residue, have been reported in adult and pediatric patients. In some cases, these complications occurred several months after use of GELFOAM.

GEL-FLOW NT should not be used for controlling postpartum bleeding or menorrhagia.

GEL-FLOW NT should not be used in conjunction with autologous blood salvage circuits or methyl-methacrylate adhesives.

After placement, absorbable hemostatic agents may be visible on imaging studies until they are fully absorbed, which could be interpreted as pseudotumor/pseudomass appearance. Pseudoinfection/pseudoabscess has also been reported in the literature. Pseudotumor/pseudomass and pseudoinfection/pseudoabscess may result in additional invasive procedures, reoperations, and prolonged hospital stays.

There have been reports of the following events associated with the use of GELFOAM absorbable gelatin powder: fever (without demonstrated infection), infection, abscess formation, giant cell granuloma, CNS compression, foreign body reaction, encapsulation of fluid, hematoma, excessive fibrosis, prolonged fixation of a tendon, toxic shock syndrome, and hearing loss (in tympanoplasty surgeries).

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.

Please see Instructions for Use for GEL-FLOW NT.

INDICATION FOR THROMBIN-JMI® (Thrombin, Topical [Bovine] U.S.P.)

THROMBIN-JMI is topical bovine thrombin indicated to aid 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.

In various types of surgeries, solutions of THROMBIN-JMI may be used in conjunction with an Absorbable Gelatin Sponge, USP for hemostasis.

IMPORTANT SAFETY INFORMATION FOR THROMBIN-JMI

WARNING: SEVERE BLEEDING AND THROMBOSIS COMPLICATIONS

- **THROMBIN-JMI can cause fatal severe bleeding or thrombosis. Thrombosis may result from the development of antibodies against bovine thrombin. Bleeding may result from the development of antibodies against factor V. These may cross-react with human factor V and lead to its deficiency.**
- **Do not re-expose patients to THROMBIN-JMI if there are known or suspected antibodies to bovine thrombin and/or factor V.**
- **Monitor patients for abnormal coagulation laboratory values, bleeding, or thrombosis.**

- Do not inject directly into the circulatory system. Because of its action in the clotting mechanism, THROMBIN-JMI can cause extensive intravascular clotting or death.
- Do not re-expose patients to THROMBIN-JMI if there are known or suspected antibodies to bovine thrombin and/or factor V.
- Do not administer to patients with a history of hypersensitivity to THROMBIN-JMI, its components and/or to material of bovine origin.
- Do not use for treatment of severe or brisk arterial bleeding.
- Allergic reactions, including anaphylactic/anaphylactoid reactions, have been reported following administration of THROMBIN-JMI.
- Institute intensive supportive measures and treat individual symptoms. Secure the airway and establish adequate respiratory exchange.
- THROMBIN-JMI causes thrombosis if it enters the circulatory system. Apply topically. DO NOT INJECT.
- Inhibitory antibodies may develop in patients and interfere with hemostasis. Monitor patients for abnormal coagulation laboratory values, bleeding, or thrombosis.

Most common adverse reactions (incidence greater than or equal to 2%) are hypersensitivity, bleeding, anemia, post-operative wound infection, thromboembolic events, hypotension, pyrexia, tachycardia and thrombocytopenia. Advise patients to consult their physician if they experience leg tenderness or swelling, chest pain, shortness of breath, or difficulty speaking or swallowing.

There is no human or animal data regarding use during pregnancy. It is also not known whether THROMBIN-JMI can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. THROMBIN-JMI should be given to a pregnant woman only if clearly needed.

Safety and effectiveness in children have not been established.

Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

ORDERING INFORMATION

THROMBIN-JMI® (Thrombin, Topical [Bovine] U.S.P.) SYRINGE SPRAY KIT

MANUFACTURER NUMBER: NDC 60793-0705-05	**PACKAGE INCLUDES:** A 5,000 IU THROMBIN-JMI vial, a 5 mL vial of diluent, a sterile transfer device, a sterile disposable syringe, and a spray tip in a sterile inner tray. **For use with GEL-FLOW NT, discard spray tip.**
UNIT OF SALE: 1 per package	

WHOLESALER PRODUCT IDENTIFICATION NUMBERS

AmerisourceBergen:	Cardinal:	McKesson Pharmacy:	McKesson Med Surg:	Morris & Dickson:	Lifeline:
10099075	4503538	1287036	870161	043547	102127

GEL-FLOW™ NT (Absorbable Gelatin Powder)

MANUFACTURER NUMBER: GTIN 00300091040016 (0009-1040-06)	**PACKAGE INCLUDES:** A prefilled sterile GEL-FLOW NT syringe containing 550 mg of absorbable gelatin powder and 2 applicator tips.
UNIT OF SALE: 6 per package	

WHOLESALER PRODUCT IDENTIFICATION NUMBERS

AmerisourceBergen:	Cardinal:	McKesson Pharmacy:	McKesson Med Surg:	Morris & Dickson:	Lifeline:	Concordance:
10186702	5436738	3900891	1106299	254102	113302	269639

GEL-FLOW™ KIT (GEL-FLOW™ NT Absorbable Gelatin Powder and Thrombin, Topical [Bovine] U.S.P., Thrombin-JMI®, 5,000 International Units Syringe Spray Kit)

MANUFACTURER NUMBER: GTIN 00300092250018 (0009-2250-01)	**PACKAGE INCLUDES:** A prefilled sterile GEL-FLOW NT syringe containing 550 mg of absorbable gelatin powder and 2 applicator tips, a 5,000 IU vial of THROMBIN-JMI, a 5 mL vial of diluent, a sterile transfer device, a sterile disposable syringe, and a spray tip in a sterile inner tray. **For use with GEL-FLOW NT, discard spray tip.**
UNIT OF SALE: 1 per package	

WHOLESALER PRODUCT IDENTIFICATION NUMBERS

AmerisourceBergen:	Cardinal:	McKesson Pharmacy:	McKesson Med Surg:	Morris & Dickson:	Lifeline:	Concordance:
10189198	5474077	3929718	1114295	400168	101511	271971

For Ordering Information, **contact your local Pfizer sales representative**.

For Medical Information, call **1-800-438-1985** or visit **pfizermedinfo.com**.

To report negative side effects of prescription drugs to the FDA, visit **fda.gov/medwatch** or call **1-800-FDA-1088**.

Please see full Important Safety Information on pages 10 and 11. Please see Instructions for Use for GEL-FLOW NT.
Please see full Prescribing Information, including BOXED WARNING, for THROMBIN-JMI.

References: 1. Doria C, Fischer CP, Wood CG, Li PM, Marra S, Hart J. Phase 3, randomized, double-blind study of plasma-derived human thrombin versus bovine thrombin in achieving hemostasis in patients undergoing surgery. *Curr Med Res Opin.* 2008;24(3):785-794. **2.** Evaluation of an absorbable surgical hemostatic agent: Thrombi-Gel® versus Gelfoam-thrombin (control). ClinicalTrials.gov website. NCT00652314. https://clinicaltrials.gov/ct2/show/NCT00652314. Accessed July 28, 2023. **3.** Chapman WC, Singla N, Genyk Y, et al. A phase 3, randomized, double-blind comparative study of the efficacy and safety of topical recombinant human thrombin and bovine thrombin in surgical hemostasis. *J Am Coll Surg.* 2007;205(2):256-265. **4.** Glickman M, Gheissari A, Money S, Martin J, Ballard JL; CoSeal Multicenter Vascular Surgery Study Group. A polymeric sealant inhibits anastomotic suture hole bleeding more rapidly than Gelfoam/thrombin: results of a randomized controlled trial. *Arch Surg.* 2002;137(3):326-331. **5.** Minkowitz H, Navarro-Puerto J, Lakshman S, et al; Clinical Investigation Study Group on Topical Thrombin (Human) Grifols in Surgery. Prospective, randomized, phase II, non-inferiority study to evaluate the safety and efficacy of topical thrombin (human) Grifols as adjunct to hemostasis during vascular, hepatic, soft tissue, and spinal open surgery. *J Am Coll Surg.* 2019;229(5):497-507.e1. **6.** Schreiber MA, Neveleff DJ. Achieving hemostasis with topical hemostats: making clinically and economically appropriate decisions in the surgical and trauma settings. *AORN J.* 2011;94(5):S1-S20. **7.** IMS data on file. **8.** GEL-FLOW NT (absorbable gelatin powder) [instructions for use]. New York, NY: Pfizer Inc.; 2022. **9.** THROMBIN-JMI (Thrombin, Topical [Bovine] U.S.P.) [prescribing information]. New York, NY: Pfizer Inc.; 2023. **10.** Widmaier EP, Raff H, Strang KT. Hemostasis: the prevention of blood loss. In: Lange M, Wheatley CH, Schreiber F, eds. *Vander's Human Physiology: The Mechanisms of Body Function.* 12th ed. New York, NY: McGraw-Hill; 2011:424-427. **11.** Oz MC, Rondinone JF, Shargill NS. Floseal Matrix: new generation topical hemostatic sealant. *J Card Surg.* 2003;18(6):486-493. **12.** Driver VR, Hanft J, Fylling CP, Beriou JM; Autologel Diabetic Foot Ulcer Study Group. A prospective, randomized, controlled trial of autologous platelet-rich plasma gel for the treatment of diabetic foot ulcers. *Ostomy Wound Manage.* 2006;52(6):68-87. **13.** Morse DC, Silva E, Bartrom J, et al. Improved bleeding scores using Gelfoam® Powder with incremental concentrations of bovine thrombin in a swine liver lesion model. *J Thromb Thrombolysis.* 2016;42(3):352-359. **14.** Adams GL, Manson RJ, Hasselblad V, Shaw LK, Lawson JH. Acute in-vivo evaluation of bleeding with Gelfoam™ plus saline and Gelfoam plus human thrombin using a liver square lesion model in swine. *J Thromb Thrombolysis.* 2009;28(1):1-5.

Pfizer