THROMBIN, TOPICAL U.S.P.
(BOVINE ORIGIN)
THROMBIN-JMI®

Thrombin, Topical (Bovine) must not be injected! Apply on the surface of bleeding tissue.

DESCRIPTION

The thrombin in Thrombin, Topical (Bovine Origin) THROMBIN-JMI® is a protein substance produced through a conversion reaction in which prothrombin of bovine origin is activated by tissue thromboplastin of bovine origin in the presence of calcium chloride. It is supplied as a sterile powder that has been freeze-dried in the final container. Also contained in the preparation are mannitol and sodium chloride. Mannitol is included to make the dried product friable and more readily soluble. The material contains no preservative.

THROMBIN-JMI® has been chromatographically purified and further processed by ultrafiltration. Analytical studies demonstrate the current manufacturing process' capability 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 significance of these findings is unknown.

CLINICAL PHARMACOLOGY

THROMBIN-JMI® requires no intermediate physiological agent for its action. It clots the fibrinogen of the blood directly. Failure to clot blood occurs in the rare case where the primary clotting defect is the absence of fibrinogen itself. The speed with which thrombin clots blood is dependent upon the concentration of both thrombin and fibrinogen.

INDICATIONS AND USAGE

THROMBIN-JMI® is indicated as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible.

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

CONTRAINDICATIONS

THROMBIN-JMI® is contraindicated in persons known to be sensitive to any of its components and/or to material of bovine origin.

Do not use for the treatment of massive or brisk arterial bleeding.

WARNING

The use of topical bovine thrombin preparations has occasionally been associated with abnormalities in hemostasis ranging from asymptomatic alterations in laboratory determinations, such as prothrombin time (PT) and partial thromboplastin time (PTT), to severe bleeding or thrombosis which rarely have been fatal. These hemostatic effects appear to be related to the formation of antibodies against bovine thrombin and/or factor V which in some cases may cross react with human factor V, potentially resulting in factor V deficiency. Repeated clinical applications of topical bovine thrombin increase the likelihood that antibodies against thrombin and/or factor V may be formed. Consultation with an expert in coagulation disorders is recommended if a patient exhibits abnormal coagulation laboratory values, abnormal bleeding, or abnormal thrombosis following the use of topical thrombin. Any interventions should consider the immunologic basis of this condition. Patients with antibodies to bovine thrombin preparations should not be re-exposed to these products.

Because of its action in the clotting mechanism, THROMBIN-JMI® must not be injected or otherwise allowed to enter large blood vessels. Extensive intravascular clotting and even death may result.

PRECAUTIONS

General – Consult the Absorbable Gelatin Sponge, USP labeling for complete information for use prior to utilizing the thrombin saturated sponge procedure.

Pregnancy – Category C — Animal reproduction studies have not been conducted with THROMBIN-JMI®. 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 indicated.

Pediatric Use – Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Allergic reactions may be encountered in persons known to be sensitive to bovine materials. Inhibitory antibodies which interfere with hemostasis may develop in a small percentage of patients. See WARNING .

DOSAGE AND ADMINISTRATION

Solutions of Thrombin, Topical (Bovine Origin), USP, THROMBIN-JMI® may be reconstituted with sterile isotonic saline at a recommended concentration of 1,000 to 2,000 International Units/mL. Where bleeding is profuse, as from abraided surfaces of liver or spleen, concentrations of 1,000 International Units per mL may be required. For general use in plastic surgery, dental extractions, skin grafting, etc. solutions containing approximately 100 International Units/mL are frequently used. Intermediate strengths to suit the needs of the case may be prepared by diluting the contents of the THROMBIN-JMI® container with an appropriate volume of sterile isotonic saline. In many situations, it may be advantageous to use THROMBIN-JMI® in a dry form on oozing surfaces. THROMBIN-JMI® may also be used with FloSeal™ NT according to the directions for use in the FloSeal™ NT package insert.

In instances where a concentration of approximately 1,000 units/mL is desired, the contents of the vial of sterile isotonic saline diluent may be transferred into the THROMBIN-JMI® container with a sterile syringe or sterile transfer device. If the transfer device is used for reconstitution, transfer the diluent in the following manner.

1. Remove the plastic cap off of the diluent vial.
2. Remove the tyvek cover from the transfer device container. Do not remove the device from the package.
3. Seat the blue end of the device on the diluent vial, pushing down until the spike penetrates the diaphragm and the device snaps in place.
4. Flip the plastic cover off on the THROMBIN-JMI® container. DO NOT REMOVE THE ALUMINUM SEAL.
5. Remove the plastic package from the transfer device, taking care to not touch the exposed end of the device.
6. Invert the vial of diluent and insert the clear end of the transfer device into the diaphragm of the THROMBIN-JMI® container.

CAUTION: Solutions should be used promptly upon removal from the container. However, the solution may be refrigerated at 2°-8°C for up to 24 hours, or may be stored at room temperature for up to 8 hours after reconstitution.

THROMBIN-JMI® PUMP SPRAY KIT

Each spray kit contains one vial of THROMBIN-JMI®, one vial of diluent and one spray pump and actuator.

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 inner tray to expose sterile contents.
3. Reconstitute the THROMBIN-JMI® to desired potency by introducing sterile isotonic saline with a sterile syringe or a sterile transfer device. If the transfer device is used, follow the previously described procedure.
4. When the THROMBIN-JMI® is completely dissolved, open vial by flipping up metal and tearing counterclockwise.
5. Remove the rubber diaphragm from vial. Remove pump with protective cap from tray and snap onto vial. Remove protective cap and attach actuator.
6. To spray, hold vial upright or at a slight angle. Several strokes of the pump will be required to expel the solution.

7. Discard unused contents and pump: DO NOT TRANSFER SPRAY PUMP TO ANOTHER VIAL.

THROMBIN-JMI® SYRINGE SPRAY KIT

Each syringe kit contains one vial of THROMBIN-JMI®, one vial of diluent and one spray tip and syringe.

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 sterile contents.
3. Using the sterile syringe equipped with a transfer device, draw the desired amount of 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® powder is completely dissolved, draw the THROMBIN-JMI® Thrombin solution into the syringe.
6. Remove the syringe from the transfer device by turning syringe counterclockwise.
7. Affix spray tip by pushing down and turning clockwise until the spray tip locks in place.
8. To spray, depress the syringe plunger in a normal fashion to dispense the THROMBIN-JMI® Thrombin solution through the tip in a fine spray.
9. Discard unused contents and syringe.

THROMBIN-JMI® EPISTAXIS KIT

Each epistaxis kit contains one vial of THROMBIN-JMI®, one vial of diluent and one nasal drug delivery device.

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 sterile contents.
3. Using the sterile syringe equipped with a transfer device, draw the desired amount of 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® powder is completely dissolved, draw the THROMBIN-JMI® Thrombin solution into the syringe.
6. Remove the syringe from the transfer device by turning syringe counterclockwise.
7. Affix the nasal drug delivery device on to the syringe by pushing the device down onto the THROMBIN-JMI® thrombin solution filled syringe and turn clockwise until the nasal drug delivery device locks in place.
8. Insert the nasal drug delivery device into the naris and spray the THROMBIN-JMI® thrombin solution onto the nasal mucosa through the nasal drug delivery device by depressing the syringe plunger using mild or moderate pressure on the syringe plunger. If feasible, the bleeding site on the patient's nasal mucosa may be placed in a dependent position during administration of THROMBIN-JMI®.

9. After administration of THROMBIN-JMI®, the device may be removed immediately or briefly held in the nasal passage.
10. Discard the unused contents, nasal drug delivery device, and the syringe.

The following techniques are suggested for the topical application of THROMBIN-JMI®.

1. The recipient surface should be sponged (not wiped) free of blood before THROMBIN-JMI® is applied.
2. A spray may be used or the surface may be flooded using a sterile syringe and small gauge needle. The most effective hemostasis results occur when the THROMBIN-JMI® mixes freely with the blood as soon as it reaches the surface.
3. Sponging of the treated surfaces should be avoided to assure that the clot remains securely in place.

THROMBIN-JMI® may be used in conjunction with Absorbable Gelatin Sponge, USP as follows:

1. Prepare THROMBIN-JMI® solution to desired strength.
2. Immerse sponge strips of the desired size in THROMBIN-JMI® solution. Knead the sponge strips vigorously with moistened, gloved fingers to remove trapped air, thereby facilitating saturation of the sponge.
3. Apply saturated sponge to bleeding area. Hold in place with a pledget of cotton or a small gauze sponge until hemostasis occurs.

HOW SUPPLIED

THROMBIN-JMI® is supplied in the following packages:

NDC 60793-215-05

Vial: 5,000 IU vial with 5 mL diluent.

NDC 60793-217-20

Vial: 20,000 IU vial with 20 mL diluent.

THROMBIN-JMI® Pump Spray Kit is supplied in the following packages:

NDC 60793-217-21

Pump Spray Kit: 20,000 IU vial with 20 mL diluent, spray pump and actuator.

THROMBIN-JMI® Syringe Spray Kit is supplied in the following packages:

NDC 60793-705-05

Syringe Spray Kit: 5,000 IU vial with 5 mL diluent, spray tip and syringe.

NDC 60793-217-22

Syringe Spray Kit: 20,000 IU vial with 20 mL diluent, spray tip and syringe.

THROMBIN-JMI® Epistaxis Kit is supplied in the following packages:

NDC 60793-205-05

Epistaxis Kit: 5,000 IU vial with 5 mL diluent, nasal drug delivery device and syringe.

STORAGE

Store THROMBIN-JMI® at 2°-25°C (36°-77°F).

Prescribing Information as of June 2011.

Distributed by: **King Pharmaceuticals, Inc.,** Bristol, TN 37620

Manufactured by: **GenTrac, Incorporated,** Middleton, Wisconsin 53562

U.S. License No. 977