#### TISSEEL FIBRIN SEALANT- fibrinogen human, human thrombin TISSEEL FIBRIN SEALANT- fibrinogen human, human thrombin solution Baxter Healthcare Corporation

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#### HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use TISSEEL safely and effectively. See full prescribing information for TISSEEL. TISSEEL [Fibrin Sealant] For Topical Use Only Frozen solution and lyophilized powder for solution for topical use only

#### Initial U.S. Approval: 1998

INDICATIONS AND USAGE Hemostasis: TISSEEL is a fibrin sealant indicated for use as an adjunct to hemostasis in adult and pediatric patients (>1 month of age) undergoing surgery when control of bleeding by conventional surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical. TISSEEL is effective in heparinized patients. (1) Sealing: TISSEEL is a fibrin sealant indicated as an adjunct to standard surgical techniques (such as suture and ligature) to prevent leakage from colonic anastomoses following the reversal of temporary colostomies. (1) DOSAGE AND ADMINISTRATION For Topical Use Only. Do Not Inject (2) Apply TISSEEL as a thin layer by dripping or spraying using cannula or spray set. (2.3, 5.2) Ensure that the amount of TISSEEL to be applied is sufficient to entirely cover the intended application area. (2.3)

DOSAGE FORMS AND STRENGTHS TISSEEL Kit (Freeze-Dried) is supplied as 2 mL, 4 mL and 10 mL (total volume) pack sizes with and without the DUPLOJECT Fibrin Sealant Preparation and Application System. (3) TISSEEL Pre-filled Syringe (Frozen) is supplied as 2 mL, 4 mL and 10 mL (total volume) pack sizes with DUO Set (AST syringe) or DUPLOJECT COMBI (PRIMA syringe). (3) **CONTRAINDICATIONS** 

- Do not inject directly into the circulatory system or into highly vascularized tissue. (4.1, 5.3)
- Do not use in individuals with a known hypersensitivity to aprotinin. (4.2, 5.1, 6)
- Do not use for the treatment of severe or brisk arterial or venous bleeding. (4.3)
- Do not spray where the minimum recommended distance from the applicator tip to the target site cannot be assured. (4.4).

#### ······ WARNINGS AND PRECAUTIONS ······

- TISSEEL contains aprotinin, a protein known to be associated with anaphylactic reactions. (4.2, 5.1, 6)
- To reduce the risk of potential life-threatening gas embolism, spray using only the appropriate pressurized gas at the recommended pressure and distance. For Open Surgical procedures, use the **EASYSPRAY** device connected to CO<sub>2</sub>, Medical Air or Nitrogen. For Minimally Invasive Surgery procedures use the **DUPLOSPRAY MIS** device connected only to CO<sub>2</sub>.(5.2)
- TISSEEL is denatured when exposed to solutions containing alcohol, iodine or heavy metals. (5.2)
- Apply only as a thin layer as excess clot thickness can negatively interfere with wound healing. (2, 5.2)
- When using TISSEEL in surgery do not inject intravascularly. (4.1, 5.3, 6.2).
- Safety has not been evaluated in neurosurgical procedures. (5.4)
- TISSEEL is made from pooled human plasma which can contain infectious agents. (5.5)

#### ----- ADVERSE REACTIONS

Hypersensitivity or allergic/anaphylactoid reactions have occurred. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Baxter Healthcare Corporation at 1-888-229-0001 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

#### ----- DRUG INTERACTIONS ------

Oxidized cellulose-containing preparations can reduce the efficacy of TISSEEL and should not be used as carrier materials. (7)

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# FULL PRESCRIBING INFORMATION

# **1 INDICATIONS AND USAGE**

**Hemostasis:** TISSEEL is a fibrin sealant indicated for use as an adjunct to hemostasis in adult and pediatric patients (>1 month of age) undergoing surgery when control of bleeding by conventional surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical. TISSEEL is effective in heparinized patients.

**Sealing:** TISSEEL is a fibrin sealant indicated as an adjunct to standard surgical techniques (such as suture and ligature) to prevent leakage from colonic anastomoses following the reversal of temporary colostomies.

# **2 DOSAGE AND ADMINISTRATION**

# FOR TOPICAL USE ONLY - DO NOT INJECT

Vials and pre-filled syringes are for single-patient use only. Discard any unused product.

# 2.1 Preparation of TISSEEL Kit (Freeze-Dried)

Do not expose to temperature above 37°C Do not microwave Do not refrigerate or freeze after reconstitution

Do not use iodine or heavy metal containing preparations such as betadine for disinfection of vial stoppers. Allow alcohol-based disinfectants to evaporate before puncturing stopper.

Use separate syringes and transfer devices for reconstituting Sealer Protein and Thrombin solutions and for application to prevent clotting.

The product must be used within 4 hours after reconstitution.

Freeze-dried Sealer Protein Concentrate and Thrombin are reconstituted in Fibrinolysis Inhibitor Solution and Calcium Chloride Solution, respectively. The Sealer Protein Solution and Thrombin Solution are then combined using the DUPLOJECT Preparation and Application System, or an equivalent delivery device cleared by FDA for use with TISSEEL, to form the Fibrin Sealant.

<u>Pre-warming TISSEEL Kit with FIBRINOTHERM device</u> See FIBRINOTHERM device manual for complete operating instructions. If a FIBRINOTHERM device is not available, contact Baxter (1-800-229-0001) for assistance.

1. Place all four vials from the TISSEEL Kit into the pre-warmed wells of the FIBRINOTHERM device, using the appropriately sized adapter ring(s), and allow the vials to warm for up to 5 minutes (room temperature product will take less time).

Preparation of Sealer Protein Solution with FIBRINOTHERM device

- 1. Remove the caps from the Sealer Protein Concentrate and the Fibrinolysis Inhibitor Solution vials.
- 2. Transfer the Aprotinin (Fibrinolysis Inhibitor Solution) into the vial containing the freeze-dried Sealer Protein Concentrate using the sterile reconstitution components (see directions provided with the device system for specific reconstitution instructions). Gently swirl the vial to ensure that the product is completely soaked.
- 3. Place the vial into the largest opening of the FIBRINOTHERM device with the appropriate adapter ring. Switch on the stirrer and allow the vial contents to stir until all Sealer Protein Concentrate is dissolved. Reconstitution is complete when no undissolved particles are visible.

#### Notes:

- If the Sealer Protein Concentrate has not fully dissolved within 20 minutes discard the vial and prepare a fresh kit.
- Keep the Sealer Protein Solution at 37°C without stirring. Stir shortly before drawing up the solution to ensure homogeneity.

# Preparation of Thrombin Solution with FIBRINOTHERM device

To reconstitute the Thrombin (Human) with the Calcium Chloride Solution; follow steps 1-3 under <u>Preparation of Sealer Protein with FIBRINOTHERM device</u>utilizing the Thrombin and Calcium Chloride vials.

#### Transferring to the Sterile Field

For transfer of the Sealer Protein and Thrombin Solutions to the sterile field, the circulating nurse should disinfect the tops of the vials with a germicidal solution and allow to dry. The scrub nurse should withdraw the sterile solutions while the circulating nurse holds the non-sterile vials. Slowly withdraw the solution, by firm constant aspiration, to reduce the risk of large air bubbles.

# 2.2 Preparation of TISSEEL Pre-Filled Syringe (Frozen)

Do not expose to temperature above 37°C Do not microwave.

Do not refrigerate or re-freeze after thawing.

Do not use TISSEEL (frozen) until it is completely thawed and warmed (liquid consistency) to 33-37°C. Do not remove the protective syringe cap until use.

AST Syringe – The plunger rod must be inserted into the syringe barrel (see ). PRIMA Syringe – The plunger is already assembled with the syringe barrel (see Figure 2).

<u>Sterile Water Bath (Quick Thawing)</u>: Transfer inner pouch to the sterile field, remove prefilled syringe from inner pouch and place directly into sterile water bath ensuring the syringe is completely immersed in the water. Maintain the product at 33-37°C until use. Once the package is opened or the product is warmed to 33-37°C, it must be used within 4 hours.

<u>Non-Sterile Water Bath</u>: Maintain the pre-filled syringe in pouches and place into a water bath outside the sterile field ensuring the pouches remain submerged. Remove from the water bath after thawing and warming, dry the external pouch and transfer inner pouch with pre-filled syringe onto the sterile field. Maintain the product at 33-37°C until use. Once the package is opened or the product is warmed to 33-37°C, it must be used within 4 hours. <u>Incubator</u>: Maintain the pre-filled syringe in pouches and place into an incubator. Remove from the incubator after thawing and warming. Transfer inner pouch with pre-filled syringe onto the sterile field. Maintain the product at 33-37°C until use. Once the package is opened or the product is warmed to 33-37°C, it must be used within 4 hours.

Pack Size	Sterile Wa (Pou Remo 33 -	ches oved)	es Water Bath ed) (In Pouches)		Incuba (In Pouc 33 - 37	hes)
	PRIMA	AST	PRIMA	AST	PRIMA	AST
	Syringe	Syringe	Syringe	Syringe	Syringe	Syringe
2 mL	5 minutes	5 minutes	15	30	40 minutes	40
	Jinnutes	Jinnutes	minutes	minutes	40 minutes	minutes
4 mL	5 minutos	5 minutes	20	40	50 minutes	85
	Jinnutes	Jinnutes	minutes	minutes	50 minutes	minutes
10 mL	10	12	35	80	90 minutes	105
	minutes	minutes	minutes	minutes	90 minutes	minutes

# Table 1: Approximate Water Bath or Incubator Thawing and<br/>Warming Times

<u>Room Temperature Thawing:</u> Unopened pouches can be stored for up to 48 hours at room temperature (15-25°C). Before use, warm the product to 33-37°C and apply immediately. The total thawing and warming time cannot exceed 48 hours.

# Table 2: Approximate Room Temperature Thawing Times

Pack Size	Room Temperature (In Pouches) 15 - 25oC PRIMA Syringe AST Syringe			
2 mL	80 minutes	60 minutes		
4 mL	90 minutes	110 minutes		
10 mL	160 minutes	160 minutes		

# Table 3: Approximate Water Bath or Incubator WarmingTimes for Thawed Product

Pack Size	Sterile Water Bath (Pouches Removed) 33 - 37°C		Non-Sterile Water Bath (In Pouches) 33 - 37°C		Incubator (In Pouches) 33 - 37°C	
	PRIMA	AST	PRIMA	AST	PRIMA	AST
	Syringe	Syringe	Syringe	Syringe	Syringe	Syringe
2 mL	2 minutes	2	5	16	16	20
2 111L	2 minutes	minutes	minutes	minutes	minutes	minutes
1 ml	2 minutos	2	8	21	21	43

4 IIIL		minutes	minutes	minutes	minutes	minutes
10 mL	1 minutos	6	12	43	35	52
TO HIE	4 minutes	minutes	minutes	minutes	minutes	minutes

# 2.3 Method of Application

TISSEEL Kit (Freeze-Dried)

Apply TISSEEL using the DUPLOJECT Fibrin Sealant Preparation and Application System or an equivalent delivery system (including open and minimally invasive spray devices) cleared by FDA for use with TISSEEL. Specific instructions for the use of TISSEEL in conjunction with each cleared delivery device are provided with the device.

TISSEEL Pre-filled Syringe Frozen

Apply pre-filled TISSEEL using the joining piece and application cannula accessory devices provided with the product or an equivalent delivery device (including open and minimally invasive spray devices) cleared by the FDA for use with TISSEEL.

DUO Set (AST Syringe) Instructions (see ):

- 1. Insert plunger into syringe barrel.
- 2. Remove all air from the double chamber syringe.
- 3. Firmly connect the two syringe nozzles to the joining piece (Y-connector) and secure it by fastening the tether strap to the syringe.
- 4. Fit an application cannula to the joining piece. Apply by depressing plunger.

DUPLOJECT COMBI (PRIMA Syringe) Instructions (see )

- 1. The plunger is attached to the syringe barrel and does not need to be inserted.
- 2. Remove all air from the double chamber syringe.
- 3. Firmly connect the two syringe nozzles to the joining piece (Y-connector) and secure it by fastening the tether strap to the syringe.
- 4. Fit an application cannula to the joining piece. Apply by depressing plunger. Note: Interruption of TISSEEL application causes clogging in the cannula. Replace the cannula immediately prior to resuming application. If the opening of the joining piece (Y-connector) facing the cannula is clogged, use the spare joining piece provided in the package.

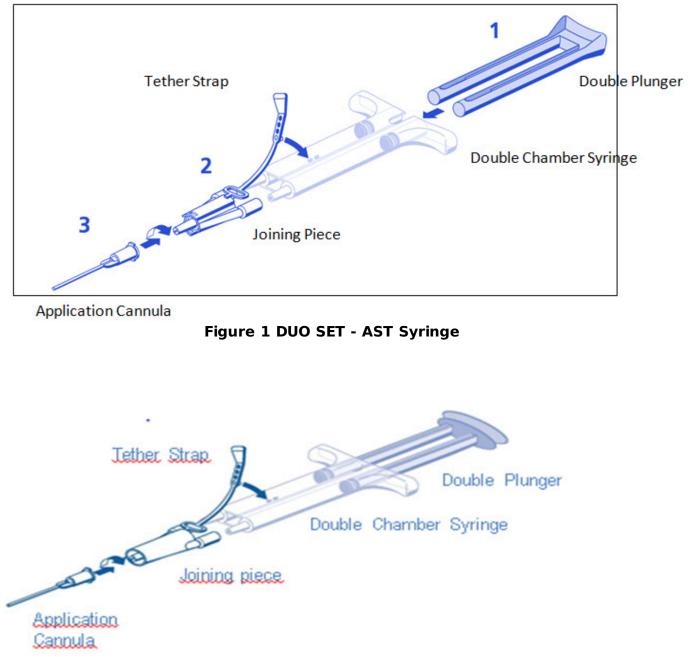


Figure 2: DUPLOJECT COMBI - PRIMA Syringe

TISSEEL must be sprayed only onto application sites that are visible. Dry the site of application as much as possible. The surface area of the wound needs to be dried using standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices). Do not use pressurized air or gas to dry the site.

When applying TISSEEL using a spray device, utilize the recommended gas, pressure and distance from tissue within the ranges recommended by the manufacturer as follows:

Surgery Spray set / Surgery Applicator tips to use	Pressure regulator to use	Gas	Distance	Spray Pressure
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Open surgery	TISSEEL /ARTISS Spray Set	EASY SPRAY Pressure Regulator	Medical grade CO2 <sup>*</sup> , Compressed Air or Nitrogen	10-15 cm	1.5-2.0 bar (21.8-29.0 psi)
Laparoscopic/ minimally invasive procedures	DUPLOSPRAY MIS Applicator 20 cm DUPLOSPRAY MIS Applicator 30 cm DUPLOSPRAY MIS Applicator 40 cm 360º Flexible Applicator 40 cm Replaceable tip	DUPLOSPRAY MIS Regulator	CO2 Only	Range 2-5 cm 3 cm recommended	1.18-1.50 bar (17-22 psi)

\* Medical grade CO2 is the preferred gas for application, however compressed Air or Nitrogen are acceptable gasses for administration of TISSEEL in open surgery.

Apply TISSEEL as a thin layer by dripping or spraying using a cannula or spray set approved for use with TISSEEL. To reduce the risk of potentially life-threatening gas embolism, spray TISSEEL using only the appropriate pressurized gas within the pressure range and distance recommended in the device Instructions For Use (see *Warnings and Precautions (5.2))*. The treating physician will determine the amount of TISSEEL to be applied based on the surface to be covered. Ensure that the amount applied is sufficient to entirely cover the intended application area. The approximate surface areas covered by each package size of TISSEEL are listed in Table 5:

#### Table 5: Surface Area Coverage

Required package size of TISSEEL	Maximum coverage using spray	Maximum coverage using cannula
2 mL	100 cm <sup>2</sup>	8 cm <sup>2</sup>
4 mL	200 cm <sup>2</sup>	16 cm <sup>2</sup>
10 mL	500 cm <sup>2</sup>	40 cm <sup>2</sup>

Avoid application beyond the intended area. Allow at least 2 minutes after application to achieve sufficient polymerization. If repeat application is needed, dry the site as much as possible before reapplying. Reapply after removing residues from the prior application or before polymerization takes place since TISSEEL may not adhere firmly to a polymerized layer.

In cases where very small volumes (1-2 drops) are required, expel and discard the first several drops from the application cannula immediately before application to ensure administration of adequately mixed TISSEEL.

# **3 DOSAGE FORMS AND STRENGTHS**

TISSEEL Kit (Freeze-Dried) is supplied as 2 mL, 4 mL and 10 mL (total volume) pack sizes with and without the DUPLOJECT Fibrin Sealant Preparation and Application System. TISSEEL Pre-Filled Syringe (Frozen) is supplied as 2 mL, 4 mL and 10 mL (total volume) pack sizes with the DUO Set (AST Syringe) or DUPLOJECT COMBI (PRIMA Syringe).

# **4 CONTRAINDICATIONS**

# 4.1 Intravascular Application

Do not inject TISSEEL directly into the circulatory system or into highly vascularized tissue. Intravascular application of TISSEEL can lead to intravascular coagulation, can result in life-threatening thromboembolic events, and can increase the likelihood and severity of acute hypersensitivity reactions in susceptible patients (see *Warnings and Precautions (5.3) and Adverse Reactions (6.2)*).

# 4.2 Aprotinin Hypersensitivity

Do not use TISSEEL in individuals with a known hypersensitivity to aprotinin (see *Warnings and Precautions (5.1) and Adverse Reactions (6)*).

# 4.3 Severe or Brisk Bleeding

Do not use TISSEEL for treatment of severe or brisk arterial or venous bleeding. In these situations, TISSEEL will be washed away in the flow of blood before hemostasis can be attained.

# 4.4 Application below minimum recommended distance from target site

Do not spray TISSEEL where the minimum recommended distance from the applicator tip to the target site cannot be assured.

# **5 WARNINGS AND PRECAUTIONS**

# 5.1 Hypersensitivity Reactions

Hypersensitivity reactions including allergic/and anaphylactoid reactions can occur with the use of TISSEEL. Cases have been reported in post marketing experience with Baxter's fibrin sealant (*see Adverse Reactions (6.2)*). In specific cases, these reactions have progressed to severe anaphylaxis. Such reactions may especially be seen if TISSEEL is applied repeatedly over time or in the same setting, or if systemic aprotinin has been administered previously. Even if the first treatment was well tolerated, this may not exclude the occurrence of an allergic reaction after a subsequent administration of TISSEEL or systemic aprotinin. Observed symptoms of allergic anaphylactic reactions to TISSEEL have included: bradycardia, tachycardia, hypotension, flushing, bronchospasm, wheezing, dyspnea, nausea, urticaria, angioedema, pruritus, erythema and paresthesia. Such reactions can also occur in patients receiving TISSEEL for the first time.

Aprotinin is included in TISSEEL for its antifibrinolytic properties. Aprotinin, a protein, is known to be associated with anaphylactic reactions. Even in the case of strict local application of aprotinin, there is a risk of anaphylactic reactions to aprotinin, particularly

in the case of previous exposure (*see Contraindications (4.2)*). TISSEEL does not contain any substances of bovine origin.

Discontinue administration of TISSEEL in the event of hypersensitivity reactions. Mild reactions can be managed with antihistamines. Severe hypotensive reactions require immediate intervention using current principles of shock therapy. Remove remaining product from the application site.

# 5.2 Application Precautions

Any application of pressurized air or gas is associated with a potential risk of air or gas embolism, tissue rupture, or gas entrapment with compression, which may be life a threatening or fatal.

Life threatening/fatal air or gas embolism has occurred when Fibrin Sealants were administered using pressurized gas with open regulator spray devices. This can occur if a spray device is used at higher than recommended pressures and in closer than recommended proximity to the tissue surface. The solubility of compressed CO<sub>2</sub> is greater than either compressed N<sub>2</sub> or Air thereby reducing the potential effect of embolization.

Regardless of the type of gas used, to reduce the incidence of embolization, spray TISSEEL using only the recommended regulator, set within the recommended pressure range, with the appropriate applicator positioned at the recommended distance in Table 4.

Monitor changes in blood pressure, pulse, oxygen saturation and endtidal CO<sub>2</sub> due to the possibility of air or gas embolism.

Use only spray catheters or applicators approved for use with TISSEEL.

TISSEEL must not be sprayed in enclosed body areas using the EASYSPRAY device and must be sprayed onto only visible application sites.

<u>For Open Surgical procedures</u>, use the EASYSPRAY Pressure Regulator connected to medical grade CO<sub>2</sub>, compressed Air or a Nitrogen compressed gas source along with the TISSEEL/ARTISS spray set, (*see Method of Application (2.3)*).

<u>For Minimally Invasive Surgery procedures</u> in enclosed body areas use of the DUPLOSPRAY MIS device connected only to compressed  $CO_2$ , along with DUPLOSPRAY applicator is recommended. The DUPLOSPRAY MIS device is specifically designed to prevent over pressurization of the body cavity through a dedicated ventline to reduce the risk of gas embolization, (*see Method of Application (2.3)*).

The sealer protein and thrombin solutions are denatured by alcohol, iodine or heavy metal ions. If any of these substances have been used to clean the wound area, the area must be thoroughly rinsed before the application of TISSEEL.

Apply TISSEEL as a thin layer as excess clot thickness can negatively interfere with wound healing.

# 5.3 Use in Surgery

When using TISSEEL in surgery, do not inject intravascularly (see Contraindications (4.1) and Adverse Reactions (6.2)).

# 5.4 Use in Neurosurgical Procedures

The safety and effectiveness of TISSEEL used alone or in combination with biocompatible carriers in neurosurgical procedures or other surgeries involving confined spaces have not been evaluated, and its use in this setting is not approved by FDA (*see Adverse Reactions (6.2) and Drug Interactions (7)*).

# 5.5 Infection Risk from Human Plasma

TISSEEL is made from human plasma. Because this product is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent 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 to Baxter Healthcare Corporation at 1-888-229-0001.

# **6 ADVERSE REACTIONS**

# 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials and may not reflect the rates observed in practice.

Increased D-Dimer levels have been observed during a clinical study in cardiovascular surgery (*see Clinical Studies (14)*), but did not exceed values reported in the literature occurring after this type of surgery. Postoperatively increased D-Dimers can result at least partly from the degradation of Fibrin Sealant.

There were no reports of serious, associated adverse reactions reported above 1% in clinical studies.

# 6.2 Post-Marketing Experience

Because adverse reactions are reported voluntarily and the population is of uncertain size, it is not always possible to reliably estimate the frequency of these reactions.

The following adverse reactions have been reported in the post-marketing experience.

<u>Immune System Disorders:</u> Hypersensitivity, including anaphylactic reaction and anaphylactic shock. Anaphylactic reactions and anaphylactic shock have included fatal outcomes.

<u>Vascular Disorders</u>:Hypotension, flushing, embolism, including cerebral artery embolism, cerebral infarction\*, air embolism\*\*

<u>Skin and subcutaneous Tissue Disorders:</u>Angioedema, erythema, impaired healing, pruritus, urticaria

Cardiac Disorders:Bradycardia, tachycardia

<u>Respiratory Disorders</u>: Bronchospasm, dyspnea, wheezing

Gastrointestinal Disorders: Nausea

Nervous System Disorders: Paresthesia

\* as a result of intravascular application into the superior petrosal sinus

\*\* As with other fibrin sealants life-threatening/fatal air or gas embolism when using devices with pressurized air or gas occurred; this event appears to be related to an inappropriate use of the spray device (e.g. at higher than recommended pressure and in close proximity to the tissue surface),

Class effect: Manifestations of hypersensitivity or allergic reactions associated with the class of fibrin sealant/hemostatic products include: application site irritation, chest discomfort, chills, headache, lethargy, restlessness and vomiting.

There have been reports of serious adverse events such as paralysis and other compressive complications possibly related to the use of fibrin sealants in combination with resorbable hemostatic agents. There have also been reports of fatalities following the misadministration of topical thrombin *(see Warnings and Precautions (5.4)).* 

# **7 DRUG INTERACTIONS**

Oxidized cellulose-containing preparations can reduce the efficacy of TISSEEL and should not be used as carrier materials. No interaction studies have been performed.

# **8 USE IN SPECIFIC POPULATIONS**

# 8.1 Pregnancy

#### **Risk Summary**

There are no direct or controlled studies of TISSEEL in pregnant women. No animal reproductive and developmental toxicity studies have been conducted with TISSEEL. It is also not known whether TISSEEL can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Some viruses, such as parvovirus B19, are particularly difficult to remove or inactivate. Parvovirus B19 most seriously affects pregnant women (fetal infection). In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

# 8.2 Lactation

#### <u>Risk Summary</u>

There is no information regarding the presence of TISSEEL in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TISSEEL and any potential adverse effects on the breastfed infant from TISSEEL or from underlying maternal condition.

# 8.4 Pediatric Use

Limited clinical study data are available with regard to the use of TISSEEL in children. Of 365 patients undergoing repeated cardiac surgery or emergency resternotomy in a clinical trial of TISSEEL, 27 pediatric patients aged 16 years or younger were treated with TISSEEL. Of these, 2 patients were less than 6 months, 2 patients were between the ages of 6 months and 2 years, 15 patients were between 3-11 years of age, and 8 patients were between 12-16 years of age. There were no differences in safety

observed between these subjects and the overall population. (seeClinical Studies (14)).

#### 8.5 Geriatric Use

Clinical studies included 218 patients aged 65 years of age or older treated with TISSEEL (159 undergoing cardiac surgery and 59 undergoing vascular surgery) (*see Clinical Studies (14)*). No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

# **11 DESCRIPTION**

TISSEEL [Fibrin Sealant] is a two-component fibrin sealant made from pooled human plasma. When combined, the two components, Sealer Protein and Thrombin mimic the final stage of the blood coagulation cascade.

#### Sealer Protein (Human)

Sealer Protein (Human) is a sterile, non-pyrogenic, vapor heated and solvent/detergent treated preparation made from pooled human plasma. Sealer Protein (Human) is provided either as a freeze-dried powder for reconstitution with Aprotinin or as a finished frozen solution pre-filled into one side of a dual-chambered syringe. The active ingredient in Sealer Protein (Human) is fibrinogen. Sealer Protein (Human) solution contains fibrinolysis inhibitor, synthetic Aprot<u>i</u>nin, that delays fibrinolysis. Aprotinin (Synthetic) is manufactured by solid phase synthesis from materials completely of non-human/non-animal origin.

#### <u>Thrombin (Human)</u>

Thrombin (Human) is a sterile, non-pyrogenic, vapor heated and solvent/detergent treated preparation made from pooled human plasma. Thrombin (Human) is also provided either as a freeze-dried powder for reconstitution with Calcium Chloride Solution or as a finished frozen solution pre-filled into one side of a dual-chambered syringe.

The reconstituted solution or pre-filled syringe contains: Sealer Protein Solution Total protein: 96 – 125 mg/mL Fibrinogen: 67 – 106 mg/mL Aprotinin (Synthetic): 2250 – 3750 KIU/mL Other ingredients include: human albumin, tri-sodium citrate, histidine, niacinamide, polysorbate 80 and water for injection. Thrombin Solution Thrombin (Human): 400 – 625 units/mL\* Calcium Chloride: 36 – 44 µmol/mL Other ingredients include: human albumin, sodium chloride and water for injection. \* The potency expressed in units is determined with a clotting assay using an inhouse internal standard that has been calibrated against the World Health Organization (WHO) Second International Standard for Thrombin, 01/580. Therefore, a unit (U) is equivalent to an International Unit (IU).

#### Viral Clearance

TISSEEL is made from pooled human plasma collected at US licensed collection centers. The vapor heat and solvent/detergent treatment steps used in the manufacturing process have been shown to be capable of significant viral reduction. No procedure, however, has been shown to be completely effective in removing viral infectivity from derivatives of human plasma (*see Warnings and Precautions (5.5)*). Validation studies were conducted using samples drawn from manufacturing intermediates for each of the two human plasma derived components. These samples were spiked with stock virus suspensions of known titers followed by further processing under conditions representative of respective manufacturing steps.

The virus reduction factors (expressed as  $\log_{10}$ ) of manufacturing steps for each of the viruses tested are shown in Table 6.

Seal	Sealer Protein Component					
Manufacturing Step	Mean Reduction Factors [ $log_{10}$ ] of Virus					
			Tested			
	HIV-1	HAV	BVDV	PRV	MMV	
Early Manufacturing Steps	n.d.	n.d.	n.d.	n.d.	2.7	
Solvent/Detergent	>5.3	n.d.	>5.7	>5.9	n.d.	
Treatment						
Vapor Heat Treatment	>5.5	>5.6	>5.7	>6.7	1.2	
Overall Reduction Factor	>10.8	>5.6	>11.4	>12.6	3.9	
(ORF)						
Th	nrombin					
Manufacturing Step	Mean Reduction Factors [log <sub>10</sub> ] of Virus					
			Tested			
	HIV-1	HAV	BVDV	PRV	MMV	
Thrombin Precursor Mass	3.2	1.5	1.8	2.5	1.2	
Capture						
Vapor Heat Treatment	>5.5	>4.9	>5.3	>6.7	1.0	
Solvent/Detergent	>5.3	n.d.	>5.5	>6.4	n.d.	
Treatment						
lon Exchange	n.d.	n.d.	n.d.	n.d.	3.6	
Chromatography						
Overall Reduction Factor	>14.0	>6.4	>12.6	>15.6	5.8	
(ORF)						

# Table 6: Reduction Factors for Virus Removal and/or Inactivation

#### n.d. = not determined

**HIV-1**: Human Immunodeficiency Virus 1; **HAV**: Hepatitis A Virus; **BVDV**: Bovine Viral Diarrhea Virus, a model for Hepatitis C Virus; **PRV**: Pseudorabies Virus, a model for lipid enveloped DNA viruses, among those is Hepatitis B Virus; **MMV**: Mouse Minute Virus, a model for B19V.

In addition, Human Parvovirus B19 (B19V) was used to investigate the upstream Thrombin precursor mass capture step, the Sealer Protein early manufacturing steps and the Thrombin and Sealer Protein vapor heating steps. Using quantitative PCR assays, the estimated B19V log reduction factors were: (a) 1.7 for the Thrombin precursor mass capture step, (b) 3.4 for Sealer Protein early manufacturing steps, (c) >4 for Thrombin vapor heat treatment and (d) 1.0 for Sealer Protein vapor heat treatment.

# **12 CLINICAL PHARMACOLOGY**

# 12.1 Mechanism of Action

Upon mixing Sealer Protein (Human) and Thrombin (Human), soluble fibrinogen is transformed into fibrin, forming a rubber-like mass that adheres to the wound surface and achieves hemostasis and sealing or gluing of tissues. TISSEEL mimics the final coagulation cascade step as it has all relevant components to form a clot. TISSEEL is effective in heparinized patients and in patients medicated with anti-platelet drugs.

# **12.2 Pharmacodynamics**

Thrombin is a highly specific protease that transforms the fibrinogen contained in Sealer Protein (Human) into fibrin. Fibrinolysis inhibitor, Aprotinin (Synthetic), is a polyvalent protease inhibitor that prevents premature degradation of fibrin. Preclinical studies with different fibrin sealant preparations simulating the fibrinolytic activity generated by extracorporeal circulation in patients during cardiovascular surgery have shown that incorporation of aprotinin in the product formulation increases resistance of the fibrin sealant clot to degradation in a fibrinolytic environment.

# **12.3 Pharmacokinetics**

Unincorporated Aprotinin and its metabolites have a half-life of 30 to 60 minutes and are eliminated by the kidney. Pharmacokinetic studies were not conducted. TISSEEL is expected to be completely resorbed in 10 to14 days

Because TISSEEL is applied only topically, systemic exposure or distribution to other organs or tissues is not expected.

# **13 NONCLINICAL TOXICOLOGY**

# 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies to evaluate the carcinogenic potential of TISSEEL or studies to determine the effect of TISSEEL on fertility have not been performed.

# **14 CLINICAL STUDIES**

# 14.1 Vascular Surgery

TISSEEL was evaluated in a prospective, controlled, randomized, single-blind, multicenter clinical study against manual compression with gauze pads in 140 subjects undergoing vascular surgery with expanded polytetrafluoroethylene (ePFTE) graft placement (arterio-arterial bypasses and AV shunts for dialysis access in the upper and lower extremity). Subjects received standardized dosages of heparin. Protamine was administered after the primary endpoint had been assessed. Long-term antiplatelet treatments were continued perioperatively at the surgeon's discretion.

Subjects were randomly assigned to TISSEEL or control when persistent bleeding at the study suture line was present after surgical hemostasis, i.e., sutures. Eligible bleedings before clamping and treatment application were defined as a minimum of 25% of the suture line bleeds or at least 5 suture line bleedings or any pulsatile or spurting needle hole bleeding. For the primary endpoint, hemostasis achieved at the study suture line at 4 minutes and maintained until surgical closure, a single application of TISSEEL was statistically significantly superior to control (p<0.0001; likelihood ratio chi-square test; 2.5% one sided) [ITT].

	-	-				
Hemostasis at the study suture line within 4 minutes and maintained						
until surgical closure						
TISSEEL Manual Compressio						
Intent to Treat Analysis	44/70 (62.9%)	22/70 (31.4%)				

# Table 7: Vascular Surgery

#### **14.2 Cardiac Surgery**

TISSEEL was evaluated in a prospective, parallel design, randomized (1:1), double-blind, multicenter clinical study against an earlier formulation of the product, TISSEEL VH, in 317 subjects undergoing cardiac surgery requiring cardiopulmonary bypass (CPB) and median sternotomy. Patients were treated with TISSEEL or the control product only when hemostasis was not achieved by conventional surgical methods. For the endpoint, hemostasis achieved at the primary treatment site within 5 minutes of treatment and maintained until closure of the surgical wound, TISSEEL was non-inferior to the earlier formulation of the product using a one-sided 97.5% confidence interval on the difference in the proportion of subjects successfully treated.

#### Table 8: Cardiac Surgery

Hemostasis within 5 minutes and maintained until surgical closure						
	TISSEEL TISSEEL VH					
Intent to Treat Analysis 127/144 (88.2%) 129/144 (89.6%)						

# **14.3 Cardiac Reoperations**

An earlier formulation of TISSEEL was evaluated in an open-label crossover study against control topical hemostatic agents in 489 patients undergoing cardiovascular reoperation or resternotomy at 11 institutions. Patients were randomized to TISSEEL or control hemostatic agents when a topical hemostatic was needed at the conclusion of surgery and after all attempts at surgical hemostasis. Patients were crossed to the alternative therapy if bleeding continued after the 5 minute endpoint. At 10 centers, TISSEEL was used after administration of protamine sulfate. At one site, TISSEEL could be used before administration of protamine sulfate. 365 of the 489 patients developed bleeding episodes requiring treatment. For the endpoint (successful hemostasis at 5 minutes), TISSEEL was statistically significantly superior to control topical hemostatic agents in these patients. Similarly, absolute time to cessation of bleeding was statistically significantly shorter for TISSEEL than for control topical hemostatic agents (p<0.0001, Gehan- Wilcoxon test, two sided).

# Table 9: Cardiac Reoperations

Hemostasis within 5 minutes				
TISSEEL Control Topical Hemostatic Agent				
82.4% (159/193) 44.5% (76/172)				
Pearson $\chi^2$ two sided; p < 0.0001; intent-to-treat analysis				

#### 14.4 Splenectomy

In a single center, open label trial, an earlier formulation of TISSEEL was compared to historical controls in patients undergoing laparotomy for blunt or penetrating traumatic injury to the spleen and/or liver. Use of TISSEEL resulted in the need for statistically significantly fewer splenectomies than control hemostatic maneuvers (Refer to Table 9). TISSEEL did not result in significantly reduced mortality in patients with blunt or penetrating trauma to the liver alone or to the liver and spleen (p=0.067,  $\chi^2$ , one sided).

Table 10: Splenectomy

Splenectomy Rate					
Injury to:	TISSEEL	Historic			
		Controls			
Spleen	0/19	14/22	p <0.001		
Spleen and liver	1/26	19/34	p <0.001		

# 14.5 Colostomy Closure

In a single center, prospective open label study of 118 patients randomized to standard of care (58 patients) or standard of care plus fibrin sealant (60 patients) for elective colostomy closure after temporary colostomy placement for treatment of traumatic injury to the colon, the earlier version of TISSEEL plus standard of care was also shown to be significantly superior to standard of care alone (p=0.0406, Jonckheere-Terpstra test for ordinal data, two sided) with regard to anastomotic complications (leakage, intra-abdominal abscess formation, re-operation, septic shock, and death).

# **16 HOW SUPPLIED/STORAGE AND HANDLING**

#### How Supplied

TISSEEL is supplied in the following pack sizes and presentations:

Pack Size	TISSEEL Kit (Freeze- Dried)	TISSEEL Kit (Freeze-Dried) with DUPLOJECT System	AST Syringe	TISSEEL Pre-Filled PRIMA Syringe (Frozen) with DUPLOJECT COMBI
2 mL	0338-4210-02	0338-4301-02	0338-8402-02	0338-9560-01

#### **Table 11: NDC Numbers**

4 mL	0338-4211-04	0338-4302-04	0338-8402-04	0338-9564-01
10 mL	0338-4212-10	0338-4303-10	0338-8402-10	0338-9568-01

TISSEEL Kit contains one vial each of:

- 1. Sealer Protein Concentrate (Human), Vapor Heated, Solvent/Detergent Treated, Freeze-Dried, Sterile
- 2. Fibrinolysis Inhibitor Solution, (Synthetic) Liquid, Sterile
- 3. Thrombin (Human), Vapor Heated, Solvent/Detergent Treated, Freeze-Dried, Sterile
- 4. Calcium Chloride Solution, Liquid, Sterile

TISSEEL Pre-Filled Dual-Chambered Syringe contains:

- 1. Sealer Protein Solution, Vapor Heated, Solvent/Detergent Treated, Frozen Solution, Sterile
- 2. Thrombin Solution, Vapor Heated, Solvent/Detergent Treated, Frozen Solution, Sterile
- 3. Sterile accessory devices (DUO Set and Plunger or DUPLOJECT COMBI)

#### Storage and Handling

TISSEEL Kit (Freeze-Dried)

Store at 2-25°C. Avoid freezing. Do not freeze or refrigerate reconstituted solutions.

TISSEEL Pre-filled Syringe (Frozen)

Store at  $\leq$  -20°C. Do not refrigerate or re-freeze after thawing. Once removed from the freezer, TISSEEL must be used within 48 hours. Prior to application, TISSEEL must be warmed to 33 - 37°C.

Once the pouches are opened or warmed to 33-37°C, they must be used within 4 hours.

Do not use after the expiration date. Discard if packaging of any components is damaged.

# **17 PATIENT COUNSELING INFORMATION**

Discuss the risks and benefits of this product with the patient since it is made from human plasma.

Instruct patients to consult their physician if symptoms of B19 virus infection appear (fever, drowsiness, chills and runny nose) followed about two weeks later by a rash and joint pain (see Use in Specific Populations (8.1)).

# Manufactured For Baxter Healthcare Corporation

Deerfield, IL 60015 USA US License No. 140

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# PACKAGE/LABEL PRINCIPAL DISPLAY PANEL



#### Fibrin Sealant TISSEEL 2 mL

NDC 0338-8402-01

#### Vapor Heated, Solvent/Detergent Treated, Frozen

#### Baxter Logo

#### Temperature sensitive - Do NOT expose above 37°C (99°F).

# **TOPICAL USE ONLY DO NOT INJECT**

Read directions for thawing and application before use.

Store at  $-20^{\circ}$ C ( $-4^{\circ}$ F) or colder. Unopened pouches may be stored for up to 48 hours at room temperature ( $15 - 25^{\circ}$ C).

#### Do not refrigerate or re-freeze.

**Rx Only** 

Contents:

#### Pre-filled syringe containing:

- Sealer Protein Solution (1): 1 mL, sterile
- Sealer Protein (Human)
- Fibrinolysis Inhibitor (Aprotinin, Synthetic), 3000 KIU/mL
- Thrombin Solution (2): 1 mL, sterile
- Thrombin (Human), 500 units/mL
- Calcium Chloride, 40 µmol/mL

#### DMC

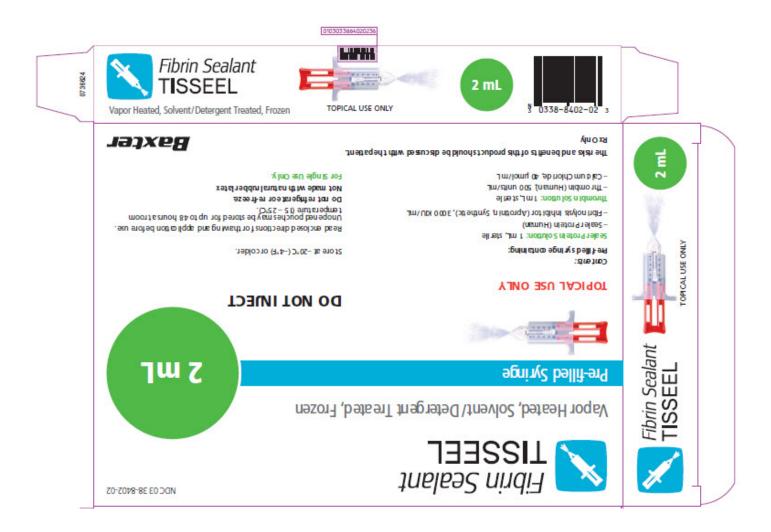
Manufactured for Baxter Healthcare Corporation Deerfield, IL 60015 USA

U.S. License No. 140 0736623

Lot No.:

Exp. Date:

Ρ





Tisseel Frozen 2 mL AST Carton Label

# 0736624

Fibrin Sealant **TISSEEL** 

Vapor Heated, Solvent/Detergent Treated, Frozen

TOPICAL USE ONLY

# 2 mL

N3 0338-8402-02 3

Fibrin Sealant **TISSEEL** 

TOPICAL USE ONLY

#### 2 mL

Fibrin Sealant TISSEEL

Vapor Heated, Solvent/Detergent Treated, Frozen

NDC 0338-8402-02

Prefilled Syringe

2 mL

# TOPICAL USE ONLY

#### Contents: Pre-filled syringe containing:

#### Sealer Protein Solution: 1 mL, sterile

- Sealer Protein (Human)
- Fibrinolysis Inhibitor (Aprotinin, Synthetic), 3000 KIU/mL

# Thrombin Solution: 1 mL, sterile

- Thrombin (Human), 500 units/mL
- Calcium Chloride, 40 μmol/mL

The risks and benefits of this product should be discussed with the patient.

Rx Only

# DO NOT INJECT

Store at -20°C (-4°F) or colder.

Read enclosed directions for thawing and application before use.

Unopened pouches may be stored for up to 48 hours at room temperature (15 –  $25^{\circ}$ C).

# Do not refrigerate or re-freeze.

# Not made with natural rubber latex

# For Single Use Only.

# Baxter Logo

Fibrin Sealant **TISSEEL** 

TOPICAL USE ONLY

# 2 mL

Fibrin Sealant **TISSEEL** 

TOPICAL USE ONLY

2 mL

# Baxter Logo

# 736624

Fibrin Sealant **TISSEEL** 

Vapor Heated, Solvent/Detergent Treated, Frozen

Pre-filled Syringe

#### 2 mL

#### TOPICAL USE ONLY DO NOT INJECT

U.S. Pat. No.: 5,962,405

#### Manufactured for Baxter Healthcare Corporation

Deerfield IL, 60015 USA 1-888-229-0001 U.S. License No. 140 Made in Austria

Reorder Number: 1501261

Baxter and Tisseel are trademarks of Baxter International Inc.

#### **Baxter Logo**





NDC 0338-4210-02

#### Fibrin Sealant TISSEEL 2 mL Vapor Heated, Solvent/Detergent Treated, Kit

GTIN (01) LOT (10) EXPIRY (17) SERIAL (21)

#### **Baxter Logo**

NDC 0338-4210-02

Barcode

Fibrin Sealant TISSEEL 2 mL Vapor Heated, Solvent/Detergent Treated, Kit

Contents:

**Sealer Protein Concentrate** (Human), Vapor Heated, Solvent/Detergent Treated, freeze dried, sterile, for 1 mL of Sealer Protein Solution 86.5 mg/mL

**Fibrinolysis Inhibitor Solution** (Synthetic), sterile, 3000 KIU of Aprotinin /mL

**Thrombin** (Human), Vapor Heated, Solvent/Detergent Treated, freeze dried, sterile, for 1 mL of Thrombin Solution 500 units/mL

#### Calcium Chloride Solution, sterile, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of reconstitution.

#### NOT FOR INJECTION. For single use only.

Not made with natural rubber latex

Rx only

# Manufactured for Baxter Healthcare Corporation

Deerfield, IL 60015 USA

U.S. License No. 140

Made in Austria

U.S. Pat. No.: 5,962,405

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0752668

Fibrin Sealant TISSEEL 2 mL Vapor Heated, Solvent/ Detergent Treated, Kit

#### 2 mL

Store at 2°C to 25°C (36°F to 77°F). Avoid freezing.







NDC 0338-4301-02





Vapor Heated, Solvent / Detergent Treated, Kit

#### Contents:

Sealer Protein Concentrate (Human), Vapor Heated, Solvent/Detergent Treated, freeze dried, sterile, for 1 mL of Sealer Protein Solution 86.5 mg/mL

Fibrinolysis Inhibitor Solution (Synthetic), sterile, 3000 KIU of Aprotinin/mL

Thrombin (Human), Vapor Heated, Solvent/Detergent Treated, freeze dried, sterile, for 1 mL of Thrombin Solution 500 units/mL

Calcium Chloride Solution, sterile, 40 µmol/mL

The risks and benefits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of reconstitution.

**Fibrin Sealant** 

TISSEEL 2 mL

NOT FOR INJECTION. For single use only. Not made with natural rubber latex Ex only

Also includes: DUPLOJECT Fibrin Sealant Preparation and Application System 2 mL / 4 mL

0752670





#### Tisseel Lyo 2mL Sleeve Carton Label

#### **Baxter Logo**

NDC 0338-4301-02

Fibrin Sealant TISSEEL 2 mL Vapor Heated, Solvent/Detergent Treated, Kit

#### Manufactured for Baxter Healthcare Corporation Deerfield, IL 60015 USA

U.S. License No. 140

Made in Austria

#### Reorder Number: 1504514

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U.S. Pat. No.: 5,962,405

**Baxter Logo** 

#### NDC 0338-4301-02

Fibrin Sealant TISSEEL 2 mL Vapor Heated, Solvent/Detergent Treated, Kit

#### TOPICAL USE ONLY DO NOT INJECT

#### **Baxter Logo**

NDC 0338-4301-02

Barcode

#### Fibrin Sealant TISSEEL 2 mL Vapor Heated, Solvent/Detergent Treated, Kit

Contents:

**Sealer Protein Concentrate** (Human), Vapor Heated, Solvent/Detergent Treated, freeze dried, sterile, for 1 mL of Sealer Protein Solution 86.5 mg/mL

**Fibrinolysis Inhibitor Solution** (Synthetic), sterile, 3000 KIU of Aprotinin /mL

**Thrombin** (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 1 mL of Thrombin Solution 500 units/mL

#### Calcium Chloride Solution, sterile, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of reconstitution.

#### NOT FOR INJECTION. For single use only.

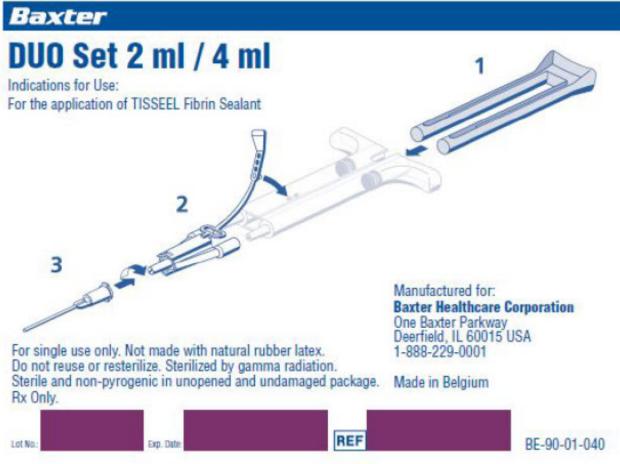
Not made with natural rubber latex Rx only

Also includes: DUPLOJECT Fibrin Sealant Preparation and Application System 2 mL / 4 mL

0752670

Barcode

Barcode N3 0338-4301-02 3



Tisseel Frozen 2 mL - 4 mL DUO Set Label

# Baxter Label

# DUO Set 2 ml / 4ml

Indications for Use:

For the application of TISSEEL Fibrin Sealant

For single use only. Not made with natural rubber latex.

Do not reuse or resterilize. Sterilized by gamma radiation.

Sterile and non-pyrogenic in unopened and undamaged package.

Rx only.

Lot No:

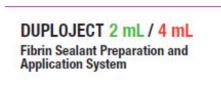
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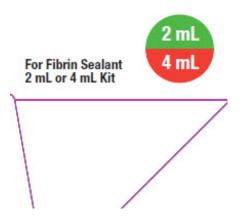
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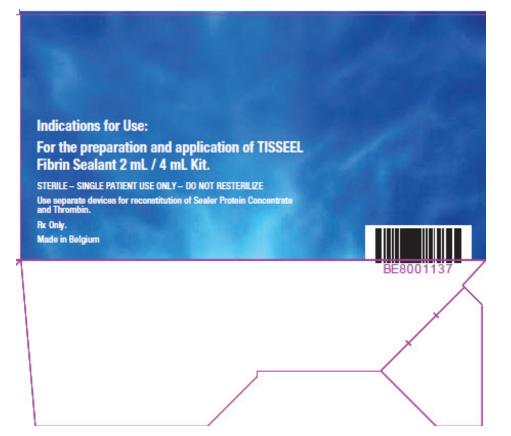
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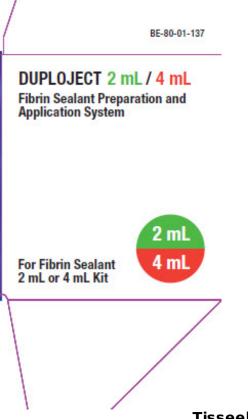
Manufactured for: **Baxter Healthcare Corporation,** One Baxter Parkway Deerfield, IL 60015 USA

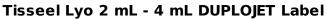












#### **Baxter Logo**

DUPLOJET 2 mL / 4 mL

Fibrin Sealant Preparation and Application System

**Baxter Logo** 

DUPLOJET 2 mL / 4 mL

# Fibrin Sealant Preparation and Application System

BAXTER, DUPLOJET and TISSEEL are trademarks of Baxter International Inc., registered in the U.S. Patent and Trademark office.

Manufactured for: **Baxter Healthcare Corporation** One Baxter Parkway Deerfield, IL 60015 USA

DUPLOJET 2 mL / 4 mL Fibrin Sealant Preparation and Application System

For Fibrin Sealant 2 mL or 4 mL Kit 2 mL 4 mL

Indications for Use: For the preparation and application of TISSEEL [Fibrin Sealant] 2 mL / 4 mL Kit.

STERILE - SINGLE PATIENT USE ONLY - DO NOT RESTERILIZE

Use separate devices for reconstruction of Sealer Protein Concentrate and Thrombin.

Rx only

Made in Belgium

Barcode

BE8001137

BE-80-01-137

DUPLOJET 2 mL / 4 mL Fibrin Sealant Preparation and Application System

For Fibrin Sealant 2 mL or 4 mL Kit

2 mL 4 mL

# Baxter

# DUPLOJECT

# Fibrin Sealant Preparation and Application System

Indications for Use: For the preparation and application of TISSEEL Fibrin Sealant kit.

Note: See TISSEEL Fibrin Sealant package insert for additional preparation and application instructions.

- 1.0 Reconstitution Instructions for the Circulating Nurse (Using the FIBRINO-THERM Heating and Stirring Device)
- 1.1 Turn on the warming unit of the FIBRINOTHERM device (amber switch).
- 1.2 Open TISSEEL Fibrin Sealant kit and place all vials into the appropriately sized heating wells of the FIBRINOTHERM device.
- 1.3 Place the Sealer Protein vial into the large magnetic stirring well fitted with the appropriately sized adapter ring (if necessary). Do not activate the stirring mechanism at this time. The indicator light will remain lit until a temperature of 37°C (98.6°F) is reached. Allow several minutes for proper warming.
- 1.4 Open Pack A of the DUPLOJECT Preparation and Application System and assemble the blue-scaled and black-scaled syringes with the needles provided.
- 1.5 Remove the flip-off caps from the blue-capped Sealer Protein Concentrate and Fibrinolysis Inhibitor Solution vials and wipe with a non-iodine based disinfectant.
- 1.6 Using the blue-scaled syringe, withdraw the Fibrinolysis Inhibitor Solution from the vial, tilting the vial slightly to facilitate removal of all solution. Inject the Fibrinolysis Inhibitor Solution into the Sealer Protein Concentrate vial. Gently swirl the vial to ensure that the freeze-dried material is fully soaked. Note: Do not invert or inject air into vials.
- 1.7 Place the Sealer Protein Concentrate vial in the stirring well and activate the stirring mechanism of the EIRPINOTHERM device (green switch). Reconstitution

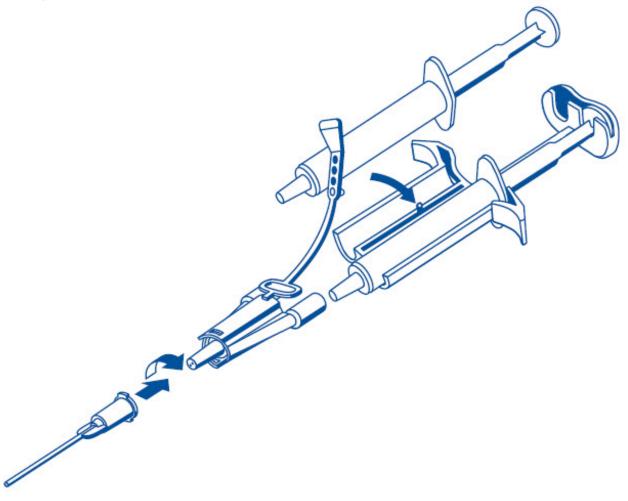
is complete when no undissolved particles are visible. If Sealer Protein is not fully dissolved after 20 minutes, discard and prepare a fresh kit. Continue with steps 8 through 11.

- 1.8 Remove the flip-off caps from the black-capped Thrombin and Calcium Chloride Solution vials and wipe with a non-iodine based disinfectant.
- 1.9 Using the black-scaled syringe, withdraw the Calcium Chloride Solution from the vial, tilting the vial slightly to facilitate removal of all solution. Inject the Calcium Chloride Solution into the Thrombin vial. Note: Do not invert or inject air into vials.
- 1.10 Swirl contents of the Thrombin vial briefly and return it to an appropriately sized heating well in the FIBRINOTHERM device.
- 1.11 Leave the Sealer Protein and Thrombin vials in the FIBRINOTHERM device until the solutions are ready to be passed into the sterile field.

#### 2.0 Preparation Instructions for the Scrub Nurse

- 2.1 Open Pack B of the DUPLOJECT Preparation and Application System into the sterile field.
- 2.2 Open Packs 1, 2, and 3.
- 2.3 Assemble the blue-scaled and black-scaled syringes with the needles provided. Note: For 10 mL DUPLOJECT systems, attach the larger needle to the bluescaled syringe.
- 2.4 While the Circulating Nurse holds the vial slightly tilted, insert needle into vial (bevel side down) and withdraw all of the Sealer Protein Solution into the blue-scaled syringe using slow, constant aspiration. Discard needle in sharps container.
- 2.5 While the Circulating Nurse holds the vial slightly tilted, insert needle into vial (bevel side down) and withdraw all of the Thrombin Solution into the black-scaled syringe using slow, constant aspiration. Discard needle in sharps container.
- 2.6 Remove any air bubbles from the syringes and ensure both syringes contain the same volume.

2.7 Snap the filled syringes into the two-syringe clip with the flanges in an up/down position, as illustrated below.



- 2.8 Attach the joining piece to the syringe nozzles, ensuring that both are firmly seated. Secure the joining piece by fastening the retaining strap to the double syringe clip. Note: For 10 ml DUPLOJECT systems, align the syringe nozzles toward the middle for proper attachment.
- 2.9 Fit one of the application cannulas onto the joining piece. A second application cannula is provided in Pack 3 as a spare.
- 2.10 DUPLOJECT Applicator is ready for use.
- 2.11 If application of TISSEEL Fibrin Sealant is interrupted, replace the cannula immediately before application is resumed. Note: If the apertures of the joining piece become clogged, Pack 4 contains one spare joining piece and two additional application cannulas.

Rx Only. DO NOT REUSE OR RESTERILIZE. NOT MADE WITH NATURAL RUBBER LATEX. STERILE AND NON-PYROGENIC IN UNOPENED AND UNDAMAGED PACKAGE. DISPOSE OF CONTAMINATED AND SHARP COMPONENTS PROPERLY.

• •

Baxter, Duploject, Fibrinotherm and Tisseel are registered trademarks of Baxter International Inc.

Manufactured for: Baxter Healthcare Corporation One Baxter Parkway Deerfield, IL 60015 USA 1-888-229-0001

Made in Belgium

Rev. Date: 2017-05-17

# **Baxter Logo**

BE 30-02-680

#### DUPLOJECT Fibrin Sealant Preparation and Application System

Indications for Use:

For the preparation and application of TISSEEL [Fibrin Sealant] kit.

## Note: See TISSEEL Fibrin Sealant package insert for additional preparation and

## application instructions.

### 1.0 Reconstitution Instructions for the Circulating Nurse (Using the FIBRINO-THERM Heating and Stirring Device)

1.1 Turn on the warming unit of the FIBRINOTHERM device (amber switch).

1.2 Open TISSEEL [Fibrin Sealant] kit and place all vials into the appropriately sized heating wells of the FIBRINOTHERM device.

1.3 Place the Sealer Protein vial into the large magnetic stirring well fitted with the appropriately sized adapter ring (if necessary). Do not activate the stirring mechanism at this time. The indicator light will remain lit until a temperature of 37°C (98.6°F) is reached. Allow several minutes for proper warming.

1.4 Open Pack A of the DUPLOIECT Preparation and Application System and assemble the blue-scaled and black-scaled syringes with the needles provided.

1.5 Remove the flip-off caps from the blue-capped Sealer Protein Concentrate and Fibrinolysis Inhibitor Solution vials and wipe with a non-iodine based disinfectant.

1.6 Using the blue-scaled syringe, withdraw the Fibrinolysis Inhibitor Solution from the vial, tilting the vial slightly to facilitate removal of all solution. Inject the Fibrinolysis Inhibitor Solution into the Sealer Protein Concentrate vial. Gently swirl the vial to ensure that the freeze-dried material is fully soaked. Note: Do not invert or inject air into vials.

1.7 Place the Sealer Protein Concentrate vial in the stirring well and activate the stirring mechanism of the FIBRINOTHERM device (green switch). Reconstitution is complete when no undissolved particles are visible. If Sealer Protein is not fully dissolved after 20 minutes, discard and prepare a fresh kit. Continue with steps 8 through 11.

1.8 Remove the flip-off caps from the black-capped Thrombin and Calcium Chloride Solution vials and wipe with a non-iodine based disinfectant.

1.9 Using the black-scaled syringe, withdraw the Calcium Chloride Solution from the vial, tilting the vial slightly to facilitate removal of all solution. Inject the Calcium Chloride Solution into the Thrombin vial. Note: Do not invert or inject air into vials.

1.10 Swirl contents of the Thrombin vial briefly and return it to an appropriately sized heating well in the FIBRINOTHERM device.

1.11 Leave the Sealer Protein and Thrombin vials in the FIBRINOTHERM device until

the solutions are ready to be passed into the sterile field.

## 2.0 Preparation Instructions for the Scrub Nurse

2.1 Open Pack B of the DUPLOJECT Preparation and Application System into the sterile field.

2.2 Open Packs 1, 2, and 3.

2.3 Assemble the blue-scaled and black-scaled syringes with the needles provided. Note: For 5 mL DUPLOJECT systems, attach the larger needle to the blue-scaled syringe.

2.4 While the Circulating Nurse holds the vial slightly tilted, insert needle into vial (bevel side down) and withdraw all of the Sealer Protein Solution into the blue-scaled syringe using slow, constant aspiration. Discard needle in sharps container.

2.5 While the Circulating Nurse holds the vial slightly tilted, insert needle into vial (bevel side down) and withdraw all of the Thrombin Solution into the black-scaled syringe using slow, constant aspiration. Discard needle in sharps container.

2.6 Remove any air bubbles from the syringes and ensure both syringes contain the same volume.

2.7 Snap the filled syringes into the two-syringe clip with the flanges in an up/down position, as illustrated below.

2.8 Attach the joining piece to the syringe nozzles, ensuring that both are firmly seated. Secure the joining piece by fastening the retaining strap to the double syringe clip. Note: Align the syringe nozzles toward the middle for proper attachment.

2.9 Fit one of the application needles onto the joining piece. A second application needle is provided in Pack 3 as a spare.

2.10 DUPLOJECT Applicator is ready for use.

2.11 If application of TISSEEL [Fibrin Sealant] is interrupted, replace the needle immediately before application is resumed. Note: If the apertures of the joining piece become clogged, Pack 4 contains one spare joining piece and two additional application needles.

Rx Only DO NOT REUSE OR RESTERILIZE. NOT MADE WITH NATURAL RUBBER LATEX.

STERILE AND NON-PYROGENIC IN UNOPENED AND UNDAMAGED PACKAGE.

DISPOSE OF CONTAMINATED AND SHARP COMPONENTS PROPERLY.

Baxter, Duploject, Fibrinotherm and Tisseel are registered trademarks of Baxter International Inc.

Manufactured for: **Baxter Healthcare Corporation** One Baxter Parkway Deerfield, IL 60015 USA 1-888-229-0001 Made in Belgium Rev. Date: 2017-05-17



#### Fibrin Sealant TISSEEL 2 mL

NDC 0338-9560-01

#### Vapor Heated, Solvent/Detergent Treated, Frozen

#### **Baxter Logo**

#### Temperature sensitive - Do NOT expose above 37°C (99°F).

### TOPICAL USE ONLY DO NOT INJECT

Read directions for thawing and application before use. Store at  $-20^{\circ}$ C ( $-4^{\circ}$ F) or colder. Unopened pouches may be stored for up to 48 hours at room temperature (15 - 25°C).

#### Do not refrigerate or re-freeze.

Rx Only

Contents:

#### Pre-filled syringe containing:

- Sealer Protein Solution (1): 1 mL, sterile

- Fibrinogen (Human), 86.5 mg/mL
- Fibrinolysis Inhibitor (Aprotinin,

Synthetic), 3000 KIU/mL

### - Thrombin Solution (2): 1 mL, sterile

- Thrombin (Human), 500 units/mL
- Calcium Chloride, 40 ìmol/mL

Manufactured for Baxter Healthcare

## Corporation

Deerfield, IL 60015 USA U.S. License No. 140 0752652

#### Barcode

Lot No.: Exp. Date:





2 mL PRIMA Carton Label

#### 0752653

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY

NDC 0338-9560-01 Barcode

Barcode 3 03389 56001 2

2 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/Detergent Treated, Frozen with Pre-filled PRIMA Syringe

#### **TOPICAL USE ONLY**

Contents: Pre-filled syringe containing: Sealer Protein Solution: 1 mL, sterile

- Fibrinogen (Human), 86.5 mg/mL
- Fibrinolysis Inhibitor (Aprotinin, Synthetic),
   3000 KIU/mL

Thrombin Solution: 1 mL, sterile

- Thrombin (Human), 500 units/mL
- Calcium Chloride, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient.

Rx Only

## DO NOT INJECT

Store at -20°C (-4°F) or colder.

Read enclosed directions for thawing and application before use.

Unopened pouches may be stored for up to 48 hours at room temperature  $(15 - 25^{\circ}C)$ .

Do not refrigerate or re-freeze.

Not made with natural rubber latex For Single Patient Use Only.

NDC 0338-9560-01

Fibrin Sealant TISSEEL Vapor Heated, Solvent/Detergent Treated, Frozen TOPICAL USE ONLY 2 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY 2 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY 2 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/Detergent Treated, Frozen with Pre-filled PRIMA Syringe

**TOPICAL USE ONLY** 

## **DO NOT INJECT**

U.S. Pat. No.: 5,962,405

Manufactured for Baxter Healthcare Corporation

Deerfield IL, 60015 USA

1-888-229-0001

U.S. License No. 140

Made in Austria

Reorder Number: 1506078

Baxter and Tisseel are trademarks of Baxter International Inc.

## 2 mL

## GTIN (01) 00303389560012

EXPIRY (17) LOT (10) SERIAL (21)

#### **Baxter Logo**

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY 2 mL



4 mL PRIMA Pouch Label

Fibrin Sealant TISSEEL 4 mL

NDC 0338-9564-01

#### Barcode

## Vapor Heated, Solvent/Detergent Treated, Frozen

## Baxter Logo

## Temperature sensitive - Do NOT expose above 37°C (99°F).

## **TOPICAL USE ONLY DO NOT INJECT**

Read directions for thawing and application before use. Store at  $-20^{\circ}$ C ( $-4^{\circ}$ F) or colder. Unopened pouches may be stored for up to 48 hours at room temperature (15 - 25°C).

## Do not refrigerate or re-freeze.

Rx Only

Contents: **Pre-filled syringe containing:** - Sealer Protein Solution (1): 2 mL, sterile - Fibrinogen (Human), 86.5 mg/mL - Fibrinolysis Inhibitor (Aprotinin,

Synthetic), 3000 KIU/mL

### - Thrombin Solution (2): 2 mL, sterile

– Thrombin (Human), 500 units/mL

- Calcium Chloride, 40 μmol/mL

## Barcode

### Manufactured for Baxter Healthcare Corporation

Deerfield, IL 60015 USA U.S. License No. 140

0752656

Barcode

Lot No.: Exp. Date:





4 mL PRIMA Carton Label

#### 0752657

Barcode 3 03389 56401 0

Fibrin Sealant TISSEEL Vapor Heated, Solvent/Detergent Treated, Frozen TOPICAL USE ONLY with Pre-filled PRIMA Syringe

#### NDC 0338-9564-01

#### **TOPICAL USE ONLY**

Contents: Pre-filled syringe containing: Sealer Protein Solution: 2 mL, sterile - Fibrinogen (Human), 86.5 mg/mL - Fibrinolysis Inhibitor (Aprotinin, Synthetic), 3000 KIU/mL

Thrombin Solution: 2 mL, sterile - Thrombin (Human), 500 units/mL - Calcium Chloride, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient.

Rx Only

## **DO NOT INJECT**

Store at -20°C (-4°F) or colder.

Read enclosed directions for thawing and application before use.

Unopened pouches may be stored for up to 48 hours at room temperature  $(15 - 25^{\circ}C)$ .

Do not refrigerate or re-freeze.

Not made with natural rubber latex For Single Patient Use Only.

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY 4 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY 4 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY 4 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/Detergent Treated, Frozen with Pre-filled PRIMA Syringe

### **TOPICAL USE ONLY**

## **DO NOT INJECT**

U.S. Pat. No.: 5,962,405

Manufactured for Baxter Healthcare Corporation

Deerfield IL, 60015 USA

1-888-229-0001

U.S. License No. 140

Made in Austria

Reorder Number: 1506079

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#### 4 mL

### Baxter Logo

GTIN (01) 00303389564010 LOT (10) EXPIRY (17) SERIAL (21)



#### 10 mL PRIMA Pouch Label

#### Fibrin Sealant TISSEEL 10 mL

NDC 0338-9568-01

## Vapor Heated, Solvent/Detergent Treated, Frozen

### Baxter Logo

Temperature sensitive - Do NOT expose above 37°C (99°F).

## **TOPICAL USE ONLY DO NOT INJECT**

Read directions for thawing and application before use.

Store at  $-20^{\circ}$ C ( $-4^{\circ}$ F) or colder. Unopened pouches may be stored for up to 48 hours at room temperature (15 – 25°C).

## Do not refrigerate or re-freeze.

Rx Only

Contents:

## Pre-filled syringe containing:

- Sealer Protein Solution (1): 5 mL, sterile
- Fibrinogen (Human), 86.5 mg/mL
- Fibrinolysis Inhibitor (Aprotinin,
- Synthetic), 3000 KIU/mL

## - Thrombin Solution (2): 5 mL, sterile

- Thrombin (Human), 500 units/mL
- Calcium Chloride, 40 ìmol/mL

## Manufactured for

#### Baxter Healthcare Corporation

Deerfield, IL 60015 USA U.S. License No. 140

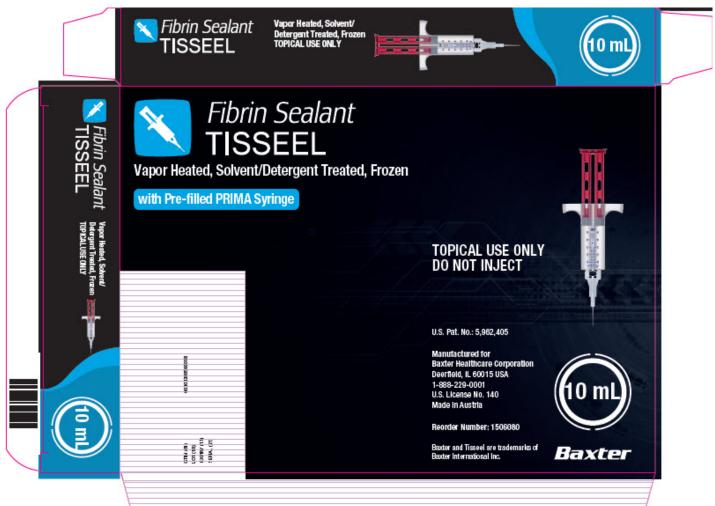
0752660

Barcode

Barcode

Lot No.: Exp. Date:





**10mL PRIMA Carton Label** 

#### 0752661

Barcode 3 03389 56801 8

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY

NDC 0338-9568-01 Barcode

10 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY

10 mL

**Fibrin Sealant** 

#### TISSEEL Vapor Heated, Solvent/Detergent Treated, Frozen with Pre-filled PRIMA Syringe

## **TOPICAL USE ONLY**

Contents: Pre-filled syringe containing: Sealer Protein Solution: 5 mL, sterile - Fibrinogen (Human), 86.5 mg/mL - Fibrinolysis Inhibitor (Aprotinin, Synthetic), 3000 KIU/mL

Thrombin Solution: 5 mL, sterile

– Thrombin (Human), 500 units/mL

- Calcium Chloride, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient.

Rx Only

## DO NOT INJECT

Store at -20°C (-4°F) or colder.

Read enclosed directions for thawing and application before use.

Unopened pouches may be stored for up to 48 hours at room temperature  $(15 - 25^{\circ}C)$ .

Do not refrigerate or re-freeze.

Not made with natural rubber latex

For Single Patient Use Only

#### Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen

TOPICAL USE ONLY

10 mL

Fibrin Sealant TISSEEL Vapor Heated, Solvent/ Detergent Treated, Frozen TOPICAL USE ONLY 10 mL

Barcode

Fibrin Sealant TISSEEL Vapor Heated, Solvent/Detergent Treated, Frozen

## with Pre-filled PRIMA Syringe

## **TOPICAL USE ONLY**

## **DO NOT INJECT**

U.S. Pat. No.: 5,962,405

Manufactured for Baxter Healthcare Corporation

Deerfield IL, 60015 USA

1-888-229-0001

U.S. License No. 140

Made in Austria

Reorder Number: 1506080

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## 10 mL

## **Baxter Logo**

GTIN (01) 00303389568018 EXPIRY (17) LOT (10) SERIAL (21)





GTIN (01) LOT (10)

EXPIRY (17)

SERIAL (21)

NDC 0338-4211-04

Fibrin Sealant TISSEEL 4 mL Vapor Heated, Solvent/Detergent Treated, Kit

#### Baxter logo

NDC 0338-4211-04 barcode

#### Fibrin Sealant TISSEEL 4 mL Vapor Heated, Solvent/Detergent Treated, Kit

Contents: Sealer Protein Concentrate (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 2 mL of Sealer Protein Solution Fibrinolysis Inhibitor Solution (Synthetic), sterile, 3000 KIU of Aprotinin /mL Thrombin (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 2 mL of Thrombin Solution 500 units/mL Calcium Chloride Solution, sterile, 40 µmol /mL The risks and benefits of this product should be discussed with the patient.

Read enclosed directions for reconstitution and application before use.

Use within four hours of reconstitution.

## NOT FOR INJECTION. For single use only.

Not made with natural rubber latex Rx only

## Manufactured for Baxter Healthcare Corporation

Deerfield, IL 60015 USA

U.S. License No. 140

Made in Austria

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U.S. Pat. No.: 5,962,405

Barcode 0752678

Fibrin Sealant TISSEEL 4 mL Vapor Heated, Solvent/ Detergent Treated, Kit

## 4 mL

Store at 2°C to 25°C (36°F to 77°F). Avoid freezing.





GTIN (01) LOT (10)

EXPIRY (17)

SERIAL (21)

NDC 0338-4212-10

Fibrin Sealant TISSEEL 10 mL Vapor Heated, Solvent/Detergent Treated, Kit

#### Baxter Logo

NDC 0338-4212-10 barcode

#### Fibrin Sealant TISSEEL 10 mL Vapor Heated, Solvent/Detergent Treated, Kit

Contents:

**Sealer Protein Concentrate** (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 5 mL of Sealer Protein Solution 86.5 mg/mL

**Fibrinolysis Inhibitor Solution** (Synthetic), sterile, 3000 KIU of Aprotinin /mL

**Thrombin** (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 5 mL of Thrombin Solution 500 units/mL

## Calcium Chloride Solution, sterile, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of reconstitution.

## NOT FOR INJECTION. For single use only.

Not made with natural rubber latex

Rx only

## Manufactured for Baxter Healthcare Corporation

Deerfield, IL 60015 USA

U.S. License No. 140

Made in Austria

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U.S. Pat. No.: 5,962,405

Barcode

0752688

Fibrin Sealant TISSEEL 10 mL Vapor Heated, Solvent/ Detergent Treated, Kit

## 10 mL

Store at 2°C to 25°C (36°F to 77°F). Avoid freezing.





NDC 0338-4302-04

#### **Fibrin Sealant** TISSEEL 4 mL

Vapor Heated, Solvent/Detergent Treated, Kit

#### Contents:

Sealer Protein Concentrate (Human), Vapor Heated, Solvent/ Detergent Treated, freeze dried, sterile, for 2 mL of Sealer Protein Solution 86.5 mg/mL

Fibrinolysis Inhibitor Solution (Synthetic), sterile, 3000 KIU of Aprotinin / mL

Thrombin (Human), Vapor Heated, Solvent/Detergent Treated, freeze dried, sterile, for 2 mL of Thrombin Solution 500 units/mL

Calcium Chloride Solution, sterile, 40 µmol/mL

The risks and benefits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of econstitution. NOT FOR INJECTION. For single use only.

Not made with natural rubber latex Rx only

Also includes: DUPLOJECT Fibrin Sealant Preparation and Application System 2 mL / 4 mL

0752680







#### **Baxter Logo**

NDC 0338-4302-04

**Fibrin Sealant TISSEEL 4 mL** Vapor Heated, Solvent/Detergent Treated, Kit

Manufactured for Baxter Healthcare Corporation Deerfield, IL 60015 USA

U.S. License No. 140

Made in Austria

## Reorder Number: 1504515

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U.S. Pat. No.: 5,962,405

## Baxter Logo

NDC 0338-4302-04

#### Fibrin Sealant TISSEEL 4 mL Vapor Heated, Solvent/Detergent Treated, Kit

TOPICAL USE ONLY DO NOT INJECT

## Baxter Logo

NDC 0338-4302-04 barcode

#### Fibrin Sealant TISSEEL 4 mL Vapor Heated, Solvent/Detergent Treated, Kit

Contents:

**Sealer Protein Concentrate** (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 2 mL of Sealer Protein Solution 86.5 mg/mL

**Fibrinolysis Inhibitor Solution** (Synthetic), sterile, 3000 KIU of Aprotinin /mL

**Thrombin** (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 2 mL of Thrombin Solution 500 units/mL

### Calcium Chloride Solution, sterile, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of reconstitution.

## NOT FOR INJECTION. For single use only.

Not made with natural rubber latex

Rx only

# Also includes: DUPLOJECT Fibrin Sealant Preparation and Application System 2 mL / 4 mL

0752680



Barcode N3 0338-4302-04 4

Barcode



NDC 0338-4303-10 

#### **Fibrin Sealant** TISSEEL 10 mL Vapor Heated, Solvent/Detergent Treated, Kit

The risks and be refits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of reconstitution.

NOT FOR INJECTION. For single use only. Not made with natural rubber latex

Rx only



#### Contents:

Sealer Protein Concentrate (Human), Vapor Healed, Solvent/Detergent Treated, freeze dried, starile, for 5 mL of Sealer Protein Solution 86.5 mg/mL Fibrinolysis Inhibitor Solution (Synthetic), starile, 3000 KIU of A protinin / mL

Thrombia (Human), Vapor Heated, Solvent/Detergent Treated, freeze dried, slerile, for 5 mL of Thrombin Solution 500 units/mL

Calcium Chleride Solution, sterile, 40 µmol/mL

Also Includes: DUPLOJECT Fibrin Sealant Preparation and Application System 10 mL

0752690







Baxter Logo

NDC 0338-4303-10

**Fibrin Sealant** TISSEEL 10 mL Vapor Heated, Solvent/Detergent Treated, Kit

Manufactured for Baxter Healthcare Corporation

Deerfield, IL 60015 USA

U.S. License No. 140

Made in Austria

## Reorder Number: 1504516

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U.S. Pat. No.: 5,962,405

## Baxter Logo

NDC 0338-4303-10

Fibrin Sealant TISSEEL 10 mL Vapor Heated, Solvent/Detergent Treated, Kit

TOPICAL USE ONLY DO NOT INJECT

## Baxter Logo

NDC 0338-4303-10

Barcode

Fibrin Sealant TISSEEL 10 mL Vapor Heated, Solvent/Detergent Treated, Kit

Contents: **Sealer Protein Concentrate** (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 5 mL of Sealer Protein Solution 86.5 mg/mL

**Fibrinolysis Inhibitor Solution** (Synthetic), sterile, 3000 KIU of Aprotinin /mL

**Thrombin** (Human), Vapor Heated, Solvent /Detergent Treated, freeze dried, sterile, for 5 mL of Thrombin Solution 500 units/mL

Calcium Chloride Solution, sterile, 40 µmol /mL

The risks and benefits of this product should be discussed with the patient. Read enclosed directions for reconstitution and application before use. Use within four hours of reconstitution. **NOT FOR INJECTION. For single use only.** 

Not made with natural rubber latex Rx only

Also includes: DUPLOJECT Fibrin Sealant Preparation and Application System 10 mL

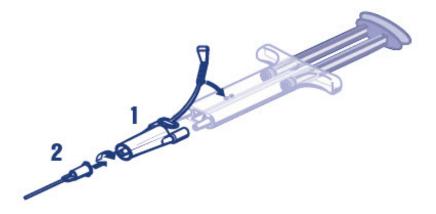
0752690

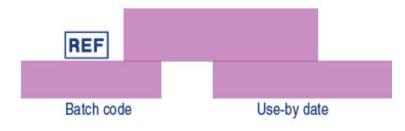
Barcode

Barcode N3 0338-4303-10 2



Indication for Use: For the application of TISSEEL Fibrin Sealant.





For single use only. Not made with natural rubber latex. Do not reuse or resterilize. Sterilized using ethylene oxide. Sterile and non-pyrogenic in unopened and undamaged package. Rx Only.

Manufactured for: Baxter Healthcare Corporation One Baxter Parkway Deerfield, IL 60015 USA 1-888-229-0001

BE-90-01-044

Made in Belgium

**Duploject Combi Label** 

#### Baxter Logo

## **DuploJect Combi**

Indication for Use: For the application of TISSEEL Fibrin Sealant.

#### REF

Batch code Use-by date

For single use only. Not made with natural rubber latex. Do not reuse or resterilize. Sterilized using ethylene oxide. Sterile and non-pyrogenic in unopened and undamaged package. Rx Only.

## Manufactured for:

#### **Baxter Healthcare Corporation** One Baxter Parkway Deerfield, IL 60015 USA

1-888-229-0001

Made in Belgium

BE-90-01-044

Produ	ict Inform	nation			
Produc	ct Type	PLAS MA DERIVATIVE	Item Code (Source)	NDC:0	338-4210
Packa	nging				
##	em ode	Package	Description	Marketing Start Date	Marketing End Date
				Start Batt	
1 NDC:0 4210-		CARTON; Type 9: Other Ty Drug/Device/Biological Pro	vpe of Part 3 Combination Product duct)		
4210-		Drug/Device/Biological Pro	vpe of Part 3 Combination Product duct)		
4210-	-02 (e.g.	Drug/Device/Biological Pro	duct)	oduct Quanti	
Quant	-02 (e.g.	Drug/Device/Biological Pro rts Package Quantity	duct)		
4210- Quant Part # Part 1	-02 (e.g.	Drug/Device/Biological Pro rts Package Quantity	duct) Total Pr		
Quant Part # Part 1 Part 2	-02 (e.g. t <b>ity of Pa</b> 1 VIAL, GLA	Drug/Device/Biological Pro rts Package Quantity SS SS	duct) Total Pr 1 mL		
4210- Quant	-02 (e.g. t <b>ity of Pa</b> 1 VIAL, GLA 1 VIAL, GLA	Drug/Device/Biological Pro rts Package Quantity SS SS SS	duct) Total Pr 1 mL 1 mL		
Quant Part # Part 1 Part 2 Part 3	-02 (e.g. t <b>ity of Pa</b> 1 VIAL, GLA 1 VIAL, GLA 1 VIAL, GLA	Drug/Device/Biological Pro rts Package Quantity SS SS SS	duct) Total Pr 1 mL 1 mL 1 mL 1 mL		
Quant Part # Part 1 Part 2 Part 3	-02 (e.g. t <b>ity of Pa</b> 1 VIAL, GLA 1 VIAL, GLA 1 VIAL, GLA	Drug/Device/Biological Pro rts Package Quantity SS SS SS	duct) Total Pr 1 mL 1 mL 1 mL 1 mL		

Pr	oduct Info	rmation					
lte	em Code (Sou	rce)	NDC:0338-7112				
Ro	ute of Admin	istration	TOPICAL				
Ac	tive Ingred	ient/Active	Moiety				
		Ingre	dient Name		Basis of Strength		Strength
	RINOGEN HUM II:N94833051K)	<b>1AN</b> (UNII: N948)	33051K) (FIBRINOGEN HUMAN -		FIBRINOGEN HUM	1AN	86.5 mg in 1 mL
Ina	active Ingre	edients					
		(1111)	Ingredient Name				Strength
	BUMIN HUMAN STIDINE (UNII: 4		∠ R)				
	ACINAMIDE (UNII: 4						
	LYSORBATE 80		ZG8H)				
TRI		ATE DIHYDRAT	E (UNII: B22547B95K)				
	ckaging			Mark	eting Start	Ma	nrketing End
#	ltem Code		ckage Description	Mark	Date	1.10	Date
	NDC:0338- 7112-01	1 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination				
M	arketing	Informat	ion				
1-1	Marketing Category	Applica	tion Number or Monograph Citation	Mark	eting Start Date	Ma	arketing End Date
	Category	Applica BLA103980		<b>Mark</b> 05/01/1	Date	Ma	
	Category				Date	Ma	
BLA	Category	BLA103980			Date	Ma	
ΒιΑ	Category	BLA103980			Date	Ma	-
BLA Pa	Category art 2 of 4 UMAN TH	BLA103980	Citation		Date	Ma	-
BLA Pa	Category	BLA103980	Citation		Date	Ma	
BLA Pa H	Category art 2 of 4 UMAN TH	BLA103980 IROMBIN n powder, for	Citation		Date	M	
BLA Pa Hu hu	Category art 2 of 4 UMAN TH man thrombin	BLA103980 BLA103980 ROMBIN n powder, for rmation	Citation		Date	M	-
BLA Pa Hu hu	Category a art 2 of 4 UMAN TH man thrombi	BLA103980 BLA103980 IROMBIN n powder, for rmation	Citation		Date	M	-

<b>Active Ingred</b>					
-	ient/Active	моюту			
	Ingre	dient Name		asis of rength	Strength
<b>HUMAN THROMBI</b> UNII:6K15ABL77G)	<b>N</b> (UNII: 6K15AB	L77G) (HUMAN THROMBIN -		THROMBIN	500 [iU] in 1 mL
Inactive Ingre	edients				
		Ingredient Name			Strength
ALBUMIN HUMAN					
SODIUM CHLORID	<b>DE</b> (UNII: 451W47	1Q8X)			
Packaging					
# Item Code	Pa	ckage Description	Marketing S Date	start	Marketing End Date
1 NDC:0338-		GLASS; Type 0: Not a Combination			
7332-01	Product				
Markating	Informat	ion			
Marketing					Mandar the or Ford
Marketing Category	Applicat	tion Number or Monograph Citation	Marketing S Date	start	Marketing End Date
BLA	BLA103980		05/01/1998		
Part 3 of 4					
FIBRINOLY		BITOR SOLUTION			
FIBRINOLY		BITOR SOLUTION			
FIBRINOLY		BITOR SOLUTION			
FIBRINOLY aprotinin liquid	SIS INHIE	BITOR SOLUTION			
FIBRINOLY aprotinin liquid	SIS INHIE	BITOR SOLUTION			
FIBRINOLY aprotinin liquid Product Infor	SIS INHIE	BITOR SOLUTION NDC:0338-7201			
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou	TSIS INHIE				
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou	TSIS INHIE	NDC:0338-7201			
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin	T <b>SIS INHIE</b> Trmation rce) istration	NDC:0338-7201			
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin	rmation rce) istration	NDC:0338-7201 TOPICAL		Street	ath
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin	TIS INHIE Tration rce) istration edients Ingred	NDC:0338-7201	3000 fill1 ir	Stren	gth
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin Inactive Ingre	rmation rce) istration edients ingred	NDC:0338-7201 TOPICAL	3000 [iU] ir		gth
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin Inactive Ingre	rmation rce) istration edients ingred	NDC:0338-7201 TOPICAL	3000 [iU] ir		gth
	rmation rce) istration edients ingred	NDC:0338-7201 TOPICAL		1 mL	
FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin Inactive Ingre APROTININ (UNII: ( WATER (UNII: 0590	rmation rce) istration edients ingred 04XPW8C0FL) QF0KO0R)	NDC:0338-7201 TOPICAL	3000 [iU] ir	1 mL	lgth Marketing End Date

7201-01	1	Due du et				
7201-01	1	Product				
Marke	tina	Informat	ion			
	-	Informat		<b>N4</b>		
	keting egory	Аррисат	tion Number or Monograph Citation	Marketiı Da		Marketing End Date
BLA		BLA103980		05/01/1998		
Part 4	l of 4					
CALCI	им с	HLORIDE	SOLUTION			
calcium		-				
		· ·				
Produc	t Infor	mation				
ltem Coc	de (Sou	rce)	NDC:0338-7401			
Route of	f Admin	istration	TOPICAL			
Inactive	e Ingre	edients				
		-	redient Name			Strength
		DE (UNII: M4I0D			40 umol in	•
		DE (UNII: M4I0D				•
		DE (UNII: M4I0D				-
WATER (U	JNII: 059C	DE (UNII: M4I0D				-
WATER (U Packag	JNII: 0590	DE (UNII: M4IOD QF0KO0R)	5VV5M)	Marketir	40 umol in	-
WATER (U Packag # Item	JNII: 0590 Jing Code	DE (UNII: M4IOD QFOKOOR) Pa	5VV5M) ckage Description	Marketir Da	40 umol in ng Start	1 mL
WATER (U Packag	JNII: 0590 Jing Code 338-	DE (UNII: M4IOD QFOKOOR) Pa	5VV5M)		40 umol in ng Start	1 mL Marketing End
WATER (U Packag # Item	JNII: 0590 Jing Code 338-	DE (UNII: M4IOD QF0KO0R) Pa 1 mL in 1 VIAL,	5VV5M) ckage Description		40 umol in ng Start	1 mL Marketing End
WATER (U Packag # Item	JNII: 0590 Jing Code 338-	DE (UNII: M4IOD QF0KO0R) Pa 1 mL in 1 VIAL,	5VV5M) ckage Description		40 umol in ng Start	1 mL Marketing End
WATER (U Packag # Item 1 NDC:03 7401-01	JNII: 0590 Jing Code 338- 1	DE (UNII: M4IOD QF0KO0R) Pa 1 mL in 1 VIAL,	GVV5M) ckage Description GLASS; Type 0: Not a Combination		40 umol in ng Start	1 mL Marketing End
WATER (U Packag # Item 1 NDC:03 7401-01 Marke Mark	JNII: 0590 Jing Code 338- 1 eting keting	DE (UNII: M4IOD FOKOOR) Pa 1 mL in 1 VIAL, Product	SVV5M) ckage Description GLASS; Type 0: Not a Combination iON tion Number or Monograph	Da Marketii	40 umol in ng Start te ng Start	1 mL Marketing End Date Marketing End
WATER (U Packag # Item 1 NDC:03 7401-01 Marke Cate	JNII: 0590 Jing Code 138- 1 2 38- 1 2 38- 1	DE (UNII: M4IOD OFOKOOR) Pa 1 mL in 1 VIAL, Product Informat Applicat	SVV5M) ckage Description GLASS; Type 0: Not a Combination ion	Da Marketii Da	40 umol in ng Start te ng Start	1 mL Marketing End Date
WATER (U Packag # Item 1 NDC:03 7401-01 Marke Cate	JNII: 0590 Jing Code 338- 1 eting keting	DE (UNII: M4IOD FOKOOR) Pa 1 mL in 1 VIAL, Product	SVV5M) ckage Description GLASS; Type 0: Not a Combination iON tion Number or Monograph	Da Marketii	40 umol in ng Start te ng Start	1 mL Marketing End Date Marketing End
WATER (U Packag # Item 1 NDC:03 7401-01 Marke Cate	JNII: 0590 Jing Code 338- 1 eting keting	DE (UNII: M4IOD OFOKOOR) Pa 1 mL in 1 VIAL, Product Informat Applicat	SVV5M) ckage Description GLASS; Type 0: Not a Combination iON tion Number or Monograph	Da Marketii Da	40 umol in ng Start te ng Start	1 mL Marketing End Date Marketing End
WATER (U Packag # Item 1 NDC:03 7401-01 Marke Cate BLA	JNII: 0590 Jing Code 338- 1 eting egory	DE (UNII: M4I0DO DFOKOOR) Pa 1 mL in 1 VIAL, Product Informat Applicat BLA103980	SVV5M) ckage Description GLASS; Type 0: Not a Combination ion tion Number or Monograph Citation	Da Marketii Da	40 umol in ng Start te ng Start	1 mL Marketing End Date Marketing End
WATER (U Packag # Item 1 NDC:03 7401-01 Marke BLA	JNII: 0590 Jing Code 338- 1 eting egory	DE (UNII: M4IOD FOKOOR) Pa 1 mL in 1 VIAL, Product Informat BLA103980 Informat	SVV5M) ckage Description GLASS; Type 0: Not a Combination ion tion Number or Monograph Citation	Da Marketii Da	40 umol in ng Start te	1 mL Marketing End Date Marketing End
WATER (U Packag # Item 1 NDC:03 7401-01 Mark Cate BLA	JNII: 0590 Jing Code 338- 1 eting egory	DE (UNII: M4IOD FOKOOR) Pa 1 mL in 1 VIAL, Product Informat BLA103980 Informat	SVV5M) ckage Description GLASS; Type 0: Not a Combination ion tion Number or Monograph Citation	Da Marketin Da 05/01/1998	40 umol in ng Start te ng Start te	1 mL Marketing End Date Marketing End Date

## TISSEEL FIBRIN SEALANT

Product Info	ormation				
Product Type	PLASM	A DERIVATIVE	Item Code (Source	NDC:0	338-4211
Packaging "Item				Markoting	Marketing
<sup>#</sup> Code		Package Descri	ption	Marketing Start Date	End Date
		/pe 9: Other Type of Pa //Biological Product)	rt 3 Combination Produc	ct	
Quantity of	Parts				
Part #	Package	Quantity		Product Quanti	ty
Part 1 1 VIAL, (			2 mL		
Part 2 1 VIAL, (			2 mL		
Part 3         1 VIAL, 0           Part 4         1 VIAL, 0			2 mL 2 mL		
SEALER P fibrinogen hur Product Info Item Code (So	ROTEIN C man powder, f ormation ource)	ONCENTRATE For solution	HUMAN		
Part 1 of 4 SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre	ROTEIN C man powder, f ormation ource) inistration	Topical	EHUMAN		
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi	ROTEIN Common powder, formation	Topical	EHUMAN	Basis of Strength	Strength
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre	ROTEIN C man powder, f ormation ource) inistration dient/Active Ingi	NDC:0338-7112 TOPICAL			Strength 86.5 mg in 1 mL
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre FIBRINOGEN HU UNIII:N94833051K	ROTEIN C man powder, f ormation ource) inistration dient/Active ing JMAN (UNII: N94	NDC:0338-7112 TOPICAL		Strength	86.5 mg
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre FIBRINOGEN HU UNIII:N94833051K	ROTEIN C man powder, f ormation ource) inistration dient/Active ing JMAN (UNII: N94	NDC:0338-7112 TOPICAL	HUMAN -	Strength	86.5 mg
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre FIBRINOGEN HU UNII:N94833051K	ROTEIN C man powder, f ormation ource) inistration dient/Active Ingu IMAN (UNII: N94 ) redients	For solution NDC:0338-7112 TOPICAL MOiety redient Name 833051K) (FIBRINOGEN Ingredient Nar	HUMAN -	Strength	86.5 mg in 1 mL
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre FIBRINOGEN HU UNII:N94833051K	ROTEIN C man powder, 1 ormation ource) inistration dient/Active ing UMAN (UNII: N94 ) redients	For solution NDC:0338-7112 TOPICAL MOiety redient Name 833051K) (FIBRINOGEN Ingredient Nar	HUMAN -	Strength	86.5 mg in 1 mL
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre FIBRINOGEN HU UNII:N94833051K Inactive Ingr ALBUMIN HUMA HISTIDINE (UNII: NIACINAMIDE (U	ROTEIN C man powder, f ormation ource) inistration dient/Active ing iMAN (UNII: N94 ) redients N (UNII: ZIF514F 4QD397987E) INII: 25X5118RD4	For solution NDC:0338-7112 TOPICAL MOiety redient Name 833051K) (FIBRINOGEN NATE	HUMAN -	Strength	86.5 mg in 1 mL
SEALER P fibrinogen hur Product Info Item Code (So Route of Admi Active Ingre FIBRINOGEN HU UNII:N94833051K Inactive Ingr ALBUMIN HUMA HISTIDINE (UNII: NIACINAMIDE (U POLYSORBATE 3	ROTEIN C man powder, 1 ormation ource) inistration dient/Active ingu MAN (UNII: N94 ) redients N (UNII: ZIF514F 4QD397987E) JNII: 25X5118RD4 80 (UNII: 60ZP3	For solution NDC:0338-7112 TOPICAL MOiety redient Name 833051K) (FIBRINOGEN NATE	HUMAN -	Strength	in 1 mL

Packaging				
# Item Code	Pa	ckage Description	Marketing Star Date	t Marketing End Date
<b>1</b> NDC:0338- 7112-02	2 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination		
Marketing	Informat	ion		
Marketing Category	Applica	tion Number or Monograph Citation	Marketing Star Date	t Marketing End Date
BLA	BLA103980		05/01/1998	
Part 2 of 4				
HUMAN TH	IROMBIN			
human thrombi	-	solution		
Product Info	mation			
Product Infoi Item Code (Sou		NDC:0338-7332		
Route of Admin		TOPICAL		
Route of Admin	Istration	IOFICAL		
Active Ingred	ient/Active	Moiety		
	Ingre	dient Name	Basis Streng	STENDT
HUMAN THROMBI UNII:6K15ABL77G)	<b>N</b> (UNII: 6K15AB	L77G) (HUMAN THROMBIN -	HUMAN THRO	MBIN 500 [iU] in 1 mL
Inactive Ingre	edients			
		Ingredient Name		Strength
ALBUMIN HUMAN				Strength
	(UNII: ZIF514RV	ZR)		Strength
	(UNII: ZIF514RV	ZR)		Strength
ALBUMIN HUMAN SODIUM CHLORIC <b>Packaging</b>	(UNII: ZIF514RV	ZR)		Strength
SODIUM CHLORIC	(UNII: ZIF514RV De (UNII: 451W47	ZR)	Marketing Star	t Marketing End
Packaging # Item Code	(UNII: ZIF514RV DE (UNII: 451W47 Pa 2 mL in 1 VIAL,	Z R) 7IQ8X)	Marketing Star Date	
Packaging # Item Code	(UNII: ZIF514RV DE (UNII: 451W47 Pa	ZR) 71Q8X) Ackage Description	-	t Marketing End
SODIUM CHLORID Packaging # Item Code	(UNII: ZIF514RV DE (UNII: 451W47 Pa 2 mL in 1 VIAL,	ZR) 71Q8X) Ackage Description	-	t Marketing End
Packaging # Item Code	(UNII: ZIF514RV DE (UNII: 451W47 Pa 2 mL in 1 VIAL, Product	ZR) 7IQ8X) CKage Description GLASS; Type 0: Not a Combination	-	t Marketing End

Category		Citation	I	Date	Date
BLA	BLA103980		05/01/199	98	
Part 3 of 4					
		BITOR SOLUTION			
aprotinin liquid	515 1111	Show Solo how			
Product Infor	mation				
ltem Code (Sou	rce)	NDC:0338-7201			
Route of Admini	istration	TOPICAL			
Inactive Ingre	dients				
	Ingred	ient Name		Str	ength
APROTININ (UNII: 0	4XPW8C0FL)		3000	[iU] in 1 mL	
WATER (UNII: 059Q	F0KO0R)				
Packaging					
# Item Code	Ра	ckage Description		ting Start Date	Marketing End Date
1 NDC:0338- 7201-02	2 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination			
Marketing	Informat	ion			
Marketing	Applica	tion Number or Monograph	Marke	ting Start	Marketing End
Category		Citation		Date	Date
BLA	BLA103980		05/01/199	98	
Part 4 of 4					
	-	SOLUTION			
calcium chloride	liquia				
Product Infor	mation				
Item Code (Sour	rce)	NDC:0338-7401			
Route of Admini	stration	TOPICAL			

		Ingredient Name		Strength
CA	ALCIUM CHLORI	<b>DE</b> (UNII: M4I0D6VV5M)	40 umol	-
	ATER (UNII: 0590			
Pa	ackaging			
#	ltem Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338- 7401-02	2 mL in 1 VIAL, GLASS; Type 0: Not a Con Product	mbination	
M	larketing	Information		
	Marketing Category	Application Number or Mono Citation	graph Marketing Start Date	Marketing End Date
ЗL	A	BLA103980	05/01/1998	
Μ	larketing	Information		
	Marketing Category	Application Number or Mono Citation	graph Marketing Start Date	Marketing End Date
BL	A	BLA103980	05/01/1998	
٦I	SSEEL FI	BRIN SEALANT		
		n, human thrombin kit		
b	rinogen huma	n, human thrombin kit		
ib		n, human thrombin kit		

Packaging							
#	em ode	Package Descri	Marketing Start Date	Marketing End Date			
	NDC:0338- 4212-101 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)						
Quant	ity of F	Parts					
Part #		Package Quantity	Total P	roduct Quantit	у		
Part 1	1 VIAL, G	LASS	5 mL				
Part 2	1 VIAL, G	LASS	5 mL				
Part 3	1 VIAL, G	LASS	5 mL				
Part 4	1 VIAL, G	LASS	5 mL				

# Part 1 of 4

# SEALER PROTEIN CONCENTRATE HUMAN

fibrinogen human powder, for solution

librinogen numa	in powder, io	Solution				
Product Infor	mation					
Item Code (Sou	rce)	NDC:0338-7112				
Route of Admini	istration	TOPICAL				
Active Ingred	ient/Active	Moiety				
	Ingre	dient Name		Basis of Strength		Strength
FIBRINOGEN HUM UNII:N94833051K)	<b>AN</b> (UNII: N9483	3051K) (FIBRINOGEN HUMAN -		FIBRINOGEN HUM		6.5 mg in 1 mL
Inactive Ingre	dients					
		Ingredient Name			9	Strength
ALBUMIN HUMAN		ZR)				
HISTIDINE (UNII: 40						
NIACINAMIDE (UNI POLYSORBATE 80		(684)				
		(UNII: B22547B95K)				
Packaging						
# Item Code	Pa	ckage Description	Mark	eting Start Date	Mar	keting End Date
1 NDC:0338- 7112-05	5 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination				
Marketing	Informati	ion				
Marketing Category		ion Number or Monograph Citation	Marl	keting Start Date	Mar	keting End Date
BLA	BLA103980		05/01/1			Butt
Part 2 of 4						
HUMAN TH						
human thrombir		solution				
Product Infor	mation					
Product Infor	mation					

	irce)	NDC:0338-7332				
Route of Admin	istration	TOPICAL				
Active Ingred	lient/Active	Moiety				
	Ingre	dient Name		Basis of Strength	Stron	gth
<b>HUMAN THROMBI</b> UNII:6K15ABL77G)	IN (UNII: 6K15AB	L77G) (HUMAN THROMBIN -		HUMAN THROMBI	IN 500 [iU] in 1 mL	
Inactive Ingre	edients					
		Ingredient Name			Strength	
ALBUMIN HUMAN						
SODIUM CHLORID	<b>JE</b> (UNII: 45104)	/1Q8X)				
Packaging						
# Item Code	Pa	ckage Description	Mark	eting Start Date	Marketing Date	End
1 NDC:0338- 7332-05	5 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination				
Marketing	Informat	ion				
Marketing		tion Number or Monograph	Mar	keting Start	Marketing	End
Marketing Category			<b>Mar</b> 05/01/1	Date	Marketing Date	End
Marketing Category BLA Part 3 of 4 FIBRINOLY	Applica BLA103980	tion Number or Monograph		Date	-	End
Marketing Category BLA Part 3 of 4 FIBRINOLY aprotinin liquid	Applica BLA103980	tion Number or Monograph Citation		Date	-	End
Marketing Category BLA Part 3 of 4 FIBRINOLY aprotinin liquid	Applica BLA103980	tion Number or Monograph Citation		Date	-	End
Marketing Category BLA Part 3 of 4 FIBRINOLY aprotinin liquid Product Infor Item Code (Sou	Applica BLA103980 SIS INHII	tion Number or Monograph Citation		Date	-	End
Marketing Category BLA Part 3 of 4 FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin	Applica BLA103980 SIS INHII SIS INHII Inrce) histration	tion Number or Monograph Citation		Date .998	Date	End
Marketing Category BLA Part 3 of 4 FIBRINOLY aprotinin liquid Product Infor Item Code (Sou Route of Admin	Applica BLA103980 SIS INHII (SIS INHII) (SIS INHII) (S	tion Number or Monograph Citation	05/01/1	Date .998 Stre	-	End
Marketing Category BLA Part 3 of 4	Applica BLA103980 SIS INHII SIS INHII Contemporation Contemporatio	tion Number or Monograph Citation	05/01/1	Date .998	Date	End

Packaging					
# Item Code	Pa	ckage Description	Marketin Dat		Marketing End Date
<b>1</b> NDC:0338- 7201-05	5 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination	Dat	e	Date
Marketing	Informat	ion			
Marketing Category	Applica	tion Number or Monograph Citation	Marketin Dat	-	Marketing End Date
BLA	BLA103980		05/01/1998		
Part 4 of 4					
CALCIUM C	HLORIDE	SOLUTION			
calcium chloride	e liquid				
Due due to buf					
Product Infor		NDC:0338-7401			
Item Code (Sou Route of Admin		TOPICAL			
Route of Admin	Istration	IOFICAL			
Inactive Ingre					
CALCIUM CHLORI		redient Name		40 umol in	Strength
WATER (UNII: 0590					1 1 1112
Packaging			Markatin	a Start	Markating End
# Item Code	Pa	ckage Description	Marketin Dat		Marketing End Date
<b>1</b> NDC:0338- 7401-05	5 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination			
Marketing	Informat	ion			
Marketing Category	Applica	tion Number or Monograph Citation	Marketin Dat		Marketing End Date
	BLA103980		05/01/1998		
BLA					
BLA					
Marketing		ion			

05/01/1998

Product Information				
Product Type PLA	SMA DERIVATIVE	Item Code (Source	) NDC:03	338-4301
Packaging				
# Item	Package Descri	ption	Marketing	Marketing
<ul> <li>Code</li> <li>NDC:0338- 4301-02</li> <li>I in 1 CARTON; (e.g., Drug/Dev</li> </ul>			Start Date	End Date
(e.g., brug, bet				
Quantity of Parts				
Part # Packag	ge Quantity	Total	Product Quantit	:y
Part 1 1 VIAL, GLASS		1 mL		
Part 2 1 VIAL, GLASS		1 mL		
Part 31 VIAL, GLASSPart 41 VIAL, GLASS		1 mL		
SEALER PROTEIN		HUMAN		
SEALER PROTEIN fibrinogen human powde		HUMAN		
SEALER PROTEIN fibrinogen human powde Product Information		HUMAN		
SEALER PROTEIN fibrinogen human powde Product Information Item Code (Source)	r, for solution	HUMAN		
SEALER PROTEIN fibrinogen human powde Product Information Item Code (Source) Route of Administration	r, for solution NDC:0338-7112 TOPICAL	EHUMAN		
SEALER PROTEIN fibrinogen human powde Product Information Item Code (Source) Route of Administration	r, for solution NDC:0338-7112 TOPICAL	EHUMAN	Basis of Strength	Strength
SEALER PROTEIN fibrinogen human powde Product Information Item Code (Source) Route of Administration Active Ingredient/Act In FIBRINOGEN HUMAN (UNII: N	r, for solution NDC:0338-7112 TOPICAL			Strength 86.5 mg in 1 mL
SEALER PROTEIN fibrinogen human powde Product Information Item Code (Source) Route of Administration Active Ingredient/Acti In FIBRINOGEN HUMAN (UNII: N UNII: N94833051K)	r, for solution NDC:0338-7112 TOPICAL		Strength	86.5 mg
Part 1 of 4 SEALER PROTEIN fibrinogen human powde Product Information Item Code (Source) Route of Administration Active Ingredient/Acti In FIBRINOGEN HUMAN (UNII: N UNII: N94833051K)	r, for solution NDC:0338-7112 TOPICAL	HUMAN -	Strength	

NIACINAMIDE (UN					
POLYSORBATE 80					
	ATE DIHYDRAT	<b>E</b> (UNII: B22547B95K)			
Packaging					
# Item Code	Pa	ckage Description	Marketing Date	Start	Marketing End Date
NDC:0338- 7112-01	1 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination			
Marketing	Informat	ion			
Marketing Category	Applica	tion Number or Monograph Citation	Marketing Date	Start	Marketing End Date
BLA	BLA103980		05/01/1998		
Part 2 of 4					
HUMAN TH	ROMBIN				
numan thrombi	n powder, for	solution			
Product Info	rmation				
ltem Code (Sou	rce)	NDC:0338-7332			
Route of Admin	istration	TOPICAL			
	•••••				
Active Ingred	ient/Active	Μοιετγ	в	asis of	
	Ingre	dient Name		trength	Strength
<b>HUMAN THROMBI</b> JNII:6K15ABL77G)	<b>N</b> (UNII: 6K15AB	L77G) (HUMAN THROMBIN -	HUMAN	THROMBIN	500 [iU] in 1 mL
nactive Ingre	edients				
		Ingredient Name			Strength
SODIUM CHLORID	E (UNII: 451W4)	(1Q0A)			
Packaging					
Packaging # Item Code	Pa	ckage Description	Marketing	Start	Marketing End
		GLASS; Type 0: Not a Combination	Marketing Date	Start	Marketing End Date

Marketing	Informat	ion		
Marketing Category	Applica	tion Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA103980		05/01/1998	
Part 3 of 4				
FIBRINOLY	SIS INHI	BITOR SOLUTION		
aprotinin liquid				
Product Infor	rmation			
ltem Code (Sou	rce)	NDC:0338-7201		
Route of Admin	istration	TOPICAL		
Inactive Ingre				
	-	lient Name		ength
	04XPW8C0FL)		3000 [iU] in 1 mL	
<b>WATER</b> (UNII: 0590	QF0KO0R)			
Packaging		ackage Description	Marketing Start	
Packaging # Item Code	Pa	ackage Description	Marketing Start Date	Marketing End Date
Packaging # Item Code	Pa			
Hermitian     Hermitian       Item Code       NDC:0338- 7201-01	Pa 1 mL in 1 VIAL, Product	, GLASS; Type 0: Not a Combination		
Packaging   #   Item Code   1   NDC:0338-   201-01   Marketing	Pa 1 mL in 1 VIAL, Product Informat	GLASS; Type 0: Not a Combination		Date
Packaging # Item Code 1 NDC:0338- 7201-01	Pa 1 mL in 1 VIAL, Product Informat	, GLASS; Type 0: Not a Combination	Date Marketing Start Date	Date
Packaging       #     Item Code       1     NDC:0338- 7201-01       NDC:0338- 7201-01     NDC:0338- 7201-01	Pa 1 mL in 1 VIAL, Product Informat	GLASS; Type 0: Not a Combination	Date Marketing Start	Marketing End
Packaging         Item Code         Image: Display structure         Image: Display structure	Pa 1 mL in 1 VIAL, Product Informat Applica	GLASS; Type 0: Not a Combination	Date Marketing Start Date	Date Marketing End
Packaging # Item Code 1 NDC:0338- 7201-01 Marketing Category BLA	Pa 1 mL in 1 VIAL, Product Informat Applica BLA103980	GLASS; Type 0: Not a Combination	Date Marketing Start Date	Date Marketing End
Packaging # Item Code 1 NDC:0338- 7201-01 Marketing Category BLA Part 4 of 4 CALCIUM C	Pa 1 mL in 1 VIAL, Product Informat Applica BLA103980	GLASS; Type 0: Not a Combination	Date Marketing Start Date	Date Marketing Enc
1 NDC:0338- 7201-01   Marketing   Marketing   Category   BLA Part 4 of 4	Pa 1 mL in 1 VIAL, Product Informat Applica BLA103980	GLASS; Type 0: Not a Combination	Date Marketing Start Date	Date Marketing Enc
Packaging # Item Code 1 NDC:0338- 7201-01 Marketing Category BLA Part 4 of 4 CALCIUM C	Pa 1 mL in 1 VIAL, Product Informat Applica BLA103980	GLASS; Type 0: Not a Combination	Date Marketing Start Date	Date Marketing End
Packaging # Item Code 1 NDC:0338- 201-01 Marketing Category BLA Part 4 of 4 CALCIUM C	Pa 1 mL in 1 VIAL, Product Informat Applica BLA103980 CHLORIDE liquid	GLASS; Type 0: Not a Combination	Date Marketing Start Date	Date Marketing End

Route of Administration	TOPICAL

Inactive Ingre	edients			
	Ingredient Name			Strength
CALCIUM CHLORI	<b>DE</b> (UNII: M4I0D6VV5M)	40	0 umol in	1 mL
WATER (UNII: 0590	QF0KO0R)			
Packaging				
# Item Code	Package Description	Marketing Date		Marketing End Date
<b>1</b> NDC:0338- 7401-01	1 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product			
Marketing	Information			
Marketing Category	Application Number or Monograph Citation	Marketing Date		Marketing End Date
BLA	BLA103980	05/01/1998		
Marketing	Information			
Marketing Category	Application Number or Monograph Citation	Marketing Date		Marketing End Date
BLA	BLA103980	05/01/1998		

TISSE	EL	<b>FIBRIN SEAL</b>	ANT							
fibrinogen human, human thrombin kit										
Produ	ct In	formation								
Produc	Product Type         PLAS MA DERIVATIVE         Item Code (Source)         NDC:0338-4302									
Packa	ging									
# Ite		Pa	ackage Descrip	tion Marke		-	Marketing			
	de				Start I	Jate	End Date			
1 NDC:0 4302-		(e.g., Drug/Device/Bio		rt 3 Combination Product						
Quant	ity o	f Parts								
Part #		Package Qua	antity	Total P	roduct Q	uantit	y			
Part 1	1 VIAL	, GLASS		2 mL						
Part 2	1 VIAL	, GLASS		2 mL						
Part 3	1 VIAL	, GLASS		2 mL						

### SEALER PROTEIN CONCENTRATE HUMAN

NDC:0338-7112

fibrinogen human powder, for solution

Product Information
Item Code (Source)

Route of Administration TOPICAL

Ingredient Name	Basis of Strength	Strength
FIBRINOGEN HUMAN (UNII: N94833051K) (FIBRINOGEN HUMAN - UNII:N94833051K)	FIBRINOGEN HUMAN	86.5 mg in 1 mL

Inactive Ingredients	
Ingredient Name	Strength
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
HISTIDINE (UNII: 4QD397987E)	
NIACINAMIDE (UNII: 25X51I8RD4)	
POLYSORBATE 80 (UNII: 60ZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	

#### Packaging

#	ltem Code	Package Description	Marketing Start Date	Marketing End Date
	NDC:0338- 7112-02	2 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

## Marketing Information

Marketing	Application Number or Monograph	Marketing Start	Marketing End
Category	Citation	Date	Date
BLA	BLA103980	05/01/1998	

### Part 2 of 4

#### **HUMAN THROMBIN**

human thrombin powder, for solution

_							
P	roduct Infor	mation					
lte	em Code (Sou	rce)	NDC:0338-7332				
Route of Administration			TOPICAL				
A	ctive Ingredi	ient/Active	Moiety				
		Ingre	dient Name		Basis ( Streng		Strength
	J <b>MAN THROMBI</b> III:6K15ABL77G)	<b>N</b> (UNII: 6K15AB	L77G) (HUMAN THROMBIN -		HUMAN THROM	<b>IBIN</b>	500 [iU] in 1 mL
In	active Ingre						
A 1			Ingredient Name			S	Strength
	BUMIN HUMAN DIUM CHLORID						
Pa	ackaging						
#	Item Code	Ра	ckage Description	Mark	eting Start Date	Ma	arketing End Date
1	NDC:0338- 7332-02	2 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination				
M	arketing	Informat	ion				
	Marketing Category	Applica	tion Number or Monograph Citation	Mar	keting Start Date	М	arketing End Date
BL	A	BLA103980		05/01/1	.998		
Ρ	art 3 of 4						
F		SIS INHII	BITOR SOLUTION				
<b>F</b> ap	<b>IBRINOLY</b> protinin liquid		BITOR SOLUTION				
F ap	IBRINOLY protinin liquid	mation					
F ap Pi	IBRINOLY protinin liquid roduct Infor	mation rce)	NDC:0338-7201				
Fi ap Pi	IBRINOLY protinin liquid	mation rce)					
F ap P Ito Ro	IBRINOLY protinin liquid roduct Infor	mation rce) istration	NDC:0338-7201				

APROTININ (UNII: (	04XPW8C0FL)		3000 [iU] in 1 mL		
<b>WATER</b> (UNII: 0590					
Packaging					
# Item Code	Pa	Marketing Start Marketing E Date Date			
<b>1</b> NDC:0338- 7201-02 2 mL in 1 VIAL Product		GLASS; Type 0: Not a Combination			
Marketing	Informat	ion			
Marketing Category	Applica	tion Number or Monograph Citation	Marketing Start Date	Marketing End Date	
BLA	BLA103980		05/01/1998		
Part 4 of 4					
CALCIUM C	HLORIDE	SOLUTION			
calcium chloride	e liquid				
Product Infoi Item Code (Sou		NDC:0338-7401			
Route of Admin	-	TOPICAL			
Inactive Ingre	edients				
	Ing	redient Name	Strength		
CALCIUM CHLORI		6VV5M)	40 umol in	1 mL	
WATER (UNII: 0590	QF0KO0R)				
Packaging					
# Item Code	Pa	ckage Description	Marketing Start Date	Marketing End Date	
1 NDC:0338- 7401-02	2 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination			
Marketing	Informat	ion			
Marketing Category	Applica	tion Number or Monograph Citation	Marketing Start Date	Marketing End Date	
BLA	BLA103980		05/01/1998		

Marketing Applicat Category					ting Start Date	Marketing End Date
LA	BLA103980			05/01/199	8	
ISSEEL FIE						
Product Inform	nation					
Product Type	PLAS MA	DERIVATIVE	ltem Code	(Source)	NE	DC:0338-4303
Packaging						
# Item Code		Package Descrip	otion		Marketin Start Dat	
		e 9: Other Type of Par Biological Product)	rt 3 Combinati	on Product		
Quantity of Pa	orte					
Part #	Package Q	Juantity		Total F	Product Qua	ntity
Part 1 1 VIAL, GLA	-	aanaty	5 mL	loturi	louuer quu	
Part 2 1 VIAL, GLA	SS		5 mL			
Part 3 1 VIAL, GLA			5 mL			
Part 4 1 VIAL, GLA	SS		5 mL			
Part 1 of 4						
SEALER PRO	OTEIN CO	NCENTRATE	HUMAN	J		
fibrinogen humai		-		-		
Product Inform	mation					
ltem Code (Sour	ce)	NDC:0338-7112				
Route of Adminis	stration	TOPICAL				
	ont/Active	Moioty				
Activo Ingradi	ent/Active	molety			Desis	
Active Ingredie	Ingre	dient Name			Basis of Strength	Strength

Inactive Ingre	edients				
		Ingredient Name			Strength
ALBUMIN HUMAN					
HISTIDINE (UNII: 4					
		20010			
POLYSORBATE 80		(UNII: B22547B95K)			
		(UNII: D22347033K)			
Packaging					
# Item Code	Pa	ckage Description	Marketing Starl Date	t Ma	arketing End Date
<b>1</b> NDC:0338- 7112-05	5 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination			
Marketing	Informat	ion			
Marketing Category	Applicat	tion Number or Monograph Citation	Marketing Start Date	t M	arketing End Date
BLA	BLA103980		05/01/1998		
Part 2 of 4					
HUMAN TH					
human thrombir	n powaer, for	Solution			
Product Infor	mation				
ltem Code (Sou	rce)	NDC:0338-7332			
Route of Admin	istration	TOPICAL			
Active Ingred	ient/Active	Moiety			
	Ingre	dient Name	Basis Streng		Strength
HUMAN THROMBI UNII:6K15ABL77G)	<b>N</b> (UNII: 6K15AB	L77G) (HUMAN THROMBIN -	HUMAN THRO	MBIN	500 [iU] in 1 mL
Inactive Ingre	edients				
		Ingredient Name		5	Strength
ALBUMIN HUMAN					
SODIUM CHLORID	<b>DE</b> (UNII: 451W47	IQ8X)			
Packaging					

				Maril 11 - 1
# Item Code	Pa	ckage Description	Marketing Start Date	Marketing End Date
1 NDC:0338- 7332-05	5 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination		
Markoting	Informat	ion		
Marketing				
Marketing Category	Applica	tion Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA103980		05/01/1998	
Part 3 of 4				
aprotinin liquid	515 INHII	BITOR SOLUTION		
Product Info	mation			
ltem Code (Sou	rce)	NDC:0338-7201		
Route of Admin	istration	TOPICAL		
Inactive Ingre	diants			
mactive mgre		ient Name	Str	ength
APROTININ (UNII: (	-		3000 [iU] in 1 mL	ength
<b>WATER</b> (UNII: 0590				
Packaging				
# Item Code	Pa	ckage Description	Marketing Start Date	Marketing End Date
<b>1</b> NDC:0338- 7201-05	5 mL in 1 VIAL, Product	GLASS; Type 0: Not a Combination		
7201 05	Troduct			
Marketing	Informat	ion		
Marketing Category	Applica	tion Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA103980		05/01/1998	
Part 4 of 4				
	_	SOLUTION		
calcium chloride	e liquid			

Pr	oduct Info	rmation				
lte	m Code (Sou	rce)	NDC:0338-7401			
Ro	ute of Admin	istration	TOPICAL			
Ina	active Ingre	edients				
		Ing	redient Name			Strength
CAL		DE (UNII: M4I0D	6VV5M)	4	40 umol in	1 mL
NA	<b>TER</b> (UNII: 0590	QF0KO0R)				
Pa	ckaging					
#	Item Code	Ра	ckage Description	Marketin Dat		Marketing End Date
	NDC:0338-	5 mL in 1 VIAL,	GLASS; Type 0: Not a Combination			
		Product				
	7401-05	Product				
	arketing Marketing	Informat	<b>ion</b> tion Number or Monograph Citation	Marketin Dat	-	Marketing End Date
Ma	arketing Marketing Category	Informat	tion Number or Monograph		-	_
Ma	arketing Marketing Category	Informat Applica	tion Number or Monograph	Dat	-	_
Ma	arketing Marketing Category	Informat Applica	tion Number or Monograph Citation	Dat	-	-
Ma	arketing Marketing Category	Informat Applica BLA103980 Informat	tion Number or Monograph Citation	Dat	ie og Start	Date
Ma Bla Ma	Arketing Category Marketing Category Marketing Category	Informat Applica BLA103980 Informat	tion Number or Monograph Citation <b>ion</b> tion Number or Monograph	Dat 05/01/1998 Marketin	ie og Start	Date Marketing End
Ma Bla Ma	Arketing Category Marketing Category Marketing Category	Informat Applica BLA103980 Informat Applica	tion Number or Monograph Citation <b>ion</b> tion Number or Monograph	Dat 05/01/1998 Marketin Dat	ie og Start	Date Marketing End
Ma BLA Ma	Arketing Marketing Category A Arketing Category	Informat Applica BLA103980 Informat Applica	tion Number or Monograph Citation ion tion Number or Monograph Citation	Dat 05/01/1998 Marketin Dat	ie og Start	Date Marketing End
	Arketing Category Marketing Category Marketing Category	Informat Applica BLA103980 Informat Applica BLA103980 BRIN SEA	tion Number or Monograph Citation ion tion Number or Monograph Citation	Dat 05/01/1998 Marketin Dat	ie og Start	Date Marketing End
Ma BLA Ma BLA	arketing Marketing Category arketing Marketing Category SSEEL FI	Informat Applica BLA103980 Informat Applica BLA103980 BRIN SEA	tion Number or Monograph Citation ion tion Number or Monograph Citation	Dat 05/01/1998 Marketin Dat	ie og Start	Date Marketing End
Ma BLA Ma BLA Dri Pro	arketing Marketing Category arketing Marketing Category SSEEL FI inogen huma	Informat Applica BLA103980 Informat Applica BLA103980 BRIN SEA	tion Number or Monograph Citation	Dat 05/01/1998 Marketin Dat 05/01/1998	ig Start te	Date Marketing End Date
Ma BLA Ma BLA	arketing Marketing Category arketing Marketing Category SSEEL FI	Informat Applica BLA103980 Informat Applica BLA103980 BRIN SEA	tion Number or Monograph Citation	Dat 05/01/1998 Marketin Dat	ig Start te	Marketing End

Active Ingredient/Active Moiety					
Ingredient Name	Basis of Strength	Strength			
FIBRINOGEN HUMAN (UNII: N94833051K) (FIBRINOGEN HUMAN - UNII:N94833051K)	FIBRINOGEN HUMAN	90 mg in 1 mL			
HUMAN THROMBIN (UNII: 6K15ABL77G) (HUMAN THROMBIN - UNII:6K15ABL77G)	HUMAN THROMBIN	500 [iU] in 1 mL			

Inactive Ingredients				
Ingredient Name	Strength			
APROTININ (UNII: 04XPW8C0FL)				
ALBUMIN HUMAN (UNII: ZIF514RVZR)				
HISTIDINE (UNII: 4QD397987E)				
NIACINAMIDE (UNII: 25X51I8RD4)				
POLYSORBATE 80 (UNII: 60ZP39ZG8H)				
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)				
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)				
SODIUM CHLORIDE (UNII: 451W47IQ8X)				
WATER (UNII: 059QF0KO0R)				

#### Packaging

#	ltem Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338- 8402-02	1 in 1 CARTON		
1	NDC:0338- 8402-01	2 mL in 1 SYRINGE, PLASTIC; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		
2	NDC:0338- 8402-04	1 in 1 CARTON		
2	NDC:0338- 8402-03	4 mL in 1 SYRINGE, PLASTIC; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		
3	NDC:0338- 8402-10	1 in 1 CARTON		
3	NDC:0338- 8402-09	10 mL in 1 SYRINGE, PLASTIC; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		
M	larketi	ng Information		
	Marketi		ng Start Ma	rketing End

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA103980	05/01/1998	

# TISSEEL FIBRIN SEALANT

fibrinogen human, human thrombin solution

Product Information					
Product Type	PLASMA DERIVATIVE	Item Code (S	ource)	NDC:03	38-9560
Route of Administration	TOPICAL				
A	N# . * . 1				
Active Ingredient/Active	Μοιετγ				
Ingro	diant Nama		Basis of		Strongth

 
 Ingredient Name
 Basis of Strength
 Strength

 FIBRINOGEN HUMAN (UNII: N94833051K) (FIBRINOGEN HUMAN EIBRINOGEN HUMAN
 86.5 mg

UN	II:N94833051K)			FIDRII		in 1 mL
	MAN THROMBIN II:6K15ABL77G)	I (UNII: 6K15ABL770	G) (HUMAN THROMBIN -	HUMA	N THROMBIN	500 [iU] in 1 mL
In	active Ingred	dients				
		lı	ngredient Name			Strength
AP	ROTININ (UNII: 04	1XPW8C0FL)				
ALI	BUMIN HUMAN (U	UNII: ZIF514RVZR)				
HIS	STIDINE (UNII: 4Q	D397987E)				
NI	ACINAMIDE (UNII:	25X51I8RD4)				
PO	LYSORBATE 80	(UNII: 60ZP39ZG8	H)			
TR	ISODIUM CITRAT	E DIHYDRATE (UI	NII: B22547B95K)			
٢N						
CA		E (UNII: M410D6VV5	5M)			
		<b>E</b> (UNII: M4I0D6VV5 : (UNII: 451W47IQ8				
so		(UNII: 451W47IQ8				
so	DIUM CHLORIDE	(UNII: 451W47IQ8				
so	DIUM CHLORIDE	(UNII: 451W47IQ8				
so w <i>i</i>	DIUM CHLORIDE	(UNII: 451W47IQ8				
so w <i>i</i>	DIUM CHLORIDE ATER (UNII: 059QF	: (UNII: 451W47IQ8. OKOOR)			Marketin Start Dat	
so w# Pa #	DIUM CHLORIDE ATER (UNII: 059QF ACKaging Item Code NDC:0338- 2 mL i	: (UNII: 451W47IQ8. :0KO0R) • Pa in 1 SYRINGE, PLAS	X)	t 3 Juct)		
so w# Pa #	DIUM CHLORIDE ATER (UNII: 059QF ACKaging Item Code NDC:0338- 2 mL i	: (UNII: 451W47IQ8. :0KO0R) • Pa in 1 SYRINGE, PLAS	X) Ackage Description STIC; Type 9: Other Type of Par	t 3 uct)		
so w# Pa #	DIUM CHLORIDE ATER (UNII: 059QF ACKaging Item Code NDC:0338- 2 mL i	: (UNII: 451W47IQ8. :0KO0R) • Pa in 1 SYRINGE, PLAS	X) Ackage Description STIC; Type 9: Other Type of Par	t 3 Jct)		
so w/ Pa #	DIUM CHLORIDE ATER (UNII: 059QF ACKaging Item Code NDC:0338- 9560-01 2 mL i Comb	: (UNII: 451W47IQ8. :0KO0R) • Pa in 1 SYRINGE, PLAS	X) Ackage Description STIC; Type 9: Other Type of Par g., Drug/Device/Biological Prod	t 3 Jct)		
so w# # 1	DIUM CHLORIDE ATER (UNII: 059QF ACKaging Item Code NDC:0338- 9560-01 2 mL i Comb	E (UNII: 451W47IQ8 TOKOOR) In 1 SYRINGE, PLAS Ination Product (e. Information	X) Ackage Description STIC; Type 9: Other Type of Par g., Drug/Device/Biological Prod	t 3 Joct) Marketing Date	Start Dat	

# TISSEEL FIBRIN SEALANT

fibrinogen human, human thrombin solution

Product Information					
Product Type	PLASMA DERIVATIVE	Item Code (S	ource)	NDC:0338-9564	
Route of Administration	TOPICAL				
	NA - 1- 4				
Active Ingredient/Active	моюту				
Ingre	dient Name		Basis of Strength		Strength
FIBRINOGEN HUMAN (UNII: N94833051K) (FIBRINOGEN HUMAN - UNII:N94833051K)			FIBRINOGEN HUN	1AN	86.5 mg in 1 mL
HUMAN THROMBIN (UNII: 6K15AB UNII:6K15ABL77G)	L77G) (HUMAN THROMBIN -		HUMAN THROMB	IN	500 [iU] in 1 mL

	edients			
	Ing	gredient Name		Strength
APROTININ (UNII:	04XPW8C0FL)			
ALBUMIN HUMAN	I (UNII: ZIF514RVZR)			
HISTIDINE (UNII: 4	QD397987E)			
NIACINAMIDE (UN	III: 25X51I8RD4)			
POLYSORBATE 8	<b>0</b> (UNII: 60ZP39ZG8H)	)		
TRISODIUM CITR	ATE DIHYDRATE (UNI	I: B22547B95K)		
CALCIUM CHLOR	IDE (UNII: M4I0D6VV5M	1)		
SODIUM CHLORI	<b>DE</b> (UNII: 451W47IQ8X)			
WATER (UNII: 059	QF0KO0R)			
Deckewing				
ltom	Pac	kage Description	Marketir Start Da	
# <b>Item</b> Code 1 NDC:0338- 4 m	L in 1 SYRINGE, PLAST	Ckage Description TIC; Type 9: Other Type of Part , Drug/Device/Biological Produ		
<ul> <li># Code</li> <li>1 NDC:0338- 4 m</li> </ul>	L in 1 SYRINGE, PLAST	- FIC; Type 9: Other Type of Part		
Item Code           1         NDC:0338- 9564-01         4 m Con	L in 1 SYRINGE, PLAST	- FIC; Type 9: Other Type of Part		
Item Code           1         NDC:0338- 9564-01         4 m Con	L in 1 SYRINGE, PLAST abination Product (e.g.	- FIC; Type 9: Other Type of Part	Start Da 9 Start	

TISSEEL FIBRIN SEA	LANT				
fibrinogen human, human thro	ombin solution				
Product Information					
Product Type	PLASMA DERIVATIVE	Item Code (S	ource)	NDC:	0338-9568
Route of Administration	TOPICAL				
Active Ingredient/Active	Moiety				
Ingre	dient Name		Basis of Strength		Strength
FIBRINOGEN HUMAN (UNII: N9483 UNII:N94833051K)	3051K) (FIBRINOGEN HUMAN	I -	FIBRINOGEN HUM	IAN	86.5 mg in 1 mL
HUMAN THROMBIN (UNII: 6K15AB UNII:6K15ABL77G)	L77G) (HUMAN THROMBIN -		HUMAN THROMBI	N	500 [iU] in 1 mL
Inactive Ingredients					
	Ingredient Name				Strength
APROTININ (UNII: 04XPW8C0FL)					
ALBUMIN HUMAN (UNII: ZIF514RV	ZR)				

HISTIDINE (UNII: 4QD397987E)

		•	5X51I8RD4)				
		-	NII: 60ZP39ZG8H)				
TR	ISODIUM C	CITRATE	DIHYDRATE (UNII: B22547B95K)				
СА	LCIUM CH	LORIDE	(UNII: M4I0D6VV5M)				
50	DIUM CHL	ORIDE (	UNII: 451W47IQ8X)				
w,	ATER (UNII:	059QF0	(OOR)				
<b>D</b> -	kaging						
Гс	ackaging	J					
#	ltem Code		Package Description		Market Start D		Marketing End Date
	NDC:0338- 9568-01		n 1 SYRINGE, PLASTIC; Type 9: Other Type of Pa ation Product (e.g., Drug/Device/Biological Produ				
n /			for which the set				
V	arketi	ng In	formation				
	Marketi Catego		Application Number or Monograph Citation	Marketing Date	-	Ма	rketing End Date
			BLA103980	05/01/1998			
BL	4		BLAIU5960	00/01/1990			

Labeler - Baxter Healthcare Corporation (005083209)

Revised: 12/2019

Baxter Healthcare Corporation