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

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_2, Medical Air or Nitrogen. For Minimally Invasive Surgery procedures use the **DUPLOSPRAY MIS** device connected only to CO_2.(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)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

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 37ºC
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.

Pre-warming TISSEEL Kit with FIBRINOTHERM device
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 Preparation of Sealer Protein with FIBRINOTHERM deviceutilizing 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 33-37ºC. 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).

Sterile Water Bath (Quick Thawing): Transfer inner pouch to the sterile field, remove pre-filled 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.

Non-Sterile Water Bath: 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.

Incubator: 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.

Table 1: Approximate Water Bath or Incubator Thawing and Warming Times

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 Syringe	AST Syringe	PRIMA Syringe	AST Syringe	PRIMA Syringe	AST Syringe
2 mL	5 minutes	5 minutes	15 minutes	30 minutes	40 minutes	40 minutes
4 mL	5 minutes	5 minutes	20 minutes	40 minutes	50 minutes	85 minutes
10 mL	10 minutes	12 minutes	35 minutes	80 minutes	90 minutes	105 minutes

Room Temperature Thawing: 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 Warming Times 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 Syringe	AST Syringe	PRIMA Syringe	AST Syringe	PRIMA Syringe	AST Syringe
2 mL	2 minutes	2 minutes	5 minutes	16 minutes	16 minutes	20 minutes
4 mL	2 minutes	2	8	21	21	43

4 mL	2 minutes	minutes	minutes	minutes	minutes	minutes
10 mL	4 minutes	6 minutes	12 minutes	43 minutes	35 minutes	52 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.

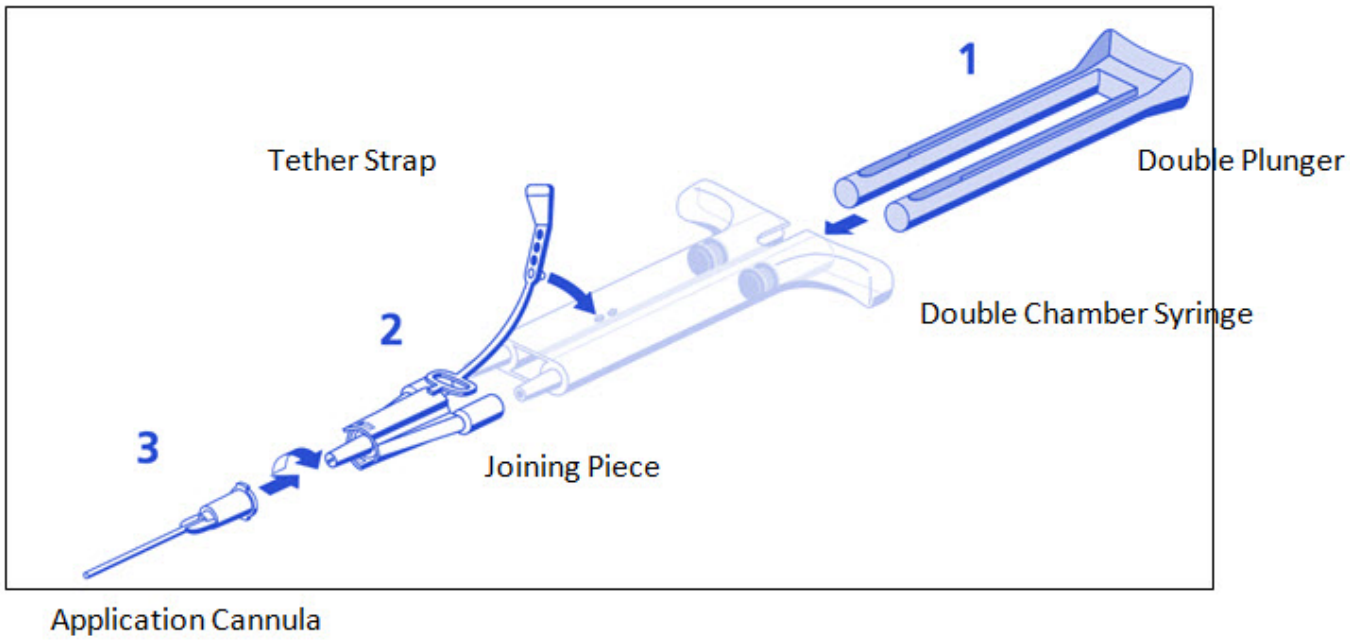


Figure 1 DUO SET - AST Syringe

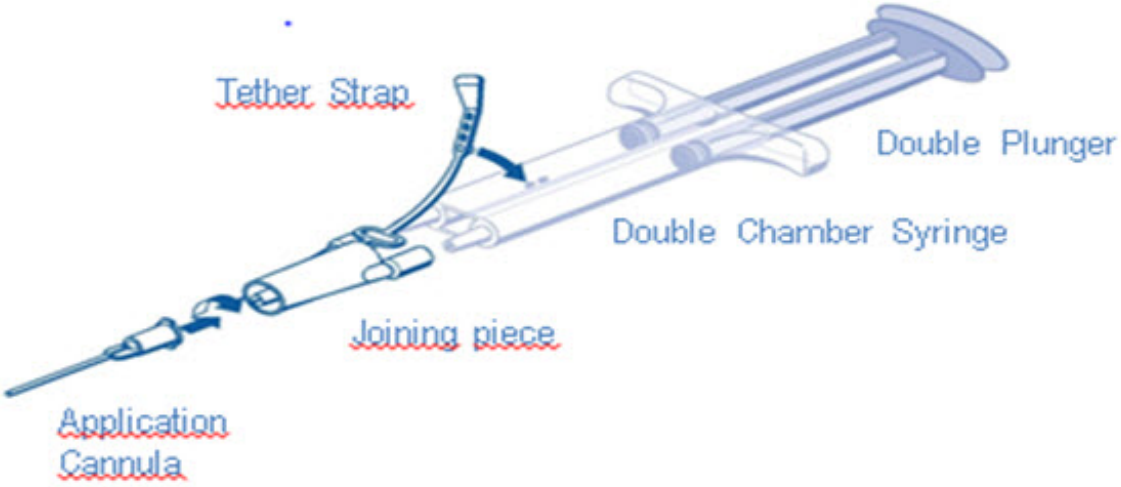


Figure 2: DUPLOJECT COMBI - PRIMA Syringe

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:

Table 4: Recommended Application Equipment, Gas and Parameters

Surgery	Spray set / Applicator tips to use	Pressure regulator to use	Gas	Distance	Spray Pressure

Open surgery	TISSEEL /ARTISS Spray Set	EASY SPRAY Pressure Regulator	Medical grade CO_2*, 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 Regulator	CO_2 Only	Range 2-5 cm 3 cm recommended	1.18-1.50 bar (17-22 psi)
	DUPLOSPRAY MIS Applicator 30 cm				
	DUPLOSPRAY MIS Applicator 40 cm				
	360º Flexible Applicator 40 cm				
	Replaceable tip				

* Medical grade CO_2 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^2	8 cm^2
4 mL	200 cm^2	16 cm^2
10 mL	500 cm^2	40 cm^2

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_2 is greater than either compressed N_2 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_2 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.

For Open Surgical procedures, use the EASYSPRAY Pressure Regulator connected to medical grade CO_2, compressed Air or a Nitrogen compressed gas source along with the TISSEEL/ARTISS spray set, (*see Method of Application (2.3)*).

For Minimally Invasive Surgery proceduresin 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 of another drug 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.

Immune System Disorders: Hypersensitivity, including anaphylactic reaction and anaphylactic shock. Anaphylactic reactions and anaphylactic shock have included fatal outcomes.
Vascular Disorders:Hypotension, flushing, embolism, including cerebral artery embolism, cerebral infarction*, air embolism**
Skin and subcutaneous Tissue Disorders:Angioedema, erythema, impaired healing, pruritus, urticaria
Cardiac Disorders:Bradycardia, tachycardia
Respiratory Disorders: 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

Risk Summary

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 Aprotinin, that delays fibrinolysis. Aprotinin (Synthetic) is manufactured by solid phase synthesis from materials completely of non-human/non-animal origin.

Thrombin (Human)
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 in-house 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.

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

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

n.d. = not determined

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].

Table 7: Vascular Surgery

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

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 χ^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, χ^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:

Table 11: NDC Numbers

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

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 ≤ -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.

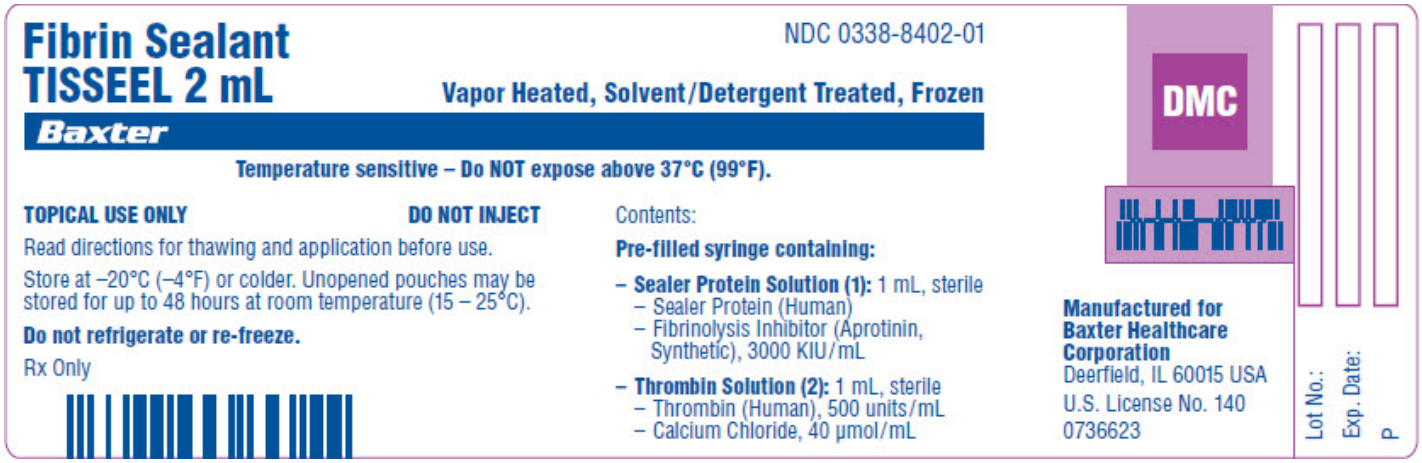
17 PATIENT COUNSELING INFORMATION

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 (s*ee Use in Specific Populations (8.1)).*

Manufactured For Baxter Healthcare Corporation
Deerfield, IL 60015 USA
US License No. 140

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL



Tiseel Frozen 2 mL AST Pouch Label

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°C (–4°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
– 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:

P

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°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 Logo

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

NDC 0338-4210-02

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

Baxter

NDC 0338-4210-02

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

Tissel Lyo 2 mL Vial Carton Label

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

Baxter and Tisseel are trademarks of Baxter International Inc.

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.

Baxter

NDC 0338-4301-02

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

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.

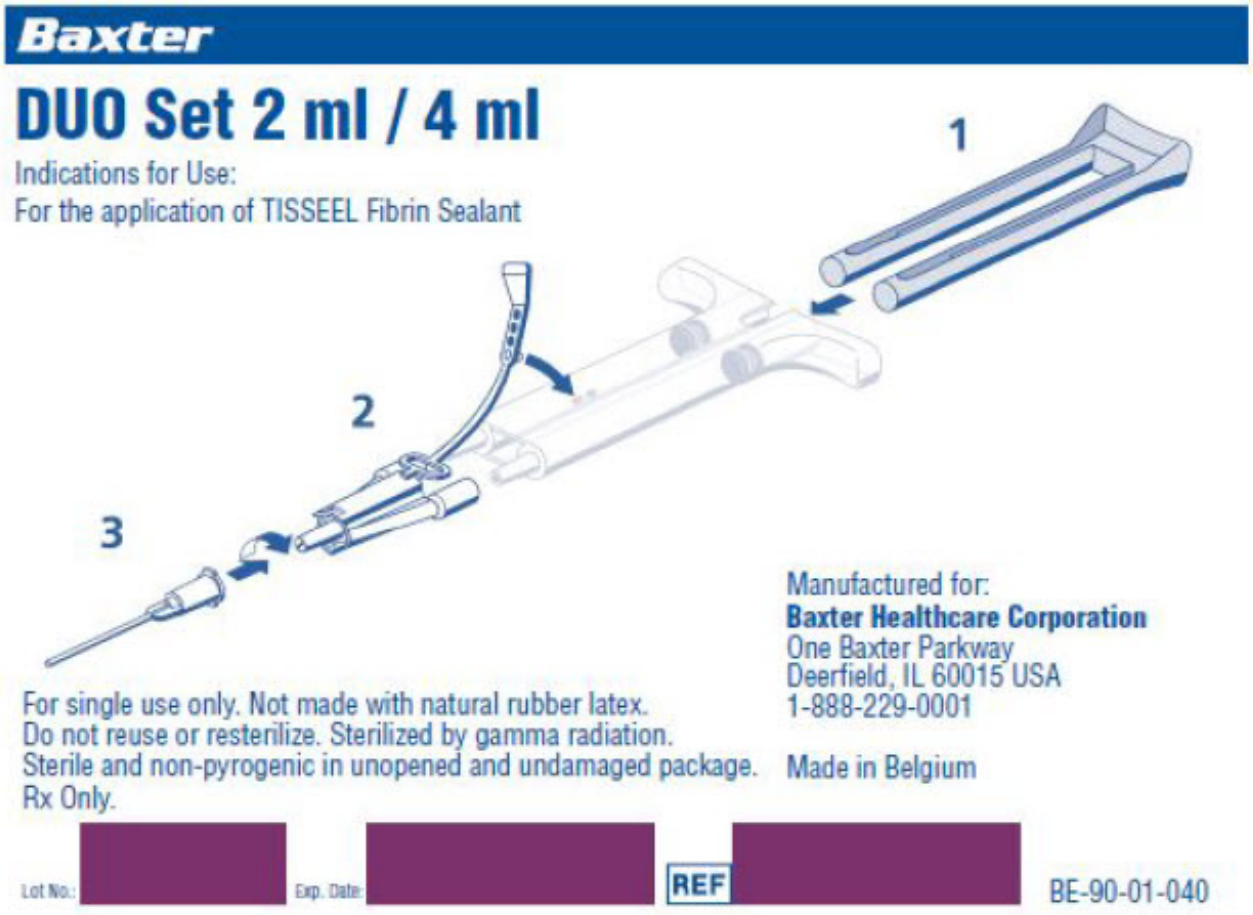
Not made with natural rubber latex
Rx only

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:

Exp. Date:

REF

BE-90-01-040

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

Made in Belgium

DUPLOJECT 2 mL / 4 mL

Fibrin Sealant Preparation and Application System

For Fibrin Sealant 2 mL or 4 mL Kit

Indications for Use:

For the preparation and application of TISSEEL Fibrin Sealant 2 mL / 4 mL Kit.

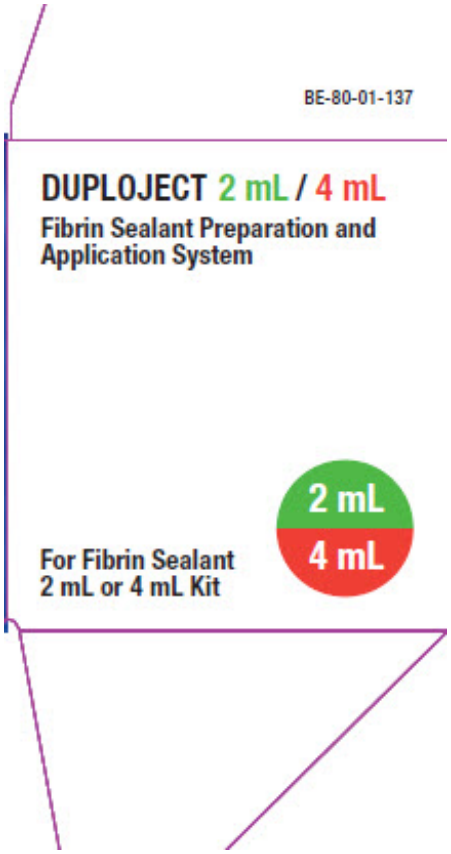
STERILE – SINGLE PATIENT USE ONLY – DO NOT RESTERILIZE

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

Rx Only.

Made in Belgium

BE8001137



Tisseel Lyo 2 mL - 4 mL DUPLOJET Label

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

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

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 FIBRINOTHERM 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 FIBRINOTHERM device (green switch). Reconstitution

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.

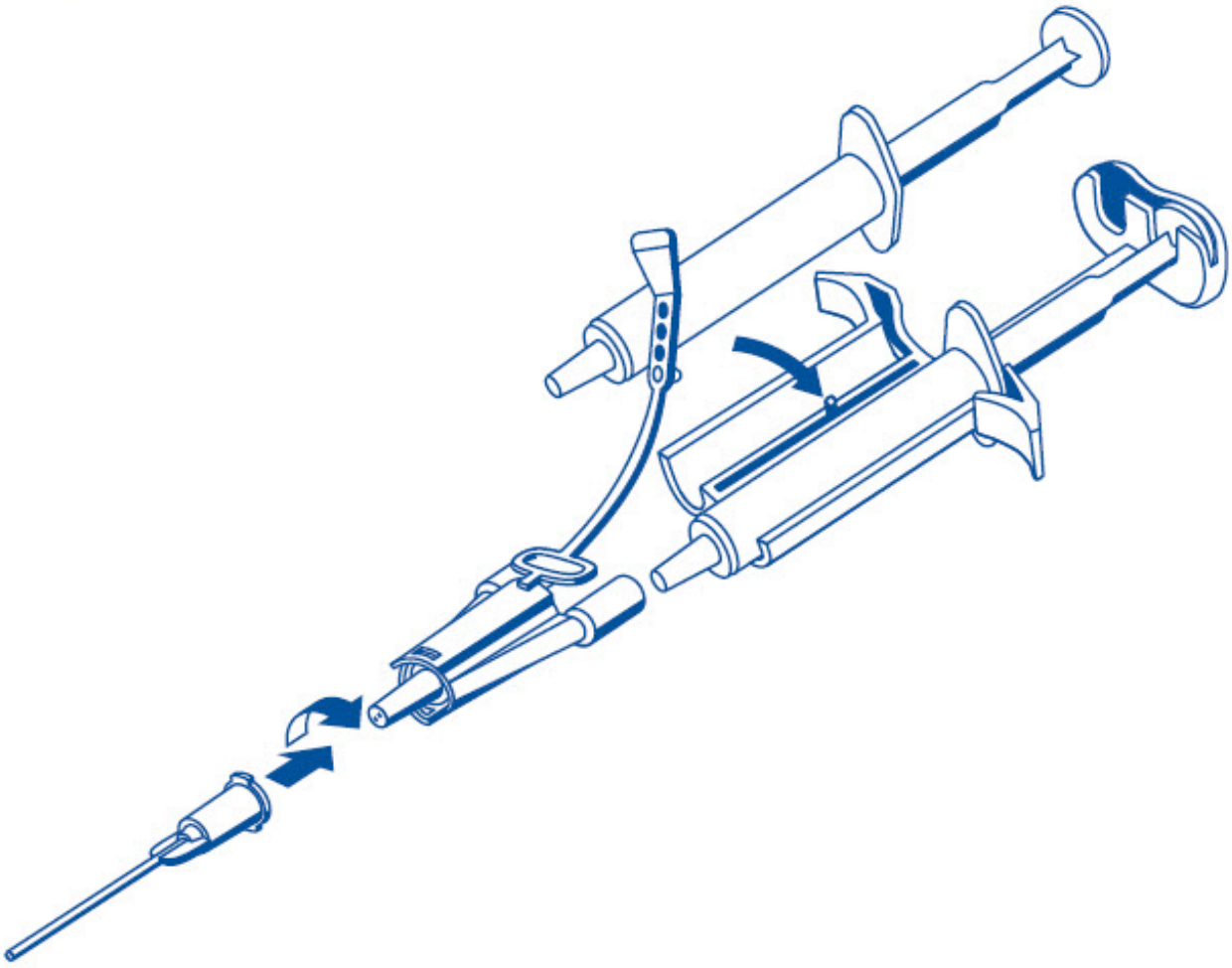
2.3 Assemble the blue-scaled and black-scaled syringes with the needles provided. Note: For 10 mL DUPLOJECT systems, attach the larger needle to the blue-scaled syringe.

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: 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.

Manufactured for:

Baxter Healthcare Corporation

One Baxter Parkway

Deerfield, IL 60015 USA

1-888-229-0001

Made in Belgium

Rev. Date: 2017-05-17

DUPLOJET IFU Label

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 FIBRINOTHERM 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 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.

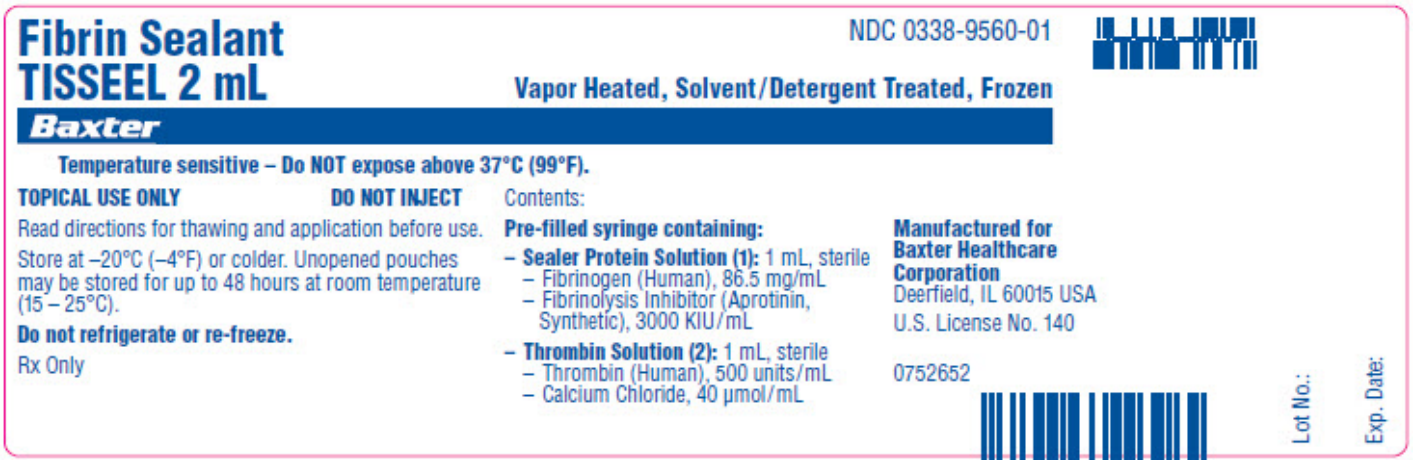
DISPOSE OF CONTAMINATED AND SHARP COMPONENTS PROPERLY.

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

1-888-229-0001

Made in Belgium

Rev. Date: 2017-05-17



2 mL PRIMA Pouch Label

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°C (–4°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°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.

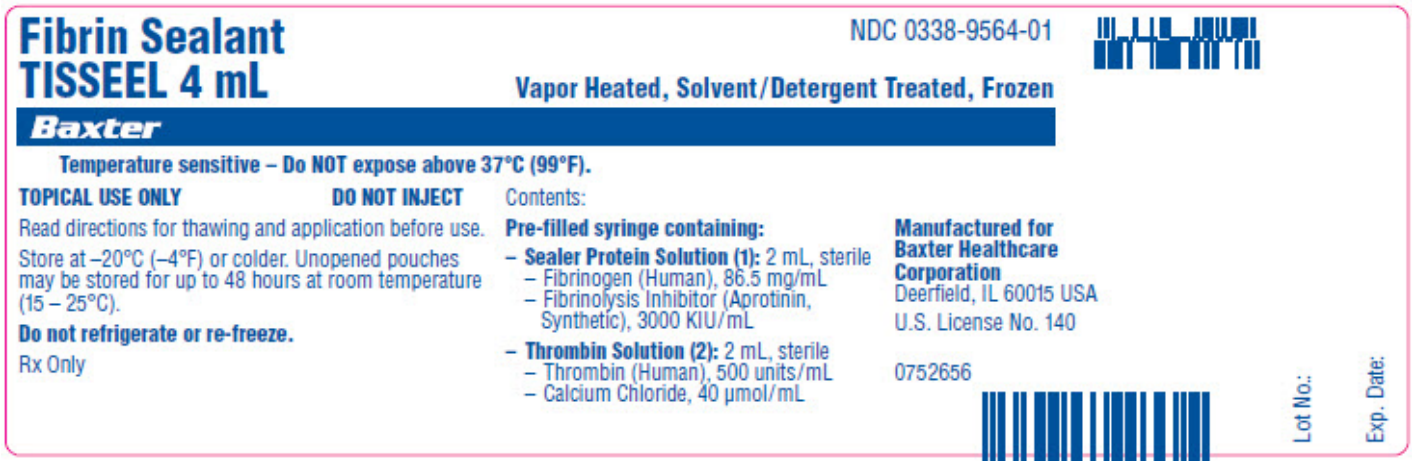
2 mL

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°C (–4°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:

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

4 mL

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° C).

Do not refrigerate or re-freeze.

Not made with natural rubber latex

For Single Patient Use Only

NDC 0338-9564-01

Baxter

3 03389564 01 0

Fibrin Sealant
TISSEEL

Vapor Heated, Solvent/
Detergent Treated, Frozen
TOPICAL USE ONLY

NDC 0338-9564-01

4 mL

0752857

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°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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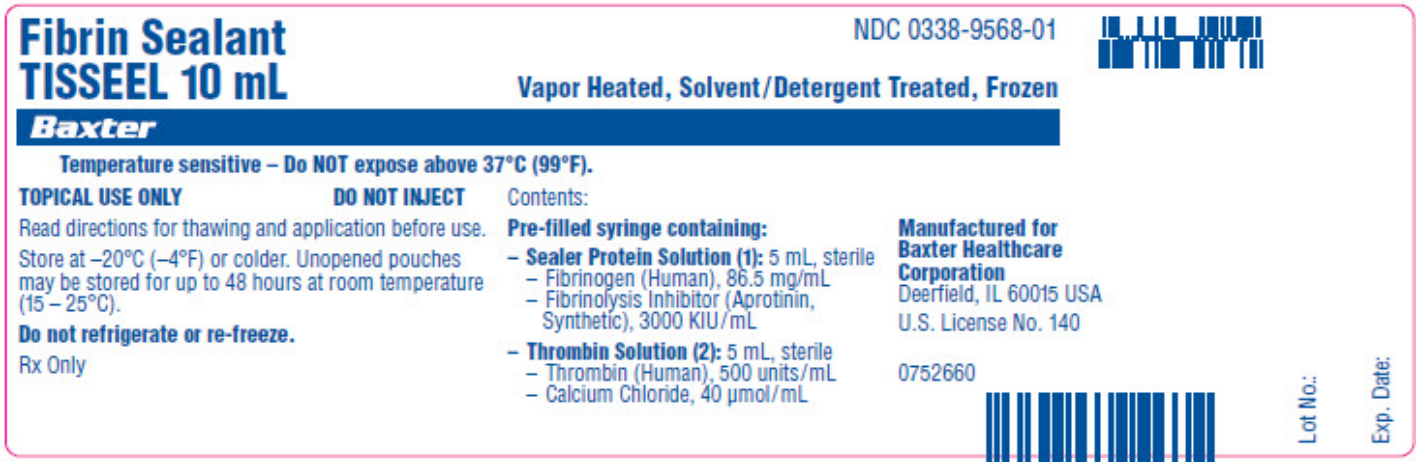
Baxter International Inc.

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°C (–4°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°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

10 mL

Baxter Logo

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

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

NDC 0338-4211-04

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

Baxter

NDC 0338-4211-04

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 reconstitution.

NOT FOR INJECTION. For single use only.

Not made with natural rubber latex

Rx only

Lyo 4mL Vial Carton Label

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

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.

Baxter

NDC 0338-4212-10

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

Lyo 10mL Vial Carton Label

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.

Baxter

NDC 0338-4302-04

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

TOPICAL USE ONLY
DO NOT INJECT

Baxter

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

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

Baxter

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 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

N 0338-4302-04 4

Lyo 4mL Sleeve Carton Label

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

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

Barcode
N3 0338-4302-04 4

Baxter

NDC 0338-4303-10

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

N 3 0338-4303-10 2

Lyo 10mL Sleeve Carton Label

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

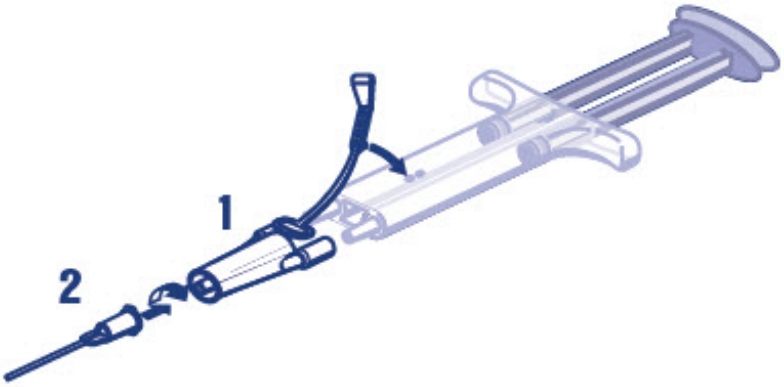
Barcode

Barcode
N3 0338-4303-10 2

Baxter

DUPLOJECT COMBI

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

Made in Belgium

BE-90-01-044

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

TISSEEL FIBRIN SEALANT

fibrinogen human, human thrombin kit

Product Information			
Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:0338-4210

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-4210-02	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL, GLASS	1 mL
Part 2	1 VIAL, GLASS	1 mL
Part 3	1 VIAL, GLASS	1 mL
Part 4	1 VIAL, GLASS	1 mL

Part 1 of 4

SEALER PROTEIN CONCENTRATE HUMAN

fibrinogen human powder, for solution

Product Information	
Item Code (Source)	NDC:0338-7112
Route of Administration	TOPICAL

Active Ingredient/Active Moiety		
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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-7112-01	1 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 2 of 4

HUMAN THROMBIN

human thrombin powder, for solution

Product Information	
Item Code (Source)	NDC:0338-7332
Route of Administration	TOPICAL

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

Inactive Ingredients	
Ingredient Name	**Strength**
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-7332-01	1 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 3 of 4

FIBRINOLYSIS INHIBITOR SOLUTION

aprotinin liquid

Product Information	
Item Code (Source)	NDC:0338-7201
Route of Administration	TOPICAL

Inactive Ingredients	
Ingredient Name	**Strength**
APROTININ (UNII: 04XPW8C0FL)	3000 [iU] in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-	1 mL in 1 VIAL, GLASS; Type 0: Not a Combination		

1	7201-01	Product		

Marketing Information

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

Part 4 of 4

CALCIUM CHLORIDE SOLUTION

calcium chloride liquid

Product Information

Item Code (Source)	NDC:0338-7401
Route of Administration	TOPICAL

Inactive Ingredients

Ingredient Name	Strength
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	40 umol in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	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 Start Date	Marketing End Date
BLA	BLA103980	05/01/1998	

Marketing Information

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 kit

Product Information			
Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:0338-4211

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-4211-04	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL, GLASS	2 mL
Part 2	1 VIAL, GLASS	2 mL
Part 3	1 VIAL, GLASS	2 mL
Part 4	1 VIAL, GLASS	2 mL

Part 1 of 4

SEALER PROTEIN CONCENTRATE HUMAN

fibrinogen human powder, for solution

Product Information	
Item Code (Source)	NDC:0338-7112
Route of Administration	TOPICAL

Active Ingredient/Active Moiety		
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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	

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

Marketing Information

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

Part 2 of 4

HUMAN THROMBIN

human thrombin powder, for solution

Product Information	
Item Code (Source)	NDC:0338-7332
Route of Administration	TOPICAL

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

Inactive Ingredients	
Ingredient Name	Strength
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7332-02	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 3 of 4

FIBRINOLYSIS INHIBITOR SOLUTION

aprotinin liquid

Product Information	
Item Code (Source)	NDC:0338-7201
Route of Administration	TOPICAL

Inactive Ingredients	
Ingredient Name	**Strength**
APROTININ (UNII: 04XPW8C0FL)	3000 [iU] in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-7201-02	2 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 4 of 4

CALCIUM CHLORIDE SOLUTION

calcium chloride liquid

Product Information	
Item Code (Source)	NDC:0338-7401
Route of Administration	TOPICAL

Inactive Ingredients	
Ingredient Name	**Strength**
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	40 umol in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-7401-02	2 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Marketing Information

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 kit

Product Information			
Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:0338-4212

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-4212-10	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL, GLASS	5 mL
Part 2	1 VIAL, GLASS	5 mL
Part 3	1 VIAL, GLASS	5 mL
Part 4	1 VIAL, GLASS	5 mL

Part 1 of 4

SEALER PROTEIN CONCENTRATE HUMAN

fibrinogen human powder, for solution

Product Information

Item Code (Source)	NDC:0338-7112
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7112-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 2 of 4

HUMAN THROMBIN

human thrombin powder, for solution

Product Information

Item Code (Source)	NDC:0338-7332
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HUMAN THROMBIN (UNII: 6K15ABL77G) (HUMAN THROMBIN - UNII:6K15ABL77G)	HUMAN THROMBIN	500 [iU] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7332-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 3 of 4

FIBRINOLYSIS INHIBITOR SOLUTION

aprotinin liquid

Product Information

Item Code (Source)	NDC:0338-7201
Route of Administration	TOPICAL

Inactive Ingredients

Ingredient Name	Strength
APROTININ (UNII: 04XPW8C0FL)	3000 [iU] in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7201-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

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

Part 4 of 4

CALCIUM CHLORIDE SOLUTION

calcium chloride liquid

Product Information	
Item Code (Source)	NDC:0338-7401
Route of Administration	TOPICAL

Inactive Ingredients	
Ingredient Name	Strength
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	40 umol in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7401-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

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

Marketing Information			
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 kit

Product Information

Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:0338-4301

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-4301-02	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, GLASS	1 mL
Part 2	1 VIAL, GLASS	1 mL
Part 3	1 VIAL, GLASS	1 mL
Part 4	1 VIAL, GLASS	1 mL

Part 1 of 4

SEALER PROTEIN CONCENTRATE HUMAN

fibrinogen human powder, for solution

Product Information

Item Code (Source)	NDC:0338-7112
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7112-01	1 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 2 of 4

HUMAN THROMBIN

human thrombin powder, for solution

Product Information

Item Code (Source)	NDC:0338-7332
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HUMAN THROMBIN (UNII: 6K15ABL77G) (HUMAN THROMBIN - UNII:6K15ABL77G)	HUMAN THROMBIN	500 [iU] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7332-01	1 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 3 of 4

FIBRINOLYSIS INHIBITOR SOLUTION

aprotinin liquid

Product Information

Item Code (Source)	NDC:0338-7201
Route of Administration	TOPICAL

Inactive Ingredients

Ingredient Name	Strength
APROTININ (UNII: 04XPW8C0FL)	3000 [iU] in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7201-01	1 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 4 of 4

CALCIUM CHLORIDE SOLUTION

calcium chloride liquid

Product Information

Item Code (Source)	NDC:0338-7401

Route of Administration	TOPICAL

Inactive Ingredients

Ingredient Name	Strength
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	40 umol in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	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 Start Date	Marketing End Date
BLA	BLA103980	05/01/1998	

Marketing Information

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 kit

Product Information

Product Type	PLASMA DERIVATIVE	Item Code (Source)	NDC:0338-4302

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-4302-04	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, GLASS	2 mL
Part 2	1 VIAL, GLASS	2 mL
Part 3	1 VIAL, GLASS	2 mL

Part 4	1 VIAL, GLASS	2 mL

Part 1 of 4

SEALER PROTEIN CONCENTRATE HUMAN

fibrinogen human powder, for solution

Product Information

Item Code (Source)	NDC:0338-7112
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	

Packaging

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

Marketing Information

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

Part 2 of 4

HUMAN THROMBIN

human thrombin powder, for solution

Product Information	
Item Code (Source)	NDC:0338-7332
Route of Administration	TOPICAL

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

Inactive Ingredients	
Ingredient Name	**Strength**
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-7332-02	2 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 3 of 4

FIBRINOLYSIS INHIBITOR SOLUTION

aprotinin liquid

Product Information	
Item Code (Source)	NDC:0338-7201
Route of Administration	TOPICAL

Inactive Ingredients	
Ingredient Name	**Strength**

APROTININ (UNII: 04XPW8C0FL)	3000 [iU] in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7201-02	2 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 4 of 4

CALCIUM CHLORIDE SOLUTION

calcium chloride liquid

Product Information

Item Code (Source)	NDC:0338-7401
Route of Administration	TOPICAL

Inactive Ingredients

Ingredient Name	Strength
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	40 umol in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7401-02	2 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Marketing Information

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 kit

Product Information

Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:0338-4303

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-4303-10	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, GLASS	5 mL
Part 2	1 VIAL, GLASS	5 mL
Part 3	1 VIAL, GLASS	5 mL
Part 4	1 VIAL, GLASS	5 mL

Part 1 of 4

SEALER PROTEIN CONCENTRATE HUMAN

fibrinogen human powder, for solution

Product Information

Item Code (Source)	NDC:0338-7112
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-7112-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 2 of 4

HUMAN THROMBIN

human thrombin powder, for solution

Product Information	
Item Code (Source)	NDC:0338-7332
Route of Administration	TOPICAL

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

Inactive Ingredients	
Ingredient Name	**Strength**
ALBUMIN HUMAN (UNII: ZIF514RVZR)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7332-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 3 of 4

FIBRINOLYSIS INHIBITOR SOLUTION

aprotinin liquid

Product Information

Item Code (Source)	NDC:0338-7201
Route of Administration	TOPICAL

Inactive Ingredients

Ingredient Name	Strength
APROTININ (UNII: 04XPW8C0FL)	3000 [iU] in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-7201-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Part 4 of 4

CALCIUM CHLORIDE SOLUTION

calcium chloride liquid

Product Information	
Item Code (Source)	NDC:0338-7401
Route of Administration	TOPICAL

Inactive Ingredients	
Ingredient Name	**Strength**
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	40 umol in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0338-7401-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

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

Marketing Information

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 (Source)**	NDC:0338-8402
Route of Administration	TOPICAL		

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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item 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)		

Marketing Information

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 (Source)**	NDC:0338-9560
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

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

UNII:N94833051K)	FIBRINOGEN HUMAN	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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-9560-01	2 mL in 1 SYRINGE, PLASTIC; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Marketing Information

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 (Source)**	NDC:0338-9564
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FIBRINOGEN HUMAN (UNII: N94833051K) (FIBRINOGEN HUMAN - UNII:N94833051K)	FIBRINOGEN HUMAN	86.5 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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-9564-01	4 mL in 1 SYRINGE, PLASTIC; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Marketing Information

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 (Source)**	NDC:0338-9568
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FIBRINOGEN HUMAN (UNII: N94833051K) (FIBRINOGEN HUMAN - UNII:N94833051K)	FIBRINOGEN HUMAN	86.5 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: 6OZP39ZG8H)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0338-9568-01	10 mL in 1 SYRINGE, PLASTIC; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Marketing Information

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

Labeler - Baxter Healthcare Corporation (005083209)

Revised: 12/2019

Baxter Healthcare Corporation