PACKAGE LEAFLET: INFORMATION FOR THE USER

TISSEEL Lyo
Powder and Solvent for Sealant
Active substances: Human fibrinogen, human thrombin, aprotinin, calcium chloride

Please read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist. See section 4

In this leaflet:

1. WHAT TISSEEL LYO IS AND WHAT IT IS USED FOR

What TISSEEL Lyo is
The name of your medicine is TISSEEL Lyo.

TISSEEL Lyo is a two-component fibrin sealant, and it contains two of the proteins that make blood clot. These proteins are called fibrinogen and thrombin. When these proteins mix during application, they form a clot where the surgeon applies them.

TISSEEL Lyo is prepared as two solutions (Sealer Protein Solution and Thrombin Solution), which mix when applied.

What TISSEEL Lyo is used for

TISSEEL Lyo is a fibrin or tissue sealant. During surgery, tissues may bleed and it may not be possible for the surgeon to control this bleeding using stitches, or by applying pressure. TISSEEL Lyo is applied to the surface of tissues either to control bleeding, or to stop (or prevent) leaks of other types of fluid by creating a watertight seal.

Reconstituted TISSEEL Lyo is used as a tissue sealant and haemostatic for surgical incisions, plastic surgical repairs, orthopaedic traumatic and dental surgery.

TISSEEL can also be applied to tension-free detached tissues to glue them together. TISSEEL Lyo can be used even if your blood does not clot properly, e.g. when you are treated with heparin against thrombosis.

The clot produced by TISSEEL Lyo is very similar to a natural blood clot and this means that it will dissolve naturally and leave no residue. However, aprotinin is added to increase the longevity of the clot and to prevent its premature dissolution.

2. BEFORE YOU USE TISSEEL LYO

Do not use TISSEEL Lyo in the following situations:

- TISSEEL Lyo must not be used for massive or brisk bleeding.
- TISSEEL Lyo must not be used to replace skin sutures intending to close surgical wounds.
- TISSEEL Lyo MUST NOT be applied into blood vessels (veins or arteries), or into tissues. As TISSEEL Lyo forms a clot where it is applied, injecting TISSEEL Lyo may cause serious reactions. TISSEEL Lyo should only be applied to the surface of tissues as thin layer where it is needed. If you are going to have coronary bypass surgery, special care needs to be taken to avoid injecting TISSEEL Lyo into blood vessels.
- If you are allergic (hypersensitive) to bovine proteins or any of the other ingredients of TISSEEL Lyo the product must not be used.

TISSEEL Lyo contains a protein, called aprotinin. Even when this protein is applied in small areas, there is a risk of a reaction known as anaphylaxis, or a severe allergic (hypersensitive) reaction.

Take special care with TISSEEL Lyo

- **Life-threatening/fatal air or gas embolism (air getting into the blood circulation which can be serious or life-threatening) has occurred very rarely with the use of spray devices employing pressure regulators to administer fibrin sealants. This appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. The risk appears to be higher when fibrin sealants are sprayed with air, as compared to CO_2 and therefore cannot be excluded with TISSEEL Lyo when sprayed in open wound surgery.**
- **Spray devices and the accessory tip provide instructions for use with recommendations for pressure ranges and to the spraying distance from the tissue surface.**
- **TISSEEL Lyo should be administered strictly according to the instructions and only with devices recommended for this product.**
- **When spraying TISSEEL Lyo, changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored for possible occurrence of gas embolism.**

- If you have ever received TISSEEL Lyo or aprotinin before, your body may have become sensitive to it. It is possible you may have an allergic reaction to this material, even if there was no reaction to the first application. If you think you have received either product in a previous operation, you have to inform your doctor about this.
- If the surgeon or operating team sees any sign of an allergic reaction during the application of TISSEEL Lyo, they will stop using TISSEEL Lyo immediately and will take the adequate measures.

Taking or Using other medicines

There are no known interactions between TISSEEL Lyo and other medicinal products. Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Oxidised cellulose-containing preparations may reduce the efficacy of TISSEEL and should not be used as carrier materials.

Taking TISSEEL Lyo with food and drink

Please ask your doctor. The doctor will decide if you are allowed to eat and drink before the application of TISSEEL Lyo.

Pregnancy, breast-feeding and fertility

Ask your doctor or pharmacist for advice before taking any medicine. Please inform your doctor before using TISSEEL Lyo if you are or could be pregnant or if you are breast- feeding. Your doctor will decide if you can use TISSEEL Lyo during pregnancy or breast-feeding.

The effects of TISSEEL Lyo on fertility have not been established.

Driving and using machines

TISSEEL Lyo will not affect your ability to drive or operate other types of machines.

Important information about some of the ingredients of TISSEEL Lyo

Important information about the potential risk of infection from donor human plasma

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.
The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non- enveloped hepatitis A virus. The measures taken may be of limited value against non- enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

It is strongly recommended that every time you receive a dose of TISSEEL the name and batch number of the product are recorded in order to maintain a record of the batches used.

3. HOW TO USE TISSEEL LYO

- TISSEEL Lyo is only applied during a surgical operation. The use of TISSEEL Lyo is restricted to experienced surgeons who have been trained in the use of TISSEEL Lyo.
- The amount of TISSEEL Lyo that will be used depends on a number of factors, including, but not limited to the type of surgery, the surface area of tissue to be treated during your operation and the way TISSEEL Lyo is applied. The surgeon will decide how much is appropriate, and will apply just enough to form a thin, even layer over the tissue. If this does not seem to be enough, a second layer can be applied.
- However, avoid a reapplication of TISSEEL to a pre-existing polymerized TISSEEL layer as TISSEEL will not adhere to a polymerized layer.
- Separate, sequential application of the two components of TISSEEL must be avoided.
- During your operation the surgeon will apply TISSEEL Lyo onto the relevant tissue surface, using the special application device provided. This device ensures that equal amounts of both components are applied at the same time – which is important for the optimal effect of TISSEEL Lyo.
- In cases where very small volumes (1 to 2 drops) of TISSEEL Lyo are administered, expel and discard the first several drops from the application cannula immediately before application, to ensure adequate mixing of the sealer protein and thrombin solutions.
- Prior to applying TISSEEL Lyo the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).
- Pressurized air or gas must not be used for drying the site.
- TISSEEL must be sprayed only onto application sites that are visible.

When applying TISSEEL Lyo using a spray device be sure to use a pressure and a distance from the tissue within the range recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of TISSEEL Lyo					
Surgery	Spray set to be used	Applicator tips to be used	Pressure regulator to be used	Recom-mended distance from target tissue	Recom-mended spray pressure
Open wound	Tisseel / Artiss Spray Set	n.a.	EasySpray	10-15cm	1.5-2.0 bar (21.5-28.5 psi).
	Tisseel / Artiss Spray Set 10 pack	n.a.	EasySpray		
		Duplospray MIS Applicator 20cm	Duplospray MIS Regulator		
			Duplospray MIS Regulator NIST B11		

Laparo-scopic/ minimally invasive procedures	n.a.	Duplospray MIS Applicator 30cm	Duplospray MIS Regulator	2 – 5 cm	1.2-1.5 bar (18-22 psi)
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 40cm	Duplospray MIS Regulator		
			Duplospray MIS Regulator NIST B11		
		Replaceable tip	Duplospray MIS Regulator		
			Duplospray MIS Regulator NIST B11		

When spraying the TISSEEL Lyo, changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see section 2).

Use in children
Safety and efficacy of the product in children have not been established.

If you take more TISSEEL Lyo than you should

TISSEEL Lyo is only applied during a surgical operation. It is applied by the surgeon and the amount of TISSEEL Lyo is determined by the surgeon.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, TISSEEL Lyo can cause side effects, although not everybody gets them. If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Side effects have been evaluated on the basis of the following frequency categories:
Very common: Affects more than one in 10.
Common: Affects 1 to 10 users in 100.
Uncommon: Affects 1 to 10 users in 1,000.
Rare: Affects 1 to 10 users in 10,000.
Very rare: Affects fewer than 1 out of 10,000 patients treated.
Not known: The frequency cannot be estimated from the available data.

In patients who are treated with fibrin sealant, hypersensitivity reactions or allergic reactions may occur. Although they are rare, they may be severe.

The first signs of an allergic reaction may include

- transient reddening of the skin (“flushing”)
- itching
- hives
- nausea, vomiting
- headache
- drowsiness
- restlessness
- burning and stinging at the application site
- tingling
- chills
- tightness of the chest
- swelling of lips, tongue, throat (which may result in difficulty to breathe and/or swallow)
- breathing difficulties
- low blood pressure
- increase or drop in pulse rate
- loss of consciousness due to a drop in blood pressure

In isolated cases, these reactions may progress to severe allergic reactions (anaphylaxis). Such reactions may be seen especially if the preparation is applied repeatedly, or administered to patients who have previously shown hypersensitivity to aprotinin or any other component of the product.

Even if repeated treatment with TISSEEL was well tolerated, a subsequent administration of TISSEEL or an infusion of aprotinin may result in severe allergic (anaphylactic) reactions.

The attending surgical team is well aware of the risk of reactions of this type and will immediately interrupt the application of TISSEEL Lyo on the occurrence of the first signs of hypersensitivity. In the case of severe symptoms emergency measures may be required.

The injection of TISSEEL into soft tissues may lead to local tissue damage.

The injection of TISSEEL into blood vessels (veins or arteries) may lead to the formation of clots (thromboses).

Intravascular application might increase the likelihood and severity of acute hypersensitivity reactions in susceptible patients.

As TISSEEL is derived from plasma from blood donations, the risk of an infection cannot be excluded completely. However, the manufacturers take numerous measures to reduce this risk (see section 2).

Antibodies against components of the fibrin sealant may occur in rare cases.

The following side effects have been observed in treatment with TISSEEL:

General areas	Side Effect	Frequency
Infections and parasitic diseases	Postoperative wound infection	Common
Blood and lymphatic system disorders	Increase of fibrin degradation products	Uncommon
Immune system disorders	Hypersensitivity reactions	Not known
	Allergic (anaphylactic) reactions	Not known
	Anaphylactic shock	Not known
	Sensation of tingling, pricking or numbness of the skin	Not known
	Tightness of the chest	Not known
	Breathing difficulties	Not known
	Itching	Not known
	Reddening of the skin	Not known
Nervous system disorders	Sensory disturbance	Common
Cardiac disorders	Increase or drop in pulse rate	Not known
Vascular disorders	Axillary venous thrombosis	Common
	Drop in blood pressure	Rare
	Bruising	Not known
	Blood clot in blood vessels	Not known
	Blockage of an artery in the brain	Not known
	Gas bubbles*	Not known
Respiratory, and thoracic disorders	Dyspnoea	Not known
Gastrointestinal disorders	Nausea	Uncommon
	Intestinal obstruction	Not known
Skin and subcutaneous tissue disorders	Skin Rash	Common
	Hives	Not known
	Impaired healing	Not known
Musculoskeletal and connective tissue disorders	Pain in extremities	Uncommon
General disorders and administration site conditions	Pain caused by the procedure	Uncommon
	Pain	Common
	Increased body temperature	Common
	Reddening of the skin	Not known
	Swelling through the accumulation of fluid in the body tissue (oedema)	Not known
Injury, poisoning and procedural complications	Accumulation of lymph or other clear bodily fluids near the operation site (seroma)	Very common
	Rapid swelling of dermis, subcutaneous tissue, mucosa and submucosa (angioedema)	Not known

* the introduction of air or gas bubbles in the blood stream have occurred when fibrin sealants are applied with devices using pressurized air or gas; this is believed to be caused by inappropriate use of the spray device (e.g. at higher than recommended pressure and in close proximity to the tissue surface.)

- The surgical team treating you will be aware of the risk of allergic reactions – if they see any symptoms, the application of TISSEEL Lyo will be stopped immediately. Severe symptoms may require emergency treatment.
- If TISSEEL Lyo is injected into soft tissues, it can cause local tissue damage.
- If TISSEEL Lyo is injected into blood vessels (veins or arteries), it can cause clots to form (thrombosis).
- As TISSEEL Lyo is made from plasma of blood donations, the risk of infection cannot be totally excluded, but the manufacturer undertakes numerous measure to reduce the risk (see section 2).
- There are also individual reports on occurrence of bleeding, blockage of bowel passageway, impaired healing, swellings caused by accumulation of fluid in body tissue, fever, and accumulation of lymph and other clear body fluids near the surgical site.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

HPRA Pharmacovigilance
Earlsfort Terrace
IRL-Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE TISSEEL LYO

- Keep out of the reach and sight of children.
- Store below +25°C. Do not freeze.
- Keep TISSEEL Lyo in the outer carton to protect from light.
- Do not use after the expiry date stated on the label.

Storing after preparation:

After reconstitution both fibrin sealant components must be used within 4 hours. Reconstituted solutions must not be refrigerated or frozen.

6. FURTHER INFORMATION

What TISSEEL Lyo contains
TISSEEL Lyo contains two components:

Component 1 = Sealer Protein Solution:
For Sealer Protein Solution the Sealer Protein Concentrate (lyophilized) has to be reconstituted with Aprotinin Solution.

1.) Sealer Protein Concentrate contains following active substances:
Human Fibrinogen, 91 mg/ml mg/ml; Human Factor XIII 0.6 - 5 IU/ml
The excipients are Human Albumin Solution, Histidine, Nicotinic Acid, Polysorbate 80, Sodium Citrate.

1.a) Aprotinin Solution (solvent for Sealer Protein Concentrate) contains following active substance:
Aprotinin 3000 KIU/ml
The excipient is Water for Injections.

Component 2 = Thrombin Solution:
For Thrombin Solution the Thrombin (lyophilized) has to be reconstituted with Calcium Chloride Solution.

2.) Thrombin (lyophilized) contains following active substance when reconstituted:
Human Thrombin, 500 IU/ml
The excipients are Human Albumin Solution and Sodium Chloride.

2.a) Calcium Chloride Solution (solvent for Thrombin Powder)
The active substance is Calcium Chloride, 40 micromoles/ml
The excipient is Water for Injections.

What TISSEEL Lyo looks like and the contents of the pack

All components of TISSEEL Lyo are filled into glass containers.

The vial containing the Sealer Protein Concentrate is equipped with a magnetic stirrer. Freeze-dried constituents are white or pale yellow powders or friable solids; liquid constituents are colorless or pale yellow.

Each pack of TISSEEL Lyo contains

- 1 vial containing Sealer Protein Concentrate – freeze-dried 91mg/ml when reconstituted
- 1 vial containing Thrombin - freeze-dried 500 IU/ml
- 1 vial containing Aprotinin Solution 3000 KIU/ml
- 1 vial containing Calcium Chloride Solution 40 micromoles/ml
- 1 kit for reconstitution and application (DUPLOJECT System) TISSEEL Lyo is available in pack sizes of 2 ml, 4 ml and 10 ml

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Baxter Holding B.V.
Kobaltweg 49,
3542CE Utrecht,
Netherlands

Manufacturer
Takeda Manufacturing Austria AG
Industriestraße 67
A-1221 Vienna
Austria

This leaflet was last approved in 01/2022

The following information is intended for medical or healthcare professionals only:

Instructions for use and handling and disposal

General

Before administering TISSEEL Lyo take care that parts of the body outside the intended application area are adequately covered, so that the medicine does not adhere to tissue at undesired sites.
To prevent TISSEEL Lyo from adhering to gloves and instruments, wet these with sodium chloride solution before contact.
In order to ensure complete blending of the sealer protein component and the thrombin component, express the first drops of the product from the application cannula immediately before use and dispose of them.

Some solutions that contain alcohol, iodine or certain types of metals (these are normally found in disinfectants or antiseptics) may reduce the ability of TISSEEL Lyo to work normally. These substances should be removed, as far as possible, before TISSEEL Lyo is applied.

The guideline for sealing surfaces is: One package of TISSEEL 2 ml (i.e. 1 ml sealer protein solution plus 1 ml thrombin solution) is sufficient for a surface of at least 10 cm^2.

The dose depends on the size of the surface to be sealed.

It is strongly recommended that every time you receive a dose of TISSEEL Lyo, the name and batch number of the product are recorded. This maintains a record of the batches used.

Preparation and reconstitution

Prior to reconstitution of the fibrin sealant components, clean the rubber stoppers of all vials. Avoid direct contact between disinfectant and product.

I. Preparation of Sealer Protein Solution(First Component)

The Sealer Protein Concentrate (lyophilized) is dissolved with the Aprotinin Solution to form the Sealer Protein Solution.

Sealer Protein Concentrate (lyophilized) is reconstituted using the FIBRINOTHERM warming and stirring device (recommended method). Alternatively, a sterile water bath at a temperature of 33-37°C can be used.

Reconstitution using the FIBRINOTHERM device:

The FIBRINOTHERM device maintains a constant temperature of 37°C. It also shortens the dissolution time of the Sealer Protein Concentrate (lyophilized) by rotating the magnetic stirrer contained in each Sealer Protein Concentrate (lyophilized) vial.

- Place the vials containing Sealer Protein Concentrate (lyophilized) and Aprotinin Solution into the appropriate openings of the temperated FIBRINOTHERM device and preheat the vials for approximately 3 minutes.

- Transfer the Aprotinin Solution into the vial containing the Sealer Protein Concentrate (lyophilized) using one needle and the blue-scaled syringe provided in the single- sterile kit for reconstitution. Place the Sealer Protein vial into the stirring well of the FIBRINOTHERM device (use the adaptor, if necessary) and stir until complete dissolution. Reconstitution is complete as soon as no particles are visible anymore when the vial is held against the light. If particles are present, keep on stirring the solution at 37°C for a few more minutes until complete dissolution. Turn off the magnetic stirrer when dissolution is complete.

Note: Excessive stirring may compromise product quality!

- Keep the Sealer Protein Solution at 37°C or at room temperature (up to +25°C) without stirring if it is not to be used immediately. Before use the solution should be warmed to 37°C. To ensure homogeneity, stir or swirl briefly before drawing up the Sealer Protein Solution into the blue-scaled syringe provided in the double-sterile kit for application.

- Withdraw the reconstituted Sealer Protein Solution from the vial under sterile conditions.

For further instructions please refer to the instructions for use of the FIBRINOTHERM device.

<u>Reconstitution using a water bath:</u>

- Preheat the vials containing the Sealer Protein Concentrate (lyophilized) and the Aprotinin Solution for approximately 3 minutes in a water bath at a temperature of 33 to 37°C. (Heating beyond 37°C must be avoided!)

- Transfer the Aprotinin Solution into the vial containing the Sealer Protein Concentrate (lyophilized) using one needle and the blue-scaled syringe provided in the single- sterile kit for reconstitution.

- Return the Sealer Protein vial to the water bath at 33 - 37°C for one minute.

- Swirl briefly but avoid excessive frothing. Then return the vial to the water bath and check periodically for complete dissolution. Reconstitution is complete as soon as no particles are visible when the vial is held against the light. If particles are present, keep the vial at 33 - 37°C for a few more minutes and agitate the solution until complete dissolution.

- Keep the Sealer Protein Solution at 33 - 37°C or at room temperature (up to +25°C) if not used immediately. Before use the solution should be warmed to 33-37°C. To ensure homogeneity, swirl briefly before drawing up the Sealer Protein Solution into the blue-scaled syringe provided in the double-sterile kit for application.

- Withdraw the reconstituted Sealer Protein Solution from the vial under sterile conditions.

Note: When using a water bath for reconstitution rather than the FIBRINOTHERM device, take special care not to submerge the vial, particularly the septum, as this can cause contamination.

II. Preparation of Thrombin Solution (Second Component)

The Thrombin (lyophilized) is dissolved with the Calcium Chloride Solution to form the Thrombin Solution. Transfer the contents of the Calcium Chloride Solution vial into the Thrombin (lyophilized) vial. Use the second needle and the black-scaled syringe provided in the single-sterile kit for reconstitution.

Swirl briefly to dissolve the lyophilized material. To warm the Thrombin Solution either the FIBRINOTHERM device or a water bath can be used. Keep the Thrombin Solution at 33 - 37°C or at room temperature (up to +25°C) if not used immediately. Before use the solution should be warmed to 33-37°C. Prior to use, draw up the Thrombin Solution from the vial, using the second needle and the black-scaled syringe provided in the double- sterile kit for application.

Note: Syringes and needles used for the reconstitution of one component must not be re- used for the reconstitution of the other component, as this would make this component set in the vial or syringe.

III. Use of reconstituted TISSEEL Lyo Components

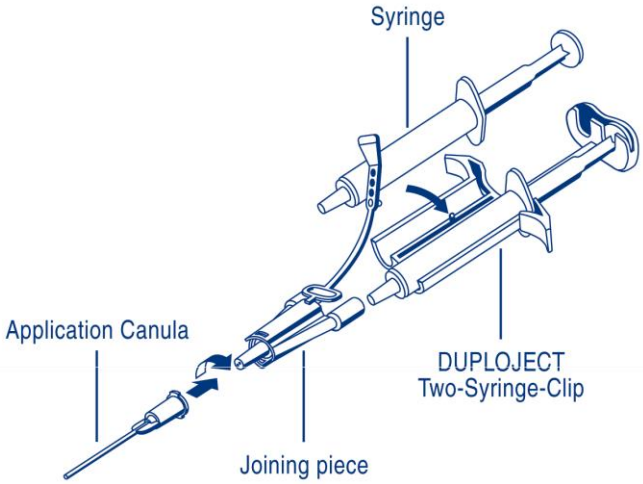
Both fibrin sealant components must be used within 4 hours of preparation. Reconstituted solutions must not be refrigerated or frozen.

Administration

The Sealer Protein and the Thrombin Solutions should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits. Inspect reconstituted products by eye for particulate matter and discoloration prior to administration.

For application, clip the two single-use syringes with the reconstituted Sealer Protein Solution and Thrombin Solution into the DUPLOJECT Two-Syringe Clip and connect this assembly to a joining piece and an application cannula. The double-sterile kit contains all devices necessary for application.
The common plunger of the DUPLOJECT Two-Syringe Clip ensures that equal volumes are fed through the joining piece, before being mixed in the application cannula and ejected.

Operating Instructions



- Place the two syringes filled with Sealer Protein Solution and with Thrombin Solution into the clip. The two syringes should be filled with equal volumes.
- Connect the nozzles of the two syringes to the joining piece, ensuring that they are firmly fixed. Secure the joining piece by fastening the tether strap to the DUPLOJECT Two-Syringe Clip. If the tether strap tears, use the spare joining piece. If none is available, further use is still possible but check that the connection is tight to prevent any risk of leaking.
- Fit an application cannula onto the joining piece.
- Do not expel the air remaining inside the joining piece or application cannula until you start actual application as the aperture of the cannula may clog.
- Apply the mixed Sealer Protein - Thrombin Solution onto the recipient surface or surfaces of the parts to be sealed.

If application of the fibrin sealant components is interrupted, clogging occurs immediately in the cannula. Replace the application cannula with a new one immediately before application is resumed. If the apertures of the joining piece are clogged, use the spare joining piece provided in the package.

Note: After mixing the sealant components, the fibrin sealant starts to set within seconds, because of the high Thrombin concentration (500 IU/ml).

Application is also possible with other accessories supplied by BAXTER that are particularly suited for, e.g., endoscopic use, minimally invasive surgery, application to large or poorly accessible areas. When using these application devices, strictly follow the Instructions for Use of the devices.
After TISSEEL has been applied, allow at least 2 minutes to achieve sufficient polymerization.

In certain applications biocompatible material, such as collagen fleece, is used as a carrier substance or for reinforcement.

Oxidized cellulose-containing preparations should not be used with TISSEEL Lyo.

When applying TISSEEL Lyo using a spray device be sure to use a pressure and a distance from the tissue within the range recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of TISSEEL Lyo					
Surgery	Spray set to be used	Applicator tips to be used	Pressure regulator to be used	Recom mended distance from target tissue	Recom-mended spray pressure
Open wound	Tisseel /Artiss Spray Set	n.a.	EasySpray	10-15cm	1.5-2.0 bar (21.5-28.5 psi).
	Tisseel / Artiss Spray Set 10 pack	n.a.	EasySpray		
Laparo-scopic/ minimally invasive procedures	n.a.	Duplospray MIS Applicator 20cm	Duplospray MIS Regulator	2 – 5 cm	1.2-1.5 bar (18-22 psi)
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 30cm	Duplospray MIS Regulator		
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 40cm	Duplospray MIS Regulator		
			Duplospray MIS Regulator NIST B11		
		Replaceable tip	Duplospray MIS Regulator		
			Duplospray MIS Regulator NIST B11		

When spraying the TISSEEL Lyo, changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see section 2).

For the application of TISSEEL Lyo in enclosed thoracic and abdominal spaces the DuploSpray MIS applicator and regulator system is recommended. Please refer to the instruction manual of the DuploSpray MIS device.

Disposal

Any unused product or waste material should be disposed of in accordance with local requirements.