**PACKAGE LEAFLET: INFORMATION FOR THE USER**

**TISSEEL**

**Ready to use**

**Solutions for Sealant**

**Active substances:** Human fibrinogen, human thrombin, aprotinin, human factor XIII, 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 you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

**In this leaflet:**



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

**What TISSEEL is**

The name of your medicine is TISSEEL.

TISSEEL is a two-component tissue 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 is prepared as two solutions (Sealer Protein Solution and Thrombin Solution), which mix when applied.

**What TISSEEL is used for**

TISSEEL 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 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.

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

The clot produced by TISSEEL 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. WHAT YOU NEED TO KNOW BEFORE YOU USE TISSEEL

**Do not use TISSEEL in the following situations:**

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

  TISSEEL 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**

- **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 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 should be administered strictly according to the instructions and only with devices recommended for this product.**
- **When spraying TISSEEL, 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 or aprotinin before, your body may have become sensitive to it. It is possible you may be allergic 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, they will stop using TISSEEL immediately and will take the adequate measures.

**Other medicines and TISSEEL**

There are no known interactions between TISSEEL 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.

**TISSEEL 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.

**Pregnancy, breast-feeding and fertility**

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Your doctor will decide if you can use TISSEEL during pregnancy or breast-feeding.

The effects of TISSEEL on fertility have not been established.

**Driving and using machines**

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

**Important information about some of the ingredients of TISSEEL**

**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

- TISSEEL is only applied during a surgical operation.–The use of TISSEEL is restricted to experienced surgeons who have been trained in the use of TISSEEL.
- The amount of TISSEEL 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 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 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.
- In cases where very small volumes (1 to 2 drops) of TISSEEL 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 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 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**

| Surgery | Spray set to be used | Applicator tips to be used | Pressure regulator to be used | Recommended distance from target tissue | Recommended spray pressure |
|---|---|---|---|---|---|
| Open wound | Tisseel / Artiss Spray Set | n.a. | EasySpray | 10-15cm | 1.5-2.0 bar (21.8-29.0 psi). |

| Surgery | Spray set to be used | Applicator tips to be used | Pressure regulator to be used | Recommended distance from target tissue | Recommended spray pressure |
|---|---|---|---|---|---|
| | Tisseel / Artiss Spray Set 10 pack | n.a. | EasySpray | | |
| Laparoscopic/ minimally invasive procedures | n.a. | Duplospray MIS Applicator 20cm | Duplospray MIS Regulator 1.5 bar | 2 – 5 cm | 1.2-1.5 bar (18-22 psi) |
| | | | | | |
| | | Duplospray MIS Applicator 30cm | | | |
| | | | | | |
| | | Duplospray MIS Applicator 40cm | | | |
| | | | | | |
| | | Replaceable tip | | | |
| | | | | | |

**When spraying the TISSEEL, 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 than you should**

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

In patients who are treated with fibrin sealant, hypersensitivity reactions or allergic reactions may occur. These side effects 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 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.

If TISSEEL is accidentally injected inside blood vessels (veins or arteries) may lead to the formation of blood 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:**

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.

**Not known:** The frequency cannot be estimated from the available data.

| 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 will be stopped immediately. Severe symptoms may require emergency treatment.
- If TISSEEL is injected into soft tissues, it can cause local tissue damage.
- If TISSEEL is injected into blood vessels (veins or arteries), it can cause clots to form (thrombosis).
- As TISSEEL is made from plasma from blood donations, the risk of infection cannot be totally excluded, but the manufacturer undertakes numerous measures 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

Website: www.hpra.ie

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

## 5. HOW TO STORE TISSEEL

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label.
- Store in a freezer at ≤–20°C without interruption until preparation for use. The cold storage chain must not be interrupted until use.
- Keep TISSEEL in the original package, to protect from light.
- After thawing, the solution must not be refrozen or refrigerated!

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

**What TISSEEL contains**

TISSEEL contains two components:

Component 1 = Sealer Protein Solution:

The active substances contained in 1ml of the Sealer Protein solution are:

Human Fibrinogen, 91 mg/ml; Aprotinin, 3000 KIU/ml; Human Factor XIII 0.6-5 IU/ml.

The excipients are Human Albumin, Histidine, Nicotinamide, Polysorbate 80, Sodium Citrate and Water for Injections.

Component 2 = Thrombin Solution:

The active substances contained in 1 ml of the Thrombin Solution are:

Human Thrombin, 500 IU/ml; Calcium Chloride, 40 micromoles/ml.

The excipients are Human Albumin, Sodium Chloride and Water for Injections.

**What TISSEEL looks like and the contents of the pack**

Solutions for sealant.

TISSEEL is supplied in a pre-filled single-use double-chamber syringe closed with a tip cap packed in two pouches (outer and inner pouch) and one device set with 2 joining pieces and 4 application cannulas.

The frozen solutions are colourless or pale yellow, opalescent.

After thawing, they are colorless to pale yellow.

TISSEEL is available in the following pack sizes of 1 syringe:

- 2 ml (1 ml of Sealer Protein Solution and 1 ml of Thrombin Solution)
- 4 ml (2 ml of Sealer Protein Solution and 2 ml of Thrombin Solution)
- 10 ml (5 ml of Sealer Protein Solution and 5 ml of Thrombin Solution)

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

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

**Instructions for use and handling and disposal**

**General**

- The inner pouch and its contents are sterile unless the integrity of the outer pouch is compromised.
- The sealer protein and the thrombin solutions should be clear or slightly opalescent.
- Do not use solutions that are cloudy, discolored, have deposits or other changes in their appearance, including the consistency of a solidified gel after thawing.
- Before the application of TISSEEL, ensure that all parts of the body outside the desired application area are sufficiently covered to prevent tissue adhesion at undesired sites.
- 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 to work normally. These substances should be removed, as far as possible, before TISSEEL is applied.

**Thawing of the frozen presentation**

- Do not use TISSEEL unless it is completely thawed and warmed (liquid consistency).
- TISSEEL must not be exposed to temperatures above 37°C and must not be microwaved.
- The protective syringe cap should not be removed until thawing and warming is complete, and application tip is ready to be attached.
- To facilitate removal of the tip cap from the syringe, rock the tip cap by moving it backward and forward, then pull the protective cap off the syringe.
- It is strongly recommended that every time you receive a dose of TISSEEL, the name and batch number of the product are recorded. This maintains a record of the batches used.

Thaw and warm the pre-filled syringes using one of the following options:

**Option 1: Quick thawing/warming methods (preparation in a single step)**

a) *Sterile Water Bath*

b) *Non-Sterile Water Bath*

c) *Incubator*

**Option 2: Thawing at Room Temperature (not above +25°C) followed by warming in Incubator (possibility of interim storage for up to 72 hours at temperatures not exceeding +25°C)**

**1. Quick thawing/warming methods**

An overview of the quick thawing/warming methods is provided in Table 1.

**Table 1: Quick Thawing /Warming Methods at 33°C – 37°C**

| Pack Size | Minimum Thawing/Warming Times | | |
|---|---|---|---|
| | **Sterile Water Bath (Pouches Removed)** | **Non-Sterile Water Bath (In Pouches)** | **Incubator (In Pouches)** |
| 2 ml | 5 min | 15 min | 40 min |
| 4 ml | 5 min | 20 min | 50 min |
| 10 ml | 10 min | 35 min | 90 min |

Note: If a water bath is used it must not exceed the temperature of +37°C.

***a) Sterile Water Bath (Recommended Method)***

- Remove the outer pouch and transfer the pre-filled syringe packed in the inner pouch, into the sterile area.
- Remove the pre-filled syringe from the inner pouch and place the syringe directly into the sterile water heated to 33°C - 37°C ensuring the syringe is completely immersed in the water (See Table 1 for minimum thawing/warming times).
- To monitor the specified temperature range, control the water temperature using a thermometer and change the water as necessary.

***b) Non-sterile water bath***

- Place the pre-filled syringe packed in both pouches, in a water bath heated to 33°C - 37°C outside the sterile area, ensuring the pouches remain immersed in the water (See Table 1 for minimum thawing/warming times).
- Remove the pouches from the water bath after thawing and warming.
- Dry and remove the outer pouch and transfer the pre-filled syringe in the inner pouch, onto the sterile area.

***c) Incubator***

- Place the pre-filled syringe, packed in both pouches, in an incubator outside the sterile area (See Table 1 for minimum thawing/warming times).
- After thawing/warming in the incubator, remove the outer pouch and transfer the pre-filled syringe, inside the inner pouch, into the sterile area.

**2. Thawing at room temperature (not above + 25°C) followed by warming in Incubator**

- Thaw the pre-filled syringe, packed in both pouches, at room temperature outside the sterile area (See Table 2 for minimum thawing times).

- Warm the pre-filled syringe, packed in both pouches, in an incubator at 33°C - 37°C outside the sterile area (See Table 2 for minimum warming times).
- After thawing/warming in the incubator, remove the outer pouch and transfer the pre-filled syringe, inside the inner pouch, into the sterile area.

**Table 2: Thawing at Room Temperature and Warming in Incubator**

| Pack Size | Minimum Thawing /Warming Times | |
|---|---|---|
| | **Thawing at room temperature (Not above 25°C)** | **Warming in Incubator (33-37°C)** |
| 2 ml | 80 minutes | 11 minutes |
| 4 ml | 90 minutes | 13 minutes |
| 10 ml | 160 minutes | 25 minutes |

**Stability after thawing**

After **thawing and warming** at temperatures between 33°C and 37°C (Options 1 and 2), the product must be used within 12 hours.

After **thawing at room temperature** (Option 2), the product can be stored for up to 72 hours at temperatures not exceeding 25°C provided it remains sealed in the original package (both pouches).

Do not re-freeze or refrigerate once thawing has been initiated.

**Handling after thawing / before application**

The product must be warmed to 33°C – 37°C before use.

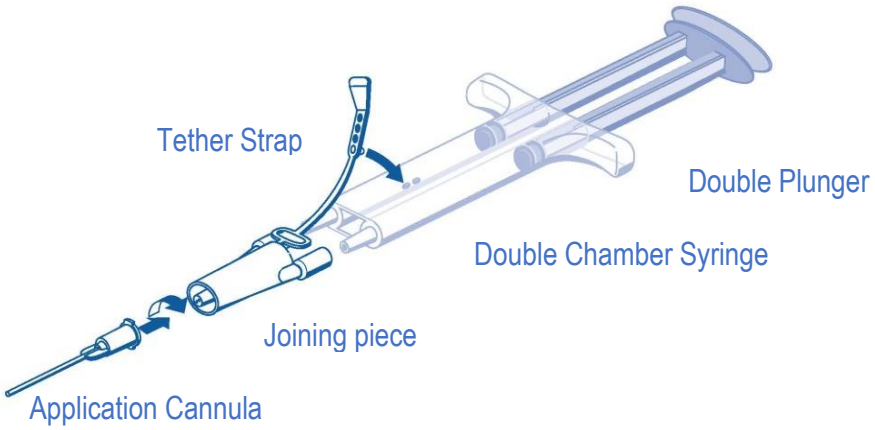
To achieve optimal blending of the two solutions and optimal solidification of the fibrin sealant, **maintain the two sealant components at 33°C - 37°C until application**.

The thawed sealer protein solution should be liquid but slightly viscous. If the solution has the consistency of a solidified gel, it must be assumed to have become denatured (possibly due to an interruption of the cold storage chain or by overheating during warming). In this case, the TISSEEL must not be used.

**Non-Spray Administration**

For application, connect the double-chamber syringe with the Sealer Protein Solution and the Thrombin Solution to a joining piece and an application cannula as provided in the accompanying set of devices. The common plunger of the double-chamber syringe ensures that the equal volumes of the two sealant components are fed through the joining piece into the application cannula where they are blended and then applied.

*Operating instructions*




- Expel all air from the syringe prior to attaching any application device.
- Align the joining piece and tether to the side of the syringe with the tether strap hole.
- Connect the nozzles of the double chamber ready-to-use syringe to the joining piece, ensuring that they are firmly attached.
    - Secure the joining piece by fastening the tether strap to the double chamber ready-to-use syringe.
    - If the tether strap tears, use the spare joining piece provided in the kit.
    - If a spare joining piece is not available, the system can still be used if care is taken to ensure that the connection is secure and leak-proof.
    - Do NOT expel the air remaining inside the joining piece.
- Attach an application cannula on to the joining piece.
    - Do NOT expel the air remaining inside the joining piece and inside the application cannula until you start the actual application because this may clog the application cannula.

**Administration**

Prior to applying TISSEEL the surface of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices). Do not use pressurized air or gas for drying the site.

- Apply the mixed sealer protein - thrombin solution on to the recipient surface or on to the surfaces of the parts to be glued by slowly pressing on the back of the common plunger.
- In surgical procedures that require the use of minimal volumes of fibrin sealant, it is recommended to expel and discard the first few drops of product.
- After TISSEEL has been applied, allow at least 2 minutes to achieve sufficient polymerization.

**Note:** If application of the fibrin sealant components is interrupted, clogging may occur in the cannula. In this case, only replace the application cannula with a new one immediately before application is resumed. If the openings of the joining piece are clogged, use the spare joining piece provided in the package.

After blending of the sealant components, the fibrin sealant starts to set within seconds due to the high thrombin concentration (500 IU/ml).

The fibrin sealant can also be applied with other accessories supplied by BAXTER which are particularly suited, for example, for endoscopic use, minimally invasive surgery or application to large or difficult-to-access areas. When using these application devices, please follow their instructions for use carefully.

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

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

**Application with Spray Device**

**When applying TISSEEL 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:**

**Table 3: Recommended pressure, distance and devices for spray application of TISSEEL**

| Surgery | Spray set to be used | Applicator tips to be used | Pressure regulator to be used | Recommended distance from target tissue | Recommended spray pressure |
|---|---|---|---|---|---|
| Open wound | Tisseel / Artiss Spray Set | n.a. | EasySpray | 10-15cm | 1.5-2.0 bar (21.8-29.0 psi). |
| | Tisseel / Artiss Spray Set 10 pack | n.a. | EasySpray | | |
| Laparoscopic/ minimally invasive procedures | n.a. | Duplospray MIS Applicator 20cm | Duplospray MIS Regulator 1.5 bar | 2 – 5 cm | 1.2-1.5 bar (18-22 psi) |
| | | | | | |
| | | Duplospray MIS Applicator 30cm | | | |
| | | | | | |
| | | Duplospray MIS Applicator 40cm | | | |
| | | | | | |
| | | Replaceable tip | | | |
| | | | | | |

**When spraying the TISSEEL, 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 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.

Equivalent spray devices, intended for specific use with TISSEEL, may also be used. When using other spray devices, follow the instructions for use that are provided with the device.

**Disposal**

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