

PACKAGE LEAFLET: INFORMATION FOR THE USER**ARTISS Solutions for Sealant****Deep frozen****Human Fibrinogen, Human Thrombin, Aprotinin,
Calcium Chloride Dihydrate.**

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- 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.

What is in this leaflet

1. What ARTISS is and what it is used for
2. What you need to know before you use ARTISS
3. How to use ARTISS
4. Possible side effects
5. How to store ARTISS
6. Contents of the pack and other information

1. What ARTISS is and what it is used for**What ARTISS is**

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

What ARTISS is used for

ARTISS is a tissue sealant.

ARTISS is applied to glue soft tissues in plastic, reconstructive and burn surgery. For example, ARTISS may be used to glue skin grafts or skin flaps to burn wounds or to glue skin to the underlying tissue in plastic surgery. Also, artificial skin may be glued to wounds with ARTISS.

The clot produced by ARTISS is very similar to a natural blood clot. This means that it will dissolve naturally and leave no residue. However, aprotinin (a protein, that delays dissolution of a clot) is added to increase the longevity of the clot and to prevent its premature dissolution.

2. What you need to know before you use ARTISS**Do not use ARTISS:**

- if you are allergic to any of the active substances or any of the other ingredients of this medicine (listed in section 6).
- ARTISS must not be used for massive or brisk bleeding.
- ARTISS is not indicated to replace skin sutures intended to close a surgical wound.
- ARTISS MUST NOT be injected into blood vessels (veins or arteries), or into tissues. As ARTISS forms a clot where it is applied, injecting ARTISS may cause serious reactions (e.g. vessel occlusion). ARTISS should only be applied to the surface of tissues as a thin layer where it is needed.
- You must not receive ARTISS if you are allergic (hypersensitive) to the active substances, to bovine protein or any of the other ingredients (see section 6) of ARTISS. It may cause serious allergic reactions. Please inform your doctor or surgeon if you know that you are allergic against aprotinin or any bovine protein.
- Spray application of ARTISS should not be used in endoscopic procedures. For laparoscopy (keyhole surgery), see section "Warnings and Precautions".

Warnings and precautions

- Talk to your doctor, pharmacist or nurse before using ARTISS.
- **Life-threatening/fatal air or gas embolism (air getting into the blood circulation which can be serious or life-threatening) has occurred 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 CO₂ and therefore cannot be excluded with ARTISS.**
- **When ARTISS is applied using a spray device, the pressure and spraying distance have to be within the range recommended by the manufacturer. ARTISS should be administered strictly according to the instructions and only with devices recommended for this product.**
- **When spraying ARTISS, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored for possible occurrence of gas embolism.**
- ARTISS must not be used with the Easy Spray/Spray Set system in enclosed body areas for serious safety reasons.
- ARTISS is not recommended for laparoscopic surgery (keyhole surgery).
- ARTISS should be applied only with CE marked application devices.
- If accessory tips are used with this product, the instructions for use of the tips should be followed.
- If you have ever received ARTISS 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 there is any sign of an allergic reaction, your doctor will stop the use of ARTISS immediately and give appropriate treatment.
- ARTISS is not indicated to stop bleeding and for sealing in situations where a fast clotting of the sealant is required. Especially in heart surgery procedures in which sealing of surgical connections between blood vessels is intended ARTISS should not be used.
- ARTISS is not indicated for use in neurosurgery and as a suture support for gastrointestinal anastomoses or vascular anastomoses as no data are available to support these indications.
- Before administration of ARTISS parts of the body outside the designated application area have to be sufficiently protected/covered to prevent unwanted tissue adhesion.
- ARTISS is applied as a thin layer. Excessive clot thickness may negatively interfere with the product's efficacy and the wound healing process.
- Your doctor will not use oxycellulose-containing preparations as carrier materials as they may reduce the efficacy of ARTISS.

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,
- the testing of each donation and pools of plasma for signs of virus/infections,
- the inclusion of 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 (foetal 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 ARTISS the name and batch number of the product are recorded in order to maintain a record of the batches used.

Other medicines and ARTISS

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

ARTISS can be used when you are receiving other medical products. There are no known interactions between ARTISS and other medicinal products.

As with comparable products or thrombin solutions, the product may be destroyed by contact with solutions containing alcohol, iodine or heavy metals (e.g. antiseptic solutions). Care should be taken to remove such substances as much as possible before applying the product.

ARTISS with food and drink

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

Pregnancy and breast-feeding

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

Driving and using machines

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

ARTISS contains Polysorbate 80

Polysorbate 80 can cause skin allergy (e.g. rash, itching).

3. How to use ARTISS

- ARTISS is only applied during a surgical operation. The use of ARTISS is restricted to experienced surgeons who have been trained in the use of ARTISS.
- The amount of ARTISS that will be used depends on a number of factors, including the type of surgery, the surface area of tissue to be treated during your operation and the way ARTISS is applied. The surgeon will decide how much is appropriate.
- During your operation, the surgeon will apply ARTISS onto the relevant tissue surface, using the special application device provided. This device ensures that equal amounts of both fibrin sealant components are applied at the same time – which is important for the optimal effect of ARTISS.
- Prior to applying ARTISS the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).
- ARTISS must be sprayed only onto application sites that are visible.
- It is recommended that the initial application covers the entire intended application area.

When applying ARTISS 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 ARTISS					
	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 surgery of sub-cutaneous tissue	Tisseel/ Artiss Spray Set	n.a.	EasySpray	10 – 15 cm	1.5 – 2.0 bar (21.5 – 28.5 psi)
	Tisseel/ Artiss Spray Set 10 pack	n.a.	EasySpray		

When spraying the ARTISS, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism (see section 2).

If you use more ARTISS than you should

ARTISS is only applied during a surgical operation. It is applied by the surgeon and the amount of ARTISS 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, this medicine can cause side effects, although not everybody gets them. The following table explains what is meant with a certain frequency, as given in the following section:

very common:	may affect more than 1 in 10 people
common:	may affect up to 1 in 10 people
uncommon:	may affect up to 1 in 100 people
rare:	may affect up to 1 in 1,000 people
very rare:	may affect up to 1 in 10,000 people
not known:	frequency cannot be estimated from the available data

- There is a slight possibility that you might have an allergic reaction to one of the components of ARTISS (see section 6). This is more likely if you have been treated with ARTISS or aprotinin during a previous operation. Allergic reactions can be serious, and it is very important that you discuss this possibility in detail with your doctor.
- Allergic reactions of the anaphylactic/anaphylactoid type may occur, frequency of this is not known. Early symptoms of allergic reactions can be: flushing, a fall in blood pressure, increased or decreased pulse rate, nausea (feeling sick), hives, itching, difficulty breathing.
- The surgical team treating you will be aware of the risk of this type of reaction – if they see any symptoms, the application of ARTISS will be stopped immediately. Severe symptoms may require emergency treatment. The frequency for allergic reactions is not known.
- If ARTISS is injected into soft tissues, it can cause local tissue damage. Frequency is not known.
- If ARTISS is injected into blood vessels (veins or arteries), it can cause clots to form (thrombosis). Frequency is not known.
- As ARTISS 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).
- Life-threatening/fatal air or gas embolism (air getting into the blood circulation which can be serious or life-threatening) has occurred 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.

Adverse reactions reported from clinical studies of ARTISS and from post-marketing experience with Baxter Fibrin Sealants are summarized in the following. Known frequencies of these adverse reactions are based on a controlled clinical study in 138 patients where skin grafts were fixed to excised burn wounds using ARTISS. None of the events observed in the clinical study were classified as serious.

Adverse Reaction	Frequency
Dermal cyst	uncommon
Itching	common
Skin graft failure	common
Gas bubbles in the vascular system (Air embolism)*	not known

* The introduction of air or gas bubbles in the blood stream (air embolism) has 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 following adverse reactions have been reported for other fibrin sealants, frequencies of those cannot be provided: Allergy, severe allergic reaction, slow heart rate, fast heart rate, decrease in blood pressure, effusion of blood, shortness of breath, sickness, hives, flushing, impaired healing, swelling, fever, and accumulation of lymph and other clear body fluids under the skin near the surgical site.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the national reporting system listed below.

United Kingdom (Northern Ireland)

The Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

Ireland

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 ARTISS

- 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 after "EXP".
- Store and transport frozen (at $\leq -20^{\circ}\text{C}$) without interruption until preparation for use.
- Keep the syringe in the original package in order to protect from light.

Storing after thawing:

Unopened pouches, thawed at room temperature, may be stored for up to 14 days at controlled room temperature (not exceeding $+25^{\circ}\text{C}$).

After thawing, the solutions must not be refrozen or refrigerated!

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What ARTISS contains

ARTISS 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 produced from the plasma of human donors; synthetic Aprotinin 3000 KIU/ml.

The excipients are Human Albumin, L-Histidine, Niacinamide, Polysorbate 80, Sodium Citrate Dihydrate and Water for Injections.

Component 2 = Thrombin Solution:

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

Human Thrombin, 4 IU/ml produced from the plasma of human donors; Calcium Chloride Dihydrate, 40 $\mu\text{mol/ml}$.

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

After mixing	1 ml	2 ml	4 ml	10 ml
Component 1: <u>Sealer protein solution</u>				
Human Fibrinogen (as clottable protein)	45.5 mg	91 mg	182 mg	455 mg
Aprotinin (synthetic)	1,500 KIU	3,000 KIU	6,000 KIU	15,000 KIU
Component 2: <u>Thrombin Solution</u>				
Human Thrombin	2 IU	4 IU	8 IU	20 IU
Calcium Chloride Dihydrate	20 μmol	40 μmol	80 μmol	200 μmol

ARTISS contains Human Factor XIII co-purified with Human Fibrinogen in a range of 0.6 – 5 IU/ml.

What ARTISS looks like and the contents of the pack

Solutions for sealant.

Frozen solutions for sealant (1 ml, 2 ml, or 5 ml of sealer protein solution and 1, 2 or 5 ml of Thrombin Solution in a single-use double-chamber syringe in a bag). Pack size of 1.

Content of package with AST Syringe:

1 ml, 2 ml or 5 ml sealer protein solution and 1 ml, 2 ml or 5 ml thrombin solution in a pre-filled single-use double chamber syringe (polypropylene) closed with a tip cap packed in two bags, and one device set with one double syringe plunger, 2 joining pieces, 4 application cannulas.

The solution is colourless or pale yellow.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

United Kingdom (Northern Ireland):

Baxter Healthcare Ltd.,

Caxton Way, Thetford, Norfolk, IP24 3SE,

United Kingdom

Ireland:

Baxter Holding B.V.

Kobaltweg 49, 3542CE Utrecht,

Netherlands

Tel +441635 206345

e-mail medinfo_uki@baxter.com

Manufacturer

Takeda Manufacturing Austria AG

Industriestraße 67

A-1221 Vienna

Austria

This medicinal product is authorized in the Member States of the EEA under the following names:

ARTISS for the following countries: AT, BE, CZ, DE, EL, ES, FI, FR, IE, IT, LU, NL, NO, PL, PT, UK(NI)

Artiss in DK, IS, SE

This leaflet was last revised in: 01/2022

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

Fertility, pregnancy and lactation

The safety of fibrin sealants/haemostatics for use in human pregnancy or breastfeeding has not been established in controlled clinical trials. Animal studies have also not been performed.

Therefore, the product should be administered to pregnant and lactating women only if clearly needed.

The effects of ARTISS on fertility have not been established.

Posology and method of administration

ARTISS is intended for hospital use only. The use of ARTISS is restricted to experienced surgeons who have been trained in the use of ARTISS.

Posology

The amount of ARTISS to be applied and the frequency of application should always be oriented towards the underlying clinical needs of the patient.

The dose to be applied is governed by variables including, but not limited to, the type of surgical intervention, the size of the area and the mode of intended application, and the number of applications.

Application of the product must be individualized by the treating physician. In clinical trials, the individual dosages have typically ranged from 0.2 – 12 ml. For some procedures (e.g. the sealing of large burned surfaces), larger volumes may be required.

The initial amount of the product to be applied at a chosen anatomic site or target surface area should be sufficient to entirely cover the intended application area. The application can be repeated, if necessary, to any small areas that may not have been previously treated. However, avoid reapplication of ARTISS to a pre-existing polymerized ARTISS layer as ARTISS will not adhere to a polymerized layer.

It is recommended that the initial application covers the entire intended application area.

As a guideline for the gluing of surfaces, 1 pack of ARTISS 2 ml (i.e., 1 ml Sealer Protein Solution plus 1 ml Thrombin Solution) will be sufficient for an area of at least 10 cm².

The skin graft should be attached to the wound bed immediately after ARTISS has been applied. The surgeon has up to 60 seconds to manipulate and position the graft prior to polymerization. After the flap or graft has been positioned, hold in the desired position by gentle compression for at least 3 minutes to ensure ARTISS sets properly and the graft or flap adheres firmly to the underlying tissue.

The required amount of ARTISS depends on the size of the surface to be covered. The approximate surface areas covered by each pack size of ARTISS by spray application are:

Approximate area requiring tissue adherence	Required pack size of ARTISS
100 cm ²	2 ml
200 cm ²	4 ml
500 cm ²	10 ml

To avoid the formation of excess granulation tissue and to ensure gradual absorption of the solidified fibrin sealant, only a thin layer of the mixed Sealer Protein – Thrombin Solution, should be applied.

ARTISS has not been administered to patients > 65 years old in clinical trials.

Paediatric Population

Currently available data are described in section 5.1 of the SmPC but no recommendation on a posology can be made.

Method of administration

For epilesional (topical) use. Do not inject.

For subcutaneous use only. ARTISS is not recommended for laparoscopic surgery. In order to ensure optimal safe use of ARTISS it should be sprayed using a pressure regulator device that delivers a maximum pressure of up to 2.0 bar (28.5 psi).

Prior to applying ARTISS the surface area 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.

ARTISS must be sprayed only onto application sites that are visible.

ARTISS should only be reconstituted and administered according to the instructions and with the devices recommended for this product.

For spray application, see section Administration below.

Before administration of ARTISS care is to be taken that parts of the body outside the designated application area are sufficiently protected/covered to prevent tissue adhesion at undesired sites.

Special precautions for disposal and other handling (final container: AST Syringe)

General

- Before the administration of ARTISS, cover all parts of the body outside the area to be treated in order to prevent tissue adhesion at undesired sites.
- To prevent ARTISS from adhering to gloves and instruments, wet these with sodium chloride solution before contact.
- As a guideline for the gluing of surfaces, 1 pack of ARTISS 2 ml (i.e., 1 ml Sealer Protein Solution plus 1 ml Thrombin Solution) will be sufficient for an area of at least 10 cm².
- The dose required depends on the size of the surface to be covered.

- Do NOT apply the two components of ARTISS separately. Both components must be applied together.
- Do NOT expose ARTISS to temperatures above 37°C. Do NOT microwave.
- Do NOT thaw the product by holding it in your hands.
- Do NOT use ARTISS until it is completely thawed and warmed to 33°C - 37°C.
- Remove the protective cap of the syringe only when thawing and warming is complete.
- Expel all air from the syringe then attach the joining piece and application cannula.

Instructions for Handling and Preparation

The inner bag and its contents are sterile unless the integrity of the outside package is compromised. Using sterile technique, transfer the sterile inner pouch and contents onto the sterile field.

The ready-to-use syringe may be thawed AND warmed using one of the following methods:

1. Rapid thawing/warming (sterile water bath) - Recommended method

2. Thawing/warming in a non-sterile water bath
3. Thawing/warming in an incubator
4. The ready-to-use syringe may also be thawed and kept at room temperature (not above 25°C) for up to 14 days. Warming is required prior to use.

1. Rapid thawing/warming (sterile water bath) - Recommended method:

It is recommended to thaw and warm the two sealant components using a sterile water bath at a temperature of 33 – 37°C.

- The water bath must not exceed a temperature of 37°C. In order to monitor the specified temperature range, control the water temperature using a thermometer and change the water as necessary.
- When using a sterile water bath for thawing and warming, remove the pre-filled syringe from the bags before placing it in the sterile water bath.

Instructions:

Bring the inner bag into the sterile area, remove the ready-to-use syringe from the inner bag and place it directly in the sterile water bath. Ensure that the content of the ready-to-use syringe is completely immersed in the water.

Table 1: Minimum thawing and warming Times using a Sterile Water Bath

Pack Size	Minimum Thawing/Warming Times 33°C to 37°C, Sterile Water Bath, Product without bags
2 ml	5 minutes
4 ml	5 minutes
10 ml	12 minutes

2) Thawing/warming in a non-sterile water bath

Instructions:

Leave the ready-to-use syringe inside both bags and place it in a water bath outside the sterile area for the appropriate length of time (see Table 2). Ensure that the bags remain immersed in the water during the entire thawing time. After thawing, remove the bags from the water bath, dry the outer bag and bring the inner bag with the ready-to-use syringe into the sterile area.

Table 2: Minimum thawing and warming times using a non-sterile water bath

Pack Size	Minimum Thawing/Warming Times 33°C to 37°C, Non-sterile Water Bath, Product in bags
2 ml	30 minutes
4 ml	40 minutes
10 ml	80 minutes

3) Thawing/warming in an incubator

Instructions:

Leave the ready-to-use syringe inside both bags and place it in an incubator outside the sterile area for the appropriate length of time (see Table 3). After thawing/warming, remove the bags from the incubator, remove the outer bag and bring the inner bag with the ready-to-use syringe into the sterile area.

Table 3: Minimum thawing and warming times in an incubator

Pack Size	Minimum Thawing/Warming Times 33°C to 37°C, Incubator, Product in bags
2 ml	40 minutes
4 ml	85 minutes
10 ml	105 minutes

4. Thawing at Room Temperature (not above +25 °C) BEFORE warming:

Instructions:

Leave the ready-to-use syringe inside both bags and thaw it at room temperature outside the sterile area for the appropriate length of time (see Table 4). Once thawed, in order to warm the product for use, warm it in the outer bag in an incubator. After thawing at room temperature, the maximum time the product can be kept (in both bags) at room temperature is 14 days.

Table 4: Minimum thawing times at Room Temperature (= RT) outside of the sterile field and additional warming times in an incubator to 33°C to 37°C

Pack Size	Minimum Thawing Times of product at room temperature (not above 25 °C) followed by additional warming, prior to use, in an incubator at 33 °C to a maximum of 37 °C Product in bags	
	Thawing at room temperature (not above 25 °C)	Warming in Incubator (33-37 °C)
2 ml	60 minutes	+15 minutes
4 ml	110 minutes	+25 minutes
10 ml	160 minutes	+35 minutes

Stability after thawing

After **thawing and warming** (at temperatures between 33°C and 37°C, methods 1, 2 and 3), chemical and physical product stability has been demonstrated for 4 hours at 33°C to 37°C.

For product **thawed** at room temperature in the unopened bag (method 4), chemical and physical product stability has been demonstrated for 14 days at temperatures no more than 25°C. Warm to 33°C to 37°C immediately before use.

From a microbiological point of view, unless the method of opening/thawing precludes the risks of microbial contamination, the product should be used immediately after being warmed to 33°C to 37°C.

If not used immediately, in-use storage times and conditions are the responsibility of the user.

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

Handling after thawing / before application

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 sealer protein and the thrombin solutions should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits. Before use, check the thawed product visually for particles, discoloration or other changes in its appearance. If one of the above occurs, dispose of the solutions.

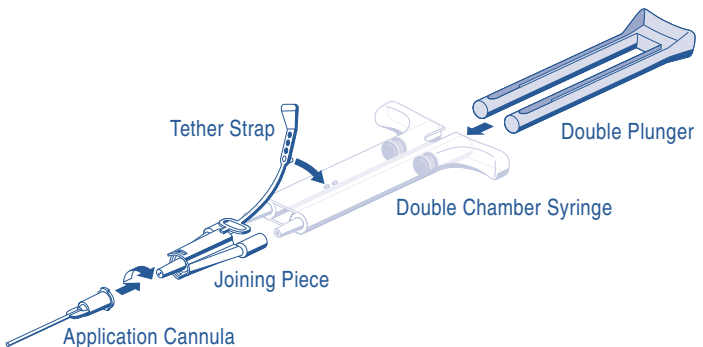
The thawed sealer protein solution should be liquid but slightly viscous. If the solution has the consistency of a solidified gel, it must be assumed to have become denatured (possibly due to an interruption of the cold storage chain or by overheating during warming). In this case, do NOT use ARTISS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

- Remove the syringe from the bags shortly before use.
- Use ARTISS only when it is thawed and warmed completely (liquid consistency).
- Remove the protective cap from the syringe immediately before application.

Non-Spray Administration with AST Syringe:

For application, connect the double chamber ready-to-use syringe with the sealer protein solution and the thrombin solution to a joining piece and an application cannula - both are provided in the set with the application devices. The common plunger of the double chamber ready-to-use syringe, likewise provided in the set with the application devices, ensures that 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 for AST Syringe:



- 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.
 - o Secure the joining piece by fastening the tether strap to the double chamber ready-to-use syringe.
 - o If the tether strap tears, use the spare joining piece provided in the kit.
 - o 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.
 - o Do NOT expel the air remaining inside the joining piece.
- Attach an application cannula on to the joining piece.

- o 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 ARTISS 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 ARTISS has been applied, allow at least 3 minutes to achieve sufficient polymerization.

Note: If application of the fibrin sealant components is interrupted, clogging may occur in the cannula. In this case, 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.

Application is also possible with other accessories supplied by BAXTER that are particularly suited for, e.g. application to large or difficult-to-access areas. When using these application devices, strictly follow the Instructions for Use of the devices.

For further preparation instructions please refer to the responsible nurse or medical doctor.

Spray application

The pressure regulator should be used in accordance with the manufacturer's instructions.

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

Recommended pressure, distance and devices for spray application of ARTISS					
	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 surgery of sub-cutaneous tissue	Tisseel/ Artiss Spray Set	n.a.	EasySpray	10 – 15 cm	1.5 – 2.0 bar (21.5 – 28.5 psi)
	Tisseel/ Artiss Spray Set 10 pack	n.a.	EasySpray		

When spraying ARTISS, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism (see sections 4.2 and 4.4).

When using accessory tips with this product, the instructions for use of the tips should be followed.

Disposal

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