TECHN. CHECK
PDD: OK
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- 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.

Application with Spray Device
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:

Table 4: Recommended pressure, distance and devices for spray application of ARTISS

Surgery	Spray set to be used	Pressure regulator to be used	Gas	Recommended distance from target tissue	Recommended spray pressure
Open wound surgery of subcutaneous tissue	Tisseel / Artiss Spray Set	EasySpray	Medical grade CO_2*, Compressed Air or Nitrogen	10 – 15 cm	1.5-2.0 bar (21.8-29.0 psi)
	Tisseel / Artiss Spray Set 10 pack	EasySpray			

* Medical grade CO_2 is the preferred gas for application, however compressed air or nitrogen are acceptable gases for administration of ARTISS in open surgery.
Equivalent spray devices, intended for specific use with ARTISS, may also be used. When using other spray devices, follow the instructions for use that are provided with the device.
When spraying ARTISS, 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 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.

7. MANUFACTURER
Takeda Manufacturing Austria AG,
Industriestrasse 67,
1221, Vienna, Austria

8. DATE OF REVISION OF THE TEXT
February 2026

Baxter

0764166

1. NAME OF THE MEDICINAL PRODUCT
ARTISS Solutions for Sealant
Deep frozen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Component 1:
Sealer Protein Solution
Human Fibrinogen 91 mg[1]/ml (as clottable protein) produced from the plasma of human donors
Aprotinin (synthetic) 3000 KIU[2]/ml

Component 2:
Thrombin Solution
Human Thrombin 4 IU[3]/ml produced from the plasma of human donors
Calcium Chloride 40 µmol/ml

1 prefilled double chamber syringe which contains Sealer Protein Solution (with Aprotinin), deep frozen 1 ml, 2 ml, 5 ml, in one chamber and Thrombin Solution (with Calcium Chloride), deep frozen 1 ml, 2 ml, 5 ml, in the other chamber results in 2 ml, 4 ml, 10 ml, total volume of product ready for use.

After mixing	1 ml	2 ml	4 ml	10 ml
Component 1: Sealer protein solution				
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: Thrombin Solution				
Human Thrombin	2 IU	4 IU	8 IU	20 IU
Calcium Chloride	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.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Solutions for Sealant
Deep frozen
Colourless to pale yellow and clear to slightly turbid solutions.
Component 1, Sealer Protein Solution: pH 6.5 – 8.0 Component 2, Thrombin Solution: pH 6.0 – 8.0

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
ARTISS is indicated as a tissue glue to adhere/seal subcutaneous tissue in plastic, reconstructive and burn surgery, as a replacement or an adjunct to sutures or staples (see 5.1). ARTISS is not indicated for hemostasis.

4.2 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 have not 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 cm^2.
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.

1 Contained in a total protein concentration of 96 - 125 mg/ml
2 1 EPU (European Pharmacopoeia Unit) corresponds to 1800 KIU (Kallidinogenase Inactivator Unit)
3 Thrombin activity is calculated using the current WHO International Standard for Thrombin.

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 but no recommendation on a posology can be made.

Method of administration
For epilesional (topical) use. Do not inject.
ARTISS is not recommended for laparoscopic surgery, see also section 4.4.
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 (29.0 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 (see section 6.6).
For spray application, see sections 4.4 and 6.6 for specific recommendations on the required pressure and distance from tissue per surgical procedure and length of applicator tips.

4.3 Contraindications
ARTISS is not indicated to replace skin sutures intended to close surgical wounds.
ARTISS alone is not indicated for the treatment of massive and brisk arterial or venous bleeding.
ARTISS must never be applied intravascularly.
ARTISS is contraindicated in the case of hypersensitivity to the active substances or to any of the excipients listed in section 6.1 (see also section 4.4. Special Warnings).
Spray application of ARTISS should not be used in endoscopic procedures. For laparoscopy, see section 4.4.

4.4 Special warnings and precautions for use
For epilesional use only. Do not apply intravascularly. Life threatening thromboembolic complications may occur if the preparation is unintentionally applied intravascularly.
Soft tissue injection of ARTISS carries the risk of local tissue damage.
Caution must be used when applying fibrin sealant using pressurized air or gas.

- 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-threatening or fatal.
- **Apply ARTISS as a thin layer. Excessive clot thickness may negatively intrfer with the product's efficacy and the wound healing process.**
- **Life-threatening/fatal air or gas embolism has occurred with the use of spray devices employing a pressure regulator to administer fibrin sealants. This event 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 ARTISS when sprayed in open wound surgery.**
- **When applying ARTISS using a spray device, be sure to use a pressure within the pressure range recommended by the spray device manufacturer (see table in section 6.6 for pressures and distances).**
- **ARTISS spray application should only be used if it is possible to accurately judge the spray distance as recommended by the manufacturer. Do not spray closer than the recommended distances. Spray distance from tissue and pressure should be within the ranges recommended by the marketing authorisation holder of this product (see table in section 6.6 for pressure and distance).**
- **When spraying ARTISS, 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 (also see section 4.2).**
- 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 use.
- Only use application devices CE marked for the administration of ARTISS.
- When using accessory tips with this product, the instructions for use of the tips should be followed.

ARTISS is not indicated for hemostasis and sealing in situations where a fast clotting of the sealant is required. Especially in cardiovascular procedures in which sealing of vascular anastomoses 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 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.
Oxycellulose-containing preparations may reduce the efficacy of ARTISS and should not be used as carrier materials (see Section 6.2). Polysorbates can cause skin allergy (e.g. rash, itching).
As with any protein-containing product, allergic type hypersensitivity reactions are possible. Signs of hypersensitivity reactions may include hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis. If these symptoms occur, the administration must be discontinued immediately.
ARTISS contains aprotinin. Even in case of strict local application, there is a risk of anaphylactic reaction linked to the presence of aprotinin. The risk seems to be higher in cases where there was previous exposure, even if it was well tolerated. Therefore, any use of aprotinin or aprotinin containing products should be recorded in the patients' records.

As synthetic aprotinin is structurally identical to bovine aprotinin the use of ARTISS in patients with allergies to bovine proteins should be carefully evaluated. In the event of anaphylactic/anaphylactoid or severe hypersensitivity reactions, administration is to be discontinued. If possible, remove any applied, polymerized product from the surgical site. Adequate medical treatment and provisions should be available for immediate use in the event of an anaphylactic reaction. State-of-the-art emergency measures are to be taken. In case of shock, standard medical treatment for shock should be implemented.
Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses.
Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses or other pathogens.
The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), and for the non-enveloped hepatitis A virus (HAV).
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 with immunodeficiency or increased erythropoiesis (e.g., hemolytic anemia).
It is strongly recommended that every time that ARTISS is administered to the patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

4.5 Interaction with other medicinal products and other forms of interaction
No formal interaction studies have been performed.
Similar to comparable products or thrombin solutions, the product may be denatured after exposure to solutions containing alcohol, iodine or heavy metals (e.g. antiseptic solutions). Such substances should be removed to the greatest possible extent before applying the product.
See section 4.4 or 6.2 for substances that can interfere with the product's performance.

4.6 Fertility, pregnancy and lactation
The safety of fibrin sealants/hemostatics for use in human pregnancy or breastfeeding has not been established in controlled clinical trials.
Experimental animal studies are insufficient to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri-and postnatal development.
Therefore, the product should be administered to pregnant and lactating women only if clearly needed.
See section 4.4 for information on Parvovirus B19 infection.
The effects of ARTISS on fertility have not been established.

4.7 Effects on ability to drive and use machines
Not relevant.

4.8 Undesirable effects
Intravascular injection could lead to thromboembolic events and disseminated intravascular coagulation (DIC) and there is also a risk of anaphylactic reactions (see section 4.4).
Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the application site, bradycardia, bronchospasm, chills, dyspnoea, flushing, generalized urticaria, headache, hives, hypotension, lethargy, nausea, pruritus, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) may occur in rare cases in patients treated with fibrin sealants/hemostatics. In isolated cases, these reactions have progressed to severe anaphylaxis. Such reactions may especially be seen if the preparation is applied repeatedly, or administered to patients known to be hypersensitive to aprotinin (see section 4.4) or any other constituents of the product.
Even if a first treatment with ARTISS was well tolerated, a subsequent administration of ARTISS or systemic administration of aprotinin may result in severe anaphylactic reactions.
Antibodies against components of fibrin sealant may rarely occur.
For safety with respect to transmissible agents, see section 4.4.
Life-threatening air or gas embolism has occurred with the use of spray devices employing a pressure regulator to administer fibrin sealant/haemostatic products. This event 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 summarized in the table below were reported from clinical studies of ARTISS and from post-marketing experience with Baxter Fibrin Sealants (marked with a p in the adverse event table). 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.
The ADRs and their frequencies are summarized below:
Common (≥1/100 to <1/10)
Uncommon (≥1/1000 to <1/100)
Not known (cannot be estimated from the available data)

Table 1: Adverse Reactions

System organ class (SOC)	Preferred MedDRA Term	Frequency
Skin and subcutaneous tissue disorders	Dermal cyst	uncommon
	Pruritus	common
Injury, poisoning and procedural complications	Skin graft failure	common
Vascular disorders	Air embolism[p] due to an inappropriate use of the spray device (see section 4.4)	not known

[p] Adverse events observed in post-marketing experience with Baxter Fibrin Sealants.

Class Reactions
Other adverse reactions associated with products of the fibrin sealant/hemostatic class include:
Hypersensitivity reactions which could manifest as application site irritation, chest discomfort, chills, headache, lethargy, restlessness and vomiting. Further class reactions are: Anaphylactic reaction, bradycardia, tachycardia, hypotension, haematoma, dyspnoea, nausea, urticaria, flushing, impaired healing, oedema, pyrexia and seroma.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose
No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: local hemostatics; combinations, ATC code: B02BC30; tissue adhesives, ATC code: V03AK
ARTISS can replace sutures or staples when used for fixation of skin grafts to burned or otherwise injured wound areas. ARTISS can be used as an adjunct to sutures or staples to adhere and seal skin flaps in cases where sutures/staples are expected to yield unsatisfactory results with respect to postoperative hematoma or seroma formation.
The fibrin adhesion system initiates the last phase of physiological blood coagulation. Conversion of fibrinogen into fibrin occurs by the splitting of fibrinogen into fibrin monomers and fibrinopeptides. The fibrin monomers aggregate and form a fibrin clot. Factor XIIIa, which is activated from factor XIII by thrombin, crosslinks fibrin. Calcium ions are required for the conversion of fibrinogen and the crosslinkage of fibrin.
As wound healing progresses, increased fibrinolytic activity is induced by plasmin, and decomposition of fibrin to fibrin degradation products is initiated. Proteolytic degradation of fibrin is inhibited by anti-fibrinolytics. Aprotinin is present in ARTISS (frozen) as an antifibrinolytic to prevent premature degradation of the clot.
For efficacy, *in vivo* studies in an animal model closely imitating the situation in patients were used. ARTISS demonstrated efficacy regarding sealing autologous split skin grafts and mesh grafts.
ARTISS was investigated for fixation of split thickness sheet skin grafts in burn patients in a prospective, randomised, controlled, multicenter clinical study. In each of the 138 patients, two comparable test sites were identified. In one test site the skin graft was fixed with ARTISS in the other test site the graft was fixed with staples (control). ARTISS proved to be non-inferior to staples with respect to the primary efficacy endpoint, complete wound closure at Day 28 was evaluated by a blinded evaluator panel from photographs. This was achieved in 55/127 patients (43.3%) treated with ARTISS (frozen) and 47/127 patients (37%) treated with staples.
With respect to secondary endpoints, ARTISS showed a significantly lower incidence and size of hematoma/seroma on Day 1 ($p < 0.0001$ for incidence as well as size). Incidence and area of engraftment on Day 5 and wound closure on Day 14, as well as area of wound closure on Day 28 were not different. ARTISS was also superior to staples with respect to patient satisfaction ($p < 0.0001$) and patients experienced significantly less anxiety about pain with ARTISS than with staples ($p < 0.0001$).
Moreover, ARTISS was significantly superior to staples with respect to the investigator's assessment of quality of graft adherence, preference of fixation method and satisfaction with graft fixation, overall quality of healing and overall rate of healing ($p < 0.0001$).
Thirty-seven (37) pediatric patients aged 1.1 to 18 years were evaluated in this trial. Eighteen (18) of these patients were 6 years old or younger.
Dosage used in clinical trials was the same for pediatric and adult patients.

5.2 Pharmacokinetic properties
ARTISS is intended for epilesional use only. Intravascular administration is contraindicated. As a consequence, intravascular pharmacokinetic studies were not performed in man.
Pharmacokinetic studies in different species of laboratory animals were not conducted. Fibrin sealants/hemostatics are metabolized in the same way as endogenous fibrin by fibrinolysis and phagocytosis.

5.3 Preclinical safety data
No preclinical safety data are available for ARTISS (thrombin 4 IU/ml). Toxicity studies were done with Fibrin Sealants containing thrombin 500 IU/ml, as representative for products containing thrombin 4 IU/ml. Single-dose toxicity studies in rats and rabbits indicated no acute toxicity of Fibrin Sealant VH S/D (500 IU/ml).
Fibrin Sealant VH S/D (500 IU/ml) also proved well tolerated in wound healing models in rats and rabbits, and in in vitro human fibroblast cultures.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Component 1: Sealer Protein Solution
Human Albumin Solution
L-Histidine
Niacinamide
Polysorbate 80 (Tween 80)
Sodium Citrate Dihydrate
Water for Injections

Component 2: Thrombin Solution
Human Albumin Solution
Sodium Chloride
Water for Injections

6.2 Incompatibilities
This medicinal product must not be mixed with other medicinal products.
Oxycellulose-containing preparations may reduce the efficacy of ARTISS and should not be used as carrier materials.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store and transport frozen (at ≤ -20°C) without interruption until preparation for use.
Keep the syringe in the outer carton in order to protect from light.
Unopened pouches, thawed at room temperature, may be stored for up to 14 days at controlled room temperature (not exceeding +25°C). Do not refreeze or refrigerate after thawing.

6.5 Nature and contents of container
Artiss is supplied in a pre-filled single-use double chamber syringe (polypropylene) 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.
Artiss is available in the following pack sizes of 1 syringe:

- 2 ml (1 ml of human fibrinogen and 1 ml of human thrombin)
- 4 ml (2 ml of human fibrinogen and 2 ml of human thrombin)
- 10 ml (5 ml of human fibrinogen and 5 ml of human thrombin)

Not all pack sizes may be marketed.
Other accessories for application of the product can be obtained from BAXTER.

6.6 Special precautions for disposal and other handling
The instructions for use are also described in the healthcare professionals' package leaflet part.

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 ARTISS, ensure that all parts of the body outside the desired application area are sufficiently covered to prevent tissue adhesion at undesired sites.

Thawing of the frozen presentation

- Do not use ARTISS unless it is completely thawed and warmed (liquid to slightly viscous consistency).
- ARTISS 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.

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 14 days at temperatures not exceeding +25°C)

1. Quick thawing/warming methods
An overview of the quick thawing/warming methods is provided in Table 2.

Table 2: 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 2 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 2 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 2 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 3 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 3 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 3: Thawing at Room Temperature and Warming in Incubator

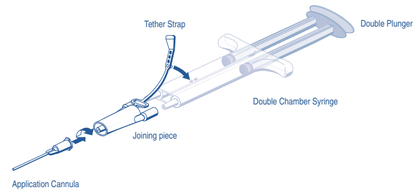
Pack Size	Minimum Thawing /Warming Times	
	Thawing at room temperature (Not above 25°C)	Warming in Incubator (33-37°C)
2 ml	80 minutes	11 minutes
4 ml	90 minutes	13 minutes
10 ml	160 minutes	25 minutes

Stability after thawing
After **thawing and warming at 33°C - 37°C**, (Options 1 and 2), the product must be used within 4 hours.
After **thawing at room temperature** (Option 2), the product can be stored up to 14 days 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, do NOT use ARTISS on any account.

Non-Spray Administration
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 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



- 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.