

אוגוסט 2026

רופא/ה, רוקח/ת, נכבד/ה,

הנדון: Tisseel Frozen**מרכיבים פעילים:**

Human fibrinogen (as clottable protein)	91 mg ¹ /ml
Human thrombin	500 IU ² /ml
Aprotinin acetate	3000 KIU ³ /ml
Calcium chloride dihydrate	40 µmol/ml

צורת מינון:

Solutions for sealant

התוויות:

Supportive treatment in adults and children from 1 month of age where standard surgical techniques appear insufficient:

- For improvement of Hemostasis.
- As a tissue glue to improve wound healing or to support sutures in vascular surgery and in gastrointestinal anastomoses.
- For tissue sealing, to improve adhesion of the separated tissue (e.g. tissue flaps, grafts, split skin grafts [mesh grafts]).

Efficacy in fully heparinized patients has been proven.

חברת בקסטר מדיקל ישראל בע"מ מבקשת להודיעכם על עדכונים בעלון לרופא של התכשיר בנדון. העלון לרופא עודכן באוגוסט 2026. להלן העדכונים (מסומן באמצעות **צבע אדום**):

4.2 Posology and method of administrationMethod of administration

In open wound surgery - a pressure regulator device that delivers a maximum pressure of no more than 2.0 bar (~~28-529.0~~ psi) should be used.

5.1 Pharmacodynamic properties

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Efficacy of TISSEEL for the fixation of subcutaneously implanted lightweight mesh has been confirmed in a randomized, controlled, multicenter trial, conducted in 2009-2012. Compared to primary suture (PS) as a control, TISSEEL was used to fix a lightweight mesh in the onlay (OMR, N=188, p=0,0016 vs. PS) as well as in the sublay position (SMR, N=185, p=0,05 vs. PS) to reinforce the tissue to prevent incisional hernia occurrence in a high-risk patient population. There was no difference between OMR and SMR (p=0,31).

6.5 Nature and contents of container~~**Content of package with PRIMA Syringe:**~~

- ~~1 ml, 2 ml or 5 ml sealer protein solution and 1 ml, 2 ml or 5 ml thrombin solution~~
TISSEEL FROZEN 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) ~~bags~~ and ~~with a one~~ device set with 2 joining pieces and 4 applications cannulas.

Pack sizes:

TISSEEL FROZEN is available in the following pack sizes of 1 syringe: ~~4 x 2 ml (1 ml + 1 ml), 1 x 4 ml (2 ml + 2 ml) and 1 x 10 ml (5 ml + 5 ml).~~

- 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)

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6.6 Special precautions for disposal and other handling**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 administration~~ of TISSEEL FROZEN, ~~cover~~ ensure that all parts of the body outside the ~~desired application area~~ are sufficiently ~~covered to be treated in order~~ to prevent tissue adhesion at undesired sites.

Thawing of the frozen presentation

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

- ~~• To prevent TISSEEL FROZEN from adhering to gloves and instruments, wet these with sodium chloride solution before contact.~~
- ~~• The guideline for sealing surfaces is: One package of TISSEEL FROZEN 2 ml (i.e. 1 ml sealer protein solution plus 1 ml thrombin solution) is sufficient for a surface of at least 10 cm².~~
- ~~• The dose required depends on the size of the surface to be sealed.~~
- ~~• Do NOT apply the two components of TISSEEL FROZEN separately. Both components must be applied together.~~
- ~~Do NOT expose~~ TISSEEL FROZEN must not be exposed to temperatures above 37°C. ~~Do NOT~~ and must not be microwaved.
- ~~• Do NOT thaw the product by holding it in your hands.~~
- ~~• Do NOT use TISSEEL FROZEN until it is completely thawed and warmed to 33°C—37°C.~~
- ~~Remove the~~ The protective syringe cap should not be removed until ~~of the syringe only when~~ thawing and warming is complete, and application tip is ready to be attached.

~~For PRIMA syringe:~~ 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.

- ~~Expel all air from the syringe then attach the joining piece and application cannula.~~

Instructions for handling and preparation:

~~Both the sealer protein solution and the thrombin solution are contained in a ready-to-use syringe. The product is packed in two sterile bags under aseptic conditions. The inner bag and its contents are sterile as long as the outer bag remains intact. 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 72 hours. Warming is required prior to use.~~

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

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

- Sterile Water Bath
- Non-Sterile Water Bath
- 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) Rapid Quick thawing/warming methods (sterile water bath) – Recommended method

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.

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
	PRIMA Syringe
2 ml	5 minutes
4 ml	5 minutes
10 ml	10 minutes

b)2) Thawing/warming in a nonNon-sSterile Wwater Bbath

- 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.

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
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	PRIMA Syringe
2-ml	15 minutes
4-ml	20 minutes
10-ml	35 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
	PRIMA Syringe
2-ml	40 minutes
4-ml	50 minutes
10-ml	90 minutes

4)2) Thawing at room temperature (not above 25°C) followed by **BEFORE** 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.

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.~~

Table 4: Minimum thawing times at room temperature outside of the sterile field and additional warming times in an incubator to 33°C to 37°C

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

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	
	PRIMA Syringe	
	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

After thawing at room temperature, the product must be used within 72 hours of removing from the freezer.

Stability after thawing

After **thawing and warming** (at temperatures between 33°C and 37°C, methods Options 1 and 2 and 3), chemical and physical product stability has been demonstrated for the product must be used within 12 hours at 33°C to 37°C.

For product After **thawed thawing** at room temperature in the unopened bag (method 4 Option 2), the product can be stored for up to chemical and physical product stability has been demonstrated for 72 hours at temperatures not exceeding 25°C, provided it remains sealed in the original package (both pouches) 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

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 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 TISSEEL FROZEN on any account.

- ~~• Remove the syringe from the bags shortly before use.~~
- ~~• Use TISSEEL FROZEN only when it is thawed and warmed completely (liquid consistency).~~
- ~~• Remove the protective cap from the syringe immediately before application. For PRIMA syringe: 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.~~

Non-Spray Administration with PRIMA Syringe:

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Administration

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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.

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.

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

Application with Spray application device

When applying TISSEEL FROZEN 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 TISSEEL FROZEN

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 - 15 cm	1.5-2.0 bar (21.58-28.529.0 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			
		Spray Set 360 Endoscopic Applicator with Snap Lock			
		Spray Set 360 Endoscopic Applicator with Tether			
		Replaceable tip			

When spraying TISSEEL FROZEN, 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).

For the application of TISSEEL FROZEN 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.

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9. Marketing Authorization Holder and Importer

Baxter Healthcare Distribution Medical Israel Ltd., 34 Jerusalem St.,
Ra'anana, Israel.

בברכה,
בקסטר מדיקל ישראל בע"מ.