ARTISS
[Solutions for Sealant]

[PROVIDES TIME FOR THE FINISHING TOUCH]

Full surface adherence eliminating dead space[3]

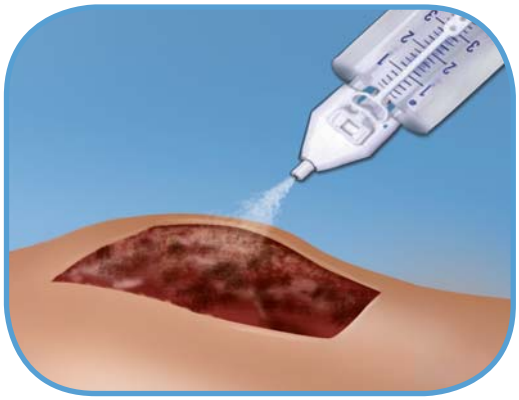
Application and Benefits in Burn Surgery

Baxter

Specifically Designed

- ARTISS [Solutions for Sealant] 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.[2]
- In addition, ARTISS is indicated as an adjunct to hemostasis on subcutaneous tissue surfaces.[2]

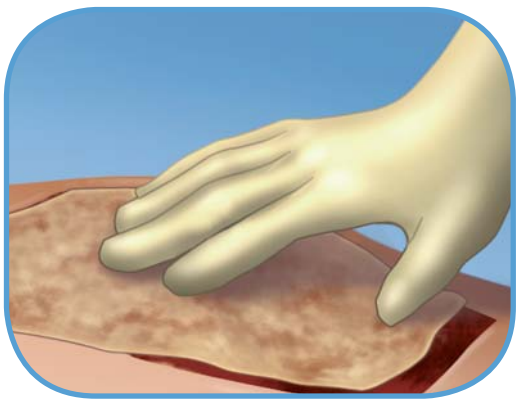
How ARTISS Works



ARTISS is applied with a spray device to achieve an even and thin layer on the wound area[3,4,7]

The wound surface should be as dry as possible before application.[1]

Upon mixing, soluble fibrinogen is transformed into a fibrin matrix that **adheres to the wound surface and to the skin graft to be affixed.**[1]
(For detailed instructions how to prepare and apply the product, please see the SmPC.)



ARTISS sets in approximately 60 seconds; allowing time to manipulate and position the graft prior to polymerization.[1,5]

After the graft has been applied, hold in the desired position by gentle compression for about 3-5 minutes to ensure ARTISS sets properly and adheres firmly to the surrounding tissue. The solidified fibrin sealant reaches its final strength in approximately 2 hours after application.[1]

The adhesive properties of **ARTISS provide full surface adherence** of the graft to the wound bed, closing the space that exists when grafts are attached using point fixation techniques such as staples.[3]

ARTISS eliminates the need for staple application or removal.[3]

ARTISS [Solutions for Sealant] – first and only fibrin sealant custom designed for tissue adherence

ARTISS is a two-component fibrin sealant matrix of human fibrinogen and contains 4 units/mL of human thrombin which sets in approximately 60 seconds:[1,5]

- allowing time to manipulate and position the graft prior to polymerization[1,3]
- providing full surface adherence of the graft to the wound bed[3]

Unlike another fast-setting, hemostatic fibrin sealant, ARTISS contains a mixture of proteins, which play important roles in the wound healing and tissue regeneration process and help to extend clot stability, such as synthetic, non-bovine aprotinin.[1,6]

According to *in-vitro* results, ARTISS clots serve as a provisional matrix that encourages adhesion and supports growth of cells involved in soft tissue repair, like keratinocytes, fibroblasts, and endothelial cells.[6]

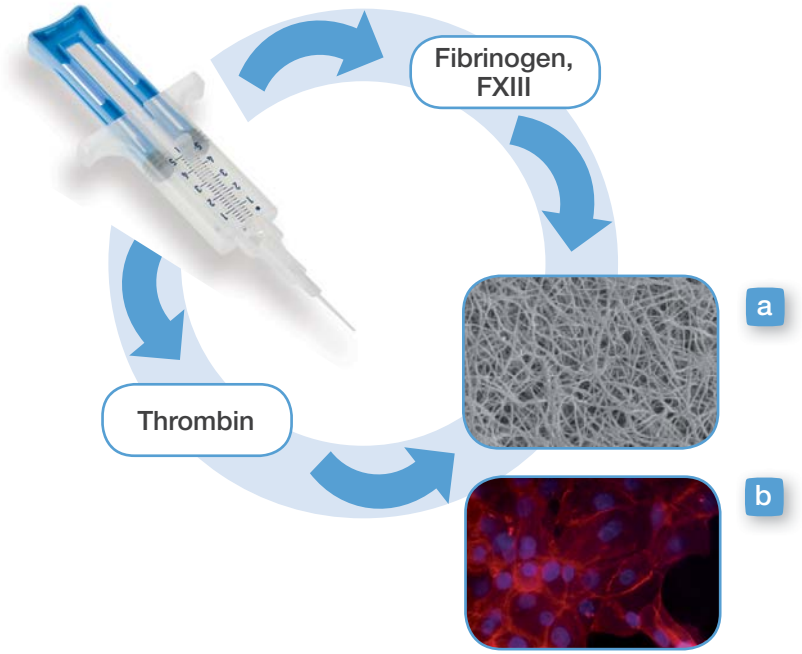


Fig. 1: Mechanism of action.

a The 2 components of Artiss imitate the last step of the coagulation cascade generating a fibrin clot with physiological clot properties[2]

b Morphology of human keratinocytes after 24 hours in contact with the Artiss clot. Red = Actin filaments; blue = Nuclei[6]

Clinical Evidence / Pivotal Study

The efficacy of ARTISS versus staples for skin graft adherence was demonstrated in a phase 3, multicenter, prospective, randomized, evaluator blinded clinical trial in 138 adult and pediatric burn patients. The study was designed to evaluate whether or not complete (100%) wound closure achieved 28 days after wound excision and skin grafting when ARTISS or staples were used.[1,3]

Study design

Each patient served as its own control, being treated with both FS 4IU VH S/D and staples on separate test sites. The test sites had to be either a single wound measuring between 2 and 8% TBSA (which could be split into two halves) or two comparable wounds each measuring between 1 and 4% TBSA. Both test sites were required to receive autologous split-thickness sheet skin grafts.

Efficacy Results

- The proportion of test sites with complete wound closure* was similar between the 2 treatments (ARTISS, 43.3%; staples, 37%).
- The lower limit of the 97.5% confidence interval of the difference between ARTISS and staples was -0.029, which is above the predefined noninferiority margin of -0.1.

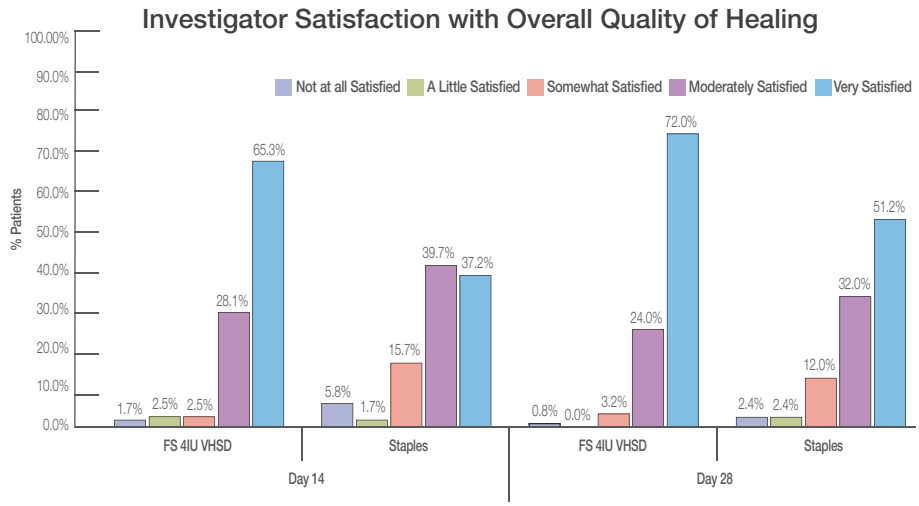
Study Conclusion

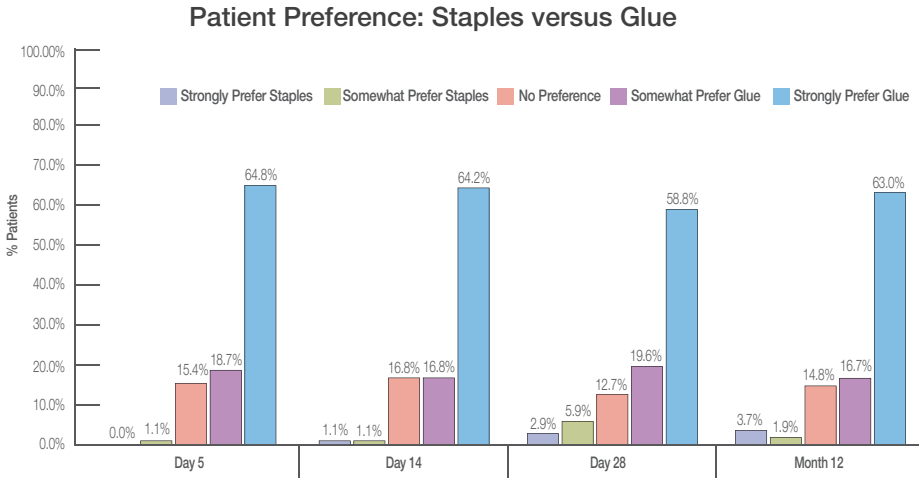
The pivotal study concluded: ARTISS is at least as efficacious as staples at the 97.5% one-sided level for complete wound closure by day 28.[3]

†Blinded Review: reviewers were burn surgeons who were not involved with the study in any other way and who were unaware of treatments used in the study, treatment assignation, time point of assessment, and identity of the patient and operating surgeon.
*Full coverage of the wound with a contiguous layer of viable epithelium.

ARTISS [Solutions for Sealant] – for skin grafting in Burn Surgery

In the study, ARTISS was favored by investigators regarding method of fixation and quality of healing, and patients preferred ARTISS over staples because of less anxiety and pain regarding staple removal.[3]





Hematoma/Seroma reduction

Significantly fewer hematoma and seroma incidences occurred on Day 1 with the use of ARTISS (29.7%) compared to the use of staples (62.3%, p<0.0001).[3]

Minimizing hematoma and seroma incidences is clinically important because of the additional procedures, and associated costs, that are required to deal with these complications.[3,4]

Patient satisfaction

58.7% of patients required additional pain medication during the staple removal process.[3]

ARTISS can help eliminate the use of staples, therefore relieving patient's anxiety about staple removal and the pain associated with it.[3,4]

Health resources needed for staple removal

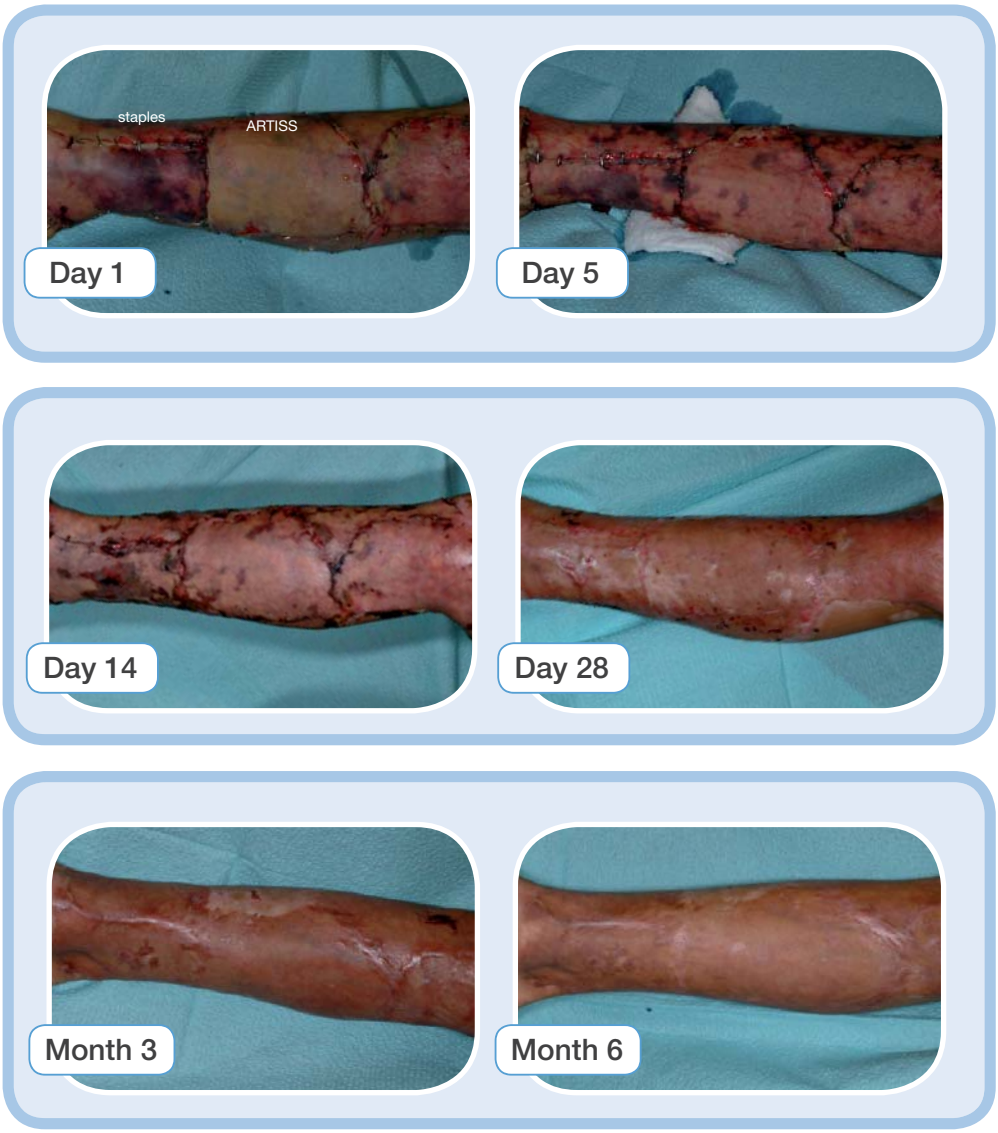
In the study it was shown that staple removal is associated with a number of health resources, that also need to be considered from an economical perspective.[3]

Health Resource Parameter	Value
Total number of staples used (median)	30 (range: 7 to 88)
Number of sessions required to remove staples (median)	1 (range: 1 to 2)
Number of persons involved in staple removal (median)	2 (range: 1 to 9)
Time (minutes) spent removing staples (median)	10 (range: 1 to 365)
Additional pain medication/sedation required for staple removal (%)	58.7% (74/126)

References:

1 ARTISS [Fibrin Sealant (Human)], full Prescribing Information, Deerfield, Illinois, 12/2010.
2 Summary of Product Characteristics for ARTISS, Solutions for Sealant SPC, Vienna Austria, Baxter International Inc. 2010
3 Foster K, Greenhalgh D, Gamelli RL, et al. FS 4IU VH S/D Clinical Group. Efficacy and safety of a fibrin sealant for adherence of autologous skin grafts to burn wounds: results of a phase 3 clinical study. J Burn Care Res. 2008; 29 (2): 293-303.
4 Gibran N, Luterman A, Herndon D, et al. Comparison of fibrin sealant and staples for attaching split-thickness autologous sheet grafts in patients with deep partial- or full-thickness burn wounds: a phase 1/2 clinical study. J Burn Care Res. 2007; 28 (3): 401-408.
5 Branski LK, Mittermayr R, Herndon DN, et al. Fibrin sealant improves graft adherence in a porcine full-thickness burn wound model, JBUR-3130 (in press).
6 Macasev D, Barry J, DiOrio J, et al. Interaction of Cells Involved in Wound Repair with Different Fibrin Sealant Matrices. J Biomater Appl. 2010. [Epub ahead of print]
7 Mittermayr R, Wasserman E, Thurnher M et al. Skin graft fixation by slow clotting fibrin sealant applied as a thin layer. Burns. 2006; 32: 305–311.

Typical Study Result



Photos taken from Baxter Library of clinical study photos.

In a phase III, multicentre, prospective, evaluator-blinded, randomized study comparing fibrin sealant with 4 I/U thrombin, vapor heated, and solvent/detergent treated (FS 4 IU VS S/D) to staples where patients served as their own control, FS 4IU VH S/D was used to affix sheet grafts at one test site (treatment) and staples used to affix sheet skin grafts at the other test site (control).[3]

ARTISS
[Solutions for Sealant]

ARTISS [Solutions for Sealant] is convenient and ready-to-use

- Prefilled syringes – ready-to-use without mixing or dilution required[7]
- Spray application for a single thin layer[3,7]
- Full surface adherence eliminating dead space[3]

ARTISS, slow-setting, vapor-heated and solvent/detergent treated fibrin sealant is developed by Baxter with over 30 years of successful fibrin sealant usage in all surgical specialties with no single case of hepatitis or HIV seropositivity. As with medicinal products manufactured from human plasma the possibility of transmitting infective agents cannot be totally excluded.[2]

Product	Quantity per pack	Article code
ARTISS [Solutions for Sealant], frozen		
2 ml (1 ml Fibrinogen Solution + 1 ml Thrombin Solution)	1	please contact your local representative for country-specific codes
4 ml (2 ml Fibrinogen Solution + 2 ml Thrombin Solution)	1	
10 ml (5 ml Fibrinogen Solution + 5 ml Thrombin Solution)	1	
EasySpray pressure regulator unit	1	0600075
Tisseel/Artiss Spray Set (10 pack)	10	0600065
Tisseel/Artiss Spray Set, single	1	0600066

This abbreviated summary of product characteristics (SmPC) is intended for international use. Please note that it may differ from the licensed SmPC in the country where you are practicing. Therefore, please always consult your country-specific SmPC or package leaflet.

ARTISS, Solutions for Sealant, deep frozen

COMPOSITION: ARTISS consists of: • Human Fibrinogen (as clottable protein) 91 mg1/ml • Synthetic Aprotinin 3000 KIU/ml • Human Thrombin 4 IU/ml • Calcium Chloride 40 µmol/ml
INDICATIONS: ARTISS is indicated as tissue glue to adhere/seal subcutaneous tissue in plastic, reconstructive and burn surgery, as replacements or adjuncts to sutures or staples. In addition, ARTISS is indicated as adjunct to hemostasis on subcutaneous tissue surfaces.
CONTRAINDICATIONS: ARTISS is not indicated to replace skin sutures intended to close surgical wound. ARTISS alone is not indicated for the treatment of massive and brisk arterial or venous bleeding. ARTISS can never be applied intravascularly. Hypersensitivity to the active substances or to any of the excipients.
SPECIAL WARNINGS AND SPECIAL 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.
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. ARTISS should only be applied as a thin layer. Excessive clot thickness may negatively interfere with the product's efficacy and the wound healing process.
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.
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 synthetic 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.
In the event of anaphylactic or severe hypersensitivity reactions, administration is to be discontinued and 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 HIV, HBV, and HCV, and for the non-enveloped 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).
UNDESIRABLE EFFECTS: Inadvertent intravascular injection could lead to thromboembolic events and DIC and there is also a risk of anaphylactic reactions. 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 or any other constituents of the product.
Even if a first treatment with ARTISS is 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. Adverse reactions reported from clinical studies as well as from postmarketing surveillance 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 were classified as serious. Unknown frequencies are based on spontaneous reports from postmarketing surveillance of Baxter's fibrin sealants.
The ADRs and their frequencies are: Common (≥1/100 to <1/10): pruritus, skin graft failure; Uncommon (≥1/1000 to <1/100): dermal cyst; Unknown (cannot be estimated from the available data): anaphylactic responses, hypersensitivity, : bradycardia, tachycardia, hypotension, haematoma, dyspnoea, nausea, urticaria, flushing, impaired healing, oedema, pyrexia, seroma.

For the Posology, incompatibilities and interactions, please refer to your locally approved full SmPC.

Medicinal products are subject to medical subscription

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