SurgiClot® Hemostatic Dressing

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INSTRUCTIONS FOR USE

DEVICE DESCRIPTION

Each SurgiClot® Hemostatic Dressing, utilizing FastClot® technology, consists of the following components:

- Non-woven Nanofiber Dextran
- Human Thrombin and Fibrinogen (Clotting Proteins)

Each 7.0 cm x 7.0 cm dressing contains 140 to 260 mg of human fibrinogen and ≥130 International Units of human thrombin.

The clotting proteins are sterile, non-pyrogenic, freeze-dried, solvent/detergent-treated, pasteurized (fibrinogen) or nano-filtered (thrombin) powder preparations made from pooled human source plasma. The pooled human source plasma is obtained from FDA-licensed plasma collection centers.

SurgiClot Hemostatic Dressing is fully dissolvable, resorbable and biocompatible.

HOW SUPPLIED

SurgiClot Hemostatic Dressing is provided as a 7.0 cm x 7.0 cm dressing in a protective plastic tray, sealed in a foil chevron pouch overpack, sterilized by gamma irradiation, and stored dry at a controlled temperature of 2°- 8°C (36°- 46°F) and at a relative humidity ≤60% until use.

Table 1 below summarizes the materials used in the device:

Table 1. SurgiClot Hemostatic Dressing Configuration

Active Dressing *(7.0 cm by 7.0 cm)*	Non-woven Nanofiber Dextran Human Thrombin Human Fibrinogen
Packaging *(15.2 cm x 21.6 cm foil chevron pouch)*	Heat-sealed foil pouch that contains: • Desiccant packet • Polyethylene, blue tinted tray • Heat-sealed Tyvek lid for tray • Label

ACTIONS

The primary mode of action of the SurgiClot Hemostatic Dressing is a physical effect to promote hemostasis. Upon topical placement of the SurgiClot dressing to cancellous bone bleeding surfaces, the non-woven nanofiber dextran material of the dressing adheres to the surface to form a physical barrier that plugs exposed marrow spaces. This has the effect of stopping blood flow.

Exposure of the dressing to blood at the dressing application site also dissolves the dextran material. As the dextran material dissolves, a further physical barrier is produced at the bleeding site when the thrombin and fibrinogen embedded in the dressing interact to form an autonomous insoluble fibrin clot. The action of the clotting proteins is ancillary to that of the dextran material.

INDICATIONS

SurgiClot Hemostatic Dressing is a medical device indicated for cancellous bone bleeding and is used as an adjunct to promote hemostasis when control of bleeding by standard surgical methods of hemostasis is ineffective or impractical. The dressing is composed of five layers of a non-woven white dextran resorbable mat that encapsulates lyophilized human-derived thrombin and fibrinogen proteins.

CONTRAINDICATIONS

Do not use SurgiClot Hemostatic Dressing in individuals with known hypersensitivity to human blood products and/or dextran.

Do not use SurgiClot Hemostatic Dressing in the presence of active infection or in contaminated areas of the body because infection may occur.

Do not apply SurgiClot Hemostatic Dressing intravascularly. Intravascular application of the SurgiClot dressing may result in life-threatening thromboembolic events.

WARNINGS and PRECAUTIONS

The use of SurgiClot is restricted to experienced physicians.

The physician should discuss the risks and benefits of this product with the patient.

No more than four (4) SurgiClot Hemostatic Dressings may be used on one adult patient.

As with other hemostatic agents, circumstances that result in a negative peripheral venous pressure (e.g. patient positioning) may draw material into the vascular system, potentially resulting in life threatening thromboembolic events.

SurgiClot Hemostatic Dressing is supplied sterile for single use only. Do not re-sterilize, e.g., autoclave. Do not reuse due to risk of contamination and reduced product efficacy.

Do not use the SurgiClot Hemostatic Dressing if the packaging has been damaged due to risk of contamination and reduced product efficacy.

Do not expose the SurgiClot Hemostatic Dressing to liquid prior to use. Exposure of the SurgiClot dressing to liquid prior to use will prematurely dissolve the dextran and reduce its efficacy.

The proteins in the SurgiClot Hemostatic Dressing can be denatured by contact with solutions containing alcohol, iodine, or heavy metal ions. If antiseptics containing such substances have been used near the site of bleeding, the SurgiClot Hemostatic Dressing should not be applied until after the application site is cleaned to remove any such substances.

Do not cut the SurgiClot Hemostatic Dressing. Cutting the dressing may result in the lyophilized proteins spilling out of the dressing.

Do not attempt to remove the SurgiClot Hemostatic Dressing once the product is applied at the bleeding site. Attempting to remove the product may disrupt the newly-formed clot.

Excess SurgiClot dressing (material not fully dissolved and/or not incorporated in the hemostatic clot) should be dissolved by gentle irrigation with a small amount of sterile non-heparinized saline at the site of application.

Performance of the SurgiClot Hemostatic Dressing following repeated (more than twice) removal and return of the fully packaged product from controlled temperature 2° - 8°C (36° - 46°F) to ambient room temperature has not been evaluated.

The safety and effectiveness of the SurgiClot Hemostatic Dressing has not been established in children and pregnant women.

The risk of antibody development with repeated applications has not been studied.

The use of SurgiClot Hemostatic Dressing in conjunction with autologous blood salvage circuits has not been evaluated.

SurgiClot Hemostatic Dressing contains thrombin and fibrinogen made from human plasma. When medical devices are made from human plasma, certain measures are put in place to prevent infections being passed on to patients; including careful selection of plasma donors to make sure those at risk of carrying infections are excluded, and testing of each plasma donation for bacteria/viruses. Manufacturers of products derived from plasma also include steps in the processing of the plasma that can inactivate or remove viruses. Despite these measures, when products prepared from human plasma are administered, the possibility of passing on bacteria/viruses cannot be totally excluded. This also applies to the Creutzfeldt-Jakob disease (CJD) agents. 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 and parvovirus B19V viruses.

SurgiClot Hemostatic Dressing contains dextran. A possible side effect is dextran-induced anaphylactoid reaction (DIAR), which is a rare but severe complication.

AII infections thought to have been transmitted by this product should be reported to St. Teresa Medical, Inc.

Do not use SurgiClot Hemostatic Dressing in place of sutures, ligature, cautery or other primary modes for control of hemostasis.

ADVERSE EVENTS (AEs)

Potential AEs associated with the SurgiClot Hemostatic Dressing include but are not limited to the following:

- Anemia
- Bacterial Infection
- Creutzfeldt-Jakob disease (CJD)
- Foreign Body Reaction/Inflammatory Response
- Pyrogenic Fever
- System Toxicity
- Thromboembolism
- Viral Infection

To report SUSPECTED ADVERSE EVENTS, contact St. Teresa Medical, Inc. at 651-789-6550 or support@stteresamedical.com.

Viral Clearance

The biological components of SurgiClot (human fibrinogen and human thrombin) are manufactured from pooled human plasma collected in FDA-licensed facilities in the United States. Human plasma is tested by FDA-licensed Nucleic Acid Tests (NAT) for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus-1 (HIV-1). NAT testing for hepatitis A virus (HAV) and parvovirus B19 is also performed. Human plasma is also tested for the presence of hepatitis B surface antigen (HBsAg), and antibodies to hepatitis C virus (anti-HCV) and human immunodeficiency viruses types 1 and 2 (anti-HIV1/2).

The manufacturing procedure for human fibrinogen and human thrombin include processing steps designed to reduce the risk of viral transmission. In particular, the virus clearance steps in the manufacture of human fibrinogen include solvent/detergent (S/D) treatment and pasteurization. The virus clearance steps in the manufacture of human thrombin include S/D treatment and nanofiltration.

The virus clearance capacity of these procedures has been validated using viruses with a range of physico-chemical characteristics. These in vitro validation studies were conducted using samples from manufacturing intermediates spiked with virus suspensions of known titers followed by further

processing under conditions equivalent to those in the respective manufacturing steps. The results of virus clearance validation studies are summarized in Table 2 and Table 3.

Table 2. Virus Reduction Factors for Human Fibrinogen

	Reduction Factor (log_{10}) of virus tested					
	Enveloped Viruses			Non-Enveloped Viruses		
Manufacturing Step	**HIV-1**	**BVDV**	**PRV**	**Polio-1**	**HAV**	**PPV**
SD Treatment	≥5.35	≥4.11	5.88	Not Tested	Not Tested	Not Tested
Pasteurization	≥6.10	≥6.08	≥3.12	≥5.82	4.55	1.03
Cumulative Virus Reduction Factor	≥11.45	≥10.19	≥9.00	≥5.82	4.55	1.03

HIV-1: Human Immunodeficiency Virus Type 1
BVDV: Bovine Viral Diarrhea Virus
PRV: Pseudorabies Virus
Polio-1: Polio-1 Virus
HAV: Hepatitis A Virus
PPV: Porcine Parvovirus

Table 3. Virus Reduction Factors for Human Thrombin

	Reduction Factor (log_{10}) of virus tested					
	Enveloped Viruses			Non-Enveloped Viruses		
Manufacturing Step	**HIV-1**	**BVDV**	**PRV**	**Polio-1**	**HAV**	**PPV**
SD Treatment	≥4.50	5.11	5.92	Not Tested	Not Tested	Not Tested
Virosart CPV Filtration	≥3.97	≥4.88	≥5.11	≥5.45	≥5.30	≥6.44
Cumulative Virus Reduction Factor	≥8.47	≥9.99	≥11.03	≥5.45	≥5.30	≥6.44

HIV-1: Human Immunodeficiency Virus Type 1
BVDV: Bovine Viral Diarrhea Virus
PRV: Pseudorabies Virus
Polio-1: Polio-1 Virus
HAV: Hepatitis A Virus
PPV: Porcine Parvovirus

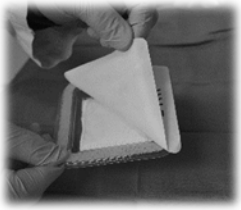
SURGICLOT® HEMOSTATIC DRESSING – INSTRUCTIONS FOR USE

1. Remove the SurgiClot Hemostatic Dressing from the refrigerator approximately 30 minutes prior to application.

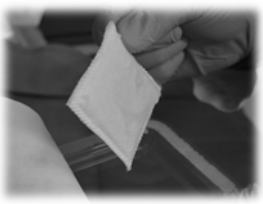
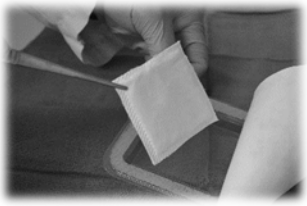
2. Before using, inspect the package for signs of damage. If the package is damaged, sterility cannot be assured. Do not use if the packaging has been damaged due to risk of contamination and reduced product efficacy. **Note:** The application of the SurgiClot Hemostatic Dressing is a sterile procedure requiring the use of sterile gloves, mask and instruments while handling the dressing.

3. Open the foil pouch and remove the tray.


4. Open the protective tray lid.



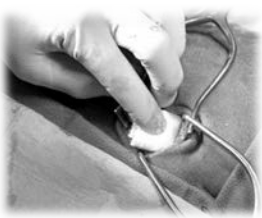
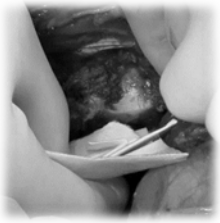
5. Using dry sterile gloves or sterile forceps, remove the SurgiClot Hemostatic Dressing from the tray.

6. Identify the source of bleeding at the bone surface. This is the target site for application of the SurgiClot Hemostatic Dressing. Remove excess blood or fluid from the site of application, if required, to improve visibility.

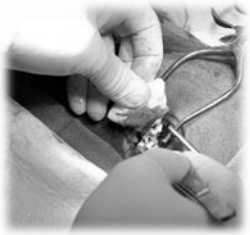
7. Fold the SurgiClot Hemostatic Dressing to match the dimensions of the site of application. The dressing can be shaped into any configuration as needed, but ensure that the dressing covers the bleeding site completely. Do not attempt to cut the SurgiClot Hemostatic Dressing because cutting the dressing may cause clotting proteins to spill out of the dressing resulting in reduced product efficacy.

8. Place the SurgiClot dressing on the bleeding site, and with the use of finger(s) or forceps, hold the dressing in place. A gauze sponge or equivalent sterile pad (e.g., Telfa pad) may be used as a backing material over the dressing to prevent adherence of the dressing to finger(s) or forceps.

9. After 2-4 minutes, carefully remove the backing material (if used) by gentle irrigation with sterile non-heparinized saline, and observe the bleeding area to determine if bleeding has

ceased. Additional SurgiClot dressings may be applied if bleeding continues; do not use more than four dressings on one adult patient.



10. Dressing dissolves in contact with fluid. If bleeding has ceased and undissolved SurgiClot material is present it can remain or apply gentle irrigation with sterile non-heparinized saline to dissolve. Do not attempt to remove the dressing material as this may cause bleeding to re-occur.
11. Unused SurgiClot material that has been removed from its packaging and exposed to blood and/or bodily fluids must be disposed of in accordance with local requirements.
12. If a backing material is used, it must be disposed of in accordance with local requirements.
13. Properly dispose of packaging material.

CLINICAL STUDY EXPERIENCE

Because clinical studies are conducted under widely varying conditions, adverse event rates observed in the clinical studies of a device cannot be directly compared to rates in the clinical studies of another device and may not reflect the rates observed in practice.

Two open-label studies assessing the safety and performance of SurgiClot Hemostatic Dressing in the treatment of cancellous bone bleeding have been conducted; a 30-subject multicenter study in patients undergoing iliac crest bone graft, pelvic osteotomy or spinal fusion surgical procedures was conducted in Europe, and a 10-subject single center study in subjects undergoing spinal fusion surgical procedures was conducted in India.

Safety

In the combined SurgiClot Hemostatic Dressing 40-subject clinical study data, the incidence of adverse events was 75% (30 subjects). The most frequently reported adverse events were anemia (14 subjects [35.0%]), abnormal lab values (13 subjects [32.5%]) and immunological reactions (9 subjects [22.5%]), see Table 4.

Table 4. Clinically Relevant Adverse Events Reported in at Least 5% of Subjects Treated with SurgiClot Hemostatic Dressing, Irrespective of Causality

Adverse Event	Occurrence N=40 n (%)
At least 1 adverse event	**30 (75%)**
Fever	2 (5.0%)
Hematoma	2 (5.0%)

Adverse Event	Occurrence N=40 n (%)
Respiratory complications	2 (5.0%)
Pain/discomfort	3 (7.5%)
Skin irritation/rash	3 (7.5%)
Hypotension	4 (10.0%)
Immunological reactions	19 (22.5%)
Abnormal lab values	13 (32.5%)
Anemia	14 (35.0%)

Other adverse events observed in less than 5% of the clinical study subjects were bleeding (mild to moderate), infection, inflammation, nausea, neurological, urinary tract infection (UTI), reduced body temperature, constipation, and tooth abscess.

Two adverse events were considered “mild” and “Possibly Related” to the use of SurgiClot Hemostatic Dressing: anemia (1 subject, 2.5%), immunological reaction – elevated eosinophil count (1 subject, 2.5%). No other adverse events were deemed to be related to the use of SurgiClot Hemostatic Dressing.

Performance

In the Intention to Treat (ITT) population (40 subjects), the proportion of subjects that achieved controlled hemostasis at 3 minutes following treatment with SurgiClot Hemostatic Dressing was 75.0% (30/40). Thirty-seven (37) out of 40 (92.5%) subjects achieved controlled hemostasis at 6 minutes following treatment with the product, see Table 5.

Table 5. Efficacy Results in Orthopedic or Spinal Surgery, ITT Population (N = 40)

Characteristics	Total number of subjects who achieved controlled hemostasis	Proportion of subjects who achieved controlled hemostasis
Hemostasis at 3 Minutes	30	0.75
Hemostasis at 6 Minutes	37	0.925

In total, 51 surgical sites were treated with the SurgiClot dressing. Of the 51 surgical sites, 41 (80.4%) achieved controlled hemostasis at 3 minutes, while 48 (94.1%) achieved controlled hemostasis at six minutes, see Table 6.

Table 6. Efficacy Results in Orthopedic or Spinal Surgery, Surgical Treatment Sites (N = 51)

Characteristics	Total number of surgical sites treated with SurgiClot® that achieved controlled hemostasis	Proportion of surgical sites treated with SurgiClot® that achieved controlled hemostasis
Hemostasis at 3 Minutes	41	0.804

Characteristics	Total number of surgical sites treated with SurgiClot® that achieved controlled hemostasis	Proportion of surgical sites treated with SurgiClot® that achieved controlled hemostasis
Hemostasis at 6 Minutes	48	0.941

STORAGE AND HANDLING CONDITIONS

SurgiClot Hemostatic Dressing shall be stored dry at controlled temperature 2°- 8°C (36°- 46°F). SurgiClot Hemostatic Dressing must be used immediately once the package is opened. Discard if packaging is damaged. Do not use after the expiration date on the package label. Do not reuse.

SYMBOL KEY


Manufacturer


Date of Manufacture

Catalog Number

Batch Code


Do Not Re-Use


Do Not Resterilize


Use-By Date


Keep Dry


Caution

Temperature Limits

Consult Instructions for Use

Sterilized Using Irradiation


For Use by A Physician Only


Do Not Use if Package is Damaged

PATENTS

International and U.S. patents US 9,399,082 and 9,555,157, Europe 2276879, other patents pending.

TRADEMARKS

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