

PerClot® Polysaccharide Hemostatic System

Instructions for Use

PerClot® Polysaccharide Hemostatic System should only be used by a physician or other licensed practitioners.

DESCRIPTION

PerClot® Polysaccharide Hemostatic System (PerClot® PHS) is a medical device composed of absorbable modified polymer (AMP®) particles and delivery applicators. AMP® particles are biocompatible, non-pyrogenic and derived from purified plant starch. The device contains no human or animal components. PerClot® PHS is intended as an absorbable hemostatic system to control bleeding during surgical procedures or following traumatic injuries. For specific surgical procedures, the system is configured in both PerClot® Standard and PerClot® Laparoscopic.

ACTION

AMP® particles have a molecular structure that rapidly absorbs water from the blood. This dehydration process causes a high concentration of platelets, red blood cells, and coagulation proteins (thrombin, fibrinogen, etc.) which accelerates the normal, physiologic clotting cascade. In contact with blood, AMP® particles support the formation of a gelled, adhesive matrix which provides a mechanical barrier to control bleeding. Absorption normally requires several days and is dependent on the amount of material applied and the site of use. AMP® particles are degraded by amylase and glucoamylase.

INDICATIONS

PerClot® PHS is indicated for use in surgical procedures (except neurological and ophthalmic) or injuries as an adjunct hemostat when control of bleeding from capillary, venous, or arteriolar vessels by pressure, ligature, and other conventional means is either ineffective or impractical.

INSTRUCTIONS FOR USE

The following instructions provide technical direction for the recommended use of all PerClot® PHS models. In addition, the techniques and procedures described here do not represent all medically acceptable protocols, nor are they intended as a substitute for physician's experience and judgment in treating specific surgical conditions.

PREPARATION

1. Visually inspect both the sealed AMP® and applicator packages. If either package has been previously opened or damaged, discard and replace with a new package.
2. Remove the applicator from the package.

3. Remove the AMP® particle dispenser (bellows) from its package. Remove the cap using a counter-clockwise turning motion (Fig.1).
4. Connect the AMP® particle dispenser firmly to the end of the applicator handle (Fig.2 and Fig.3). The system is now ready for use.
5. Pump the dispenser to deliver AMP® particles directly to the site of bleeding (Fig. 4).

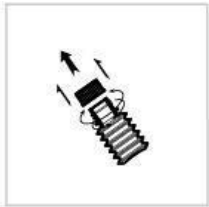


Fig.1



Fig.2



Fig.3

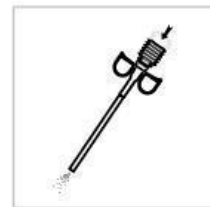


Fig.4

PerClot® Standard

Used during open surgical procedure.

Application Technique

For maximum efficacy, the following techniques are recommended:

1. Remove all excess blood from the intended site by blotting, wiping, or suctioning. Identify and expose the source of bleeding. Removing excess blood is critical to maximizing the hemostatic performance as it allows AMP® particles direct contact with the site and source of active bleeding.
2. Immediately apply a liberal amount of AMP® particles directly to the source of bleeding. Thoroughly cover the bleeding wound with AMP® particles.
3. When managing deep wounds, the applicator tip must be close to the source of the bleeding. In this situation, use caution to avoid contacting the applicator tip with blood as this may occlude the applicator. If this occurs, discard and use a new PerClot® Standard applicator.
4. For profuse bleeding, apply direct pressure over the wound for several minutes following AMP® particle application. Some materials such as standard gauze may adhere to the gelled clot matrix. Irrigation with saline before carefully removing the gauze is recommended. The use of a non-adhering substrate to apply pressure is recommended.
5. If bleeding continues, remove excess particles and repeat the procedure.
6. Once hemostasis is achieved, remove excess AMP® particles carefully and completely by irrigation and aspiration.

PerClot® Laparoscopic

Used in laparoscopic and laparoscopic-assisted procedure.



An illustration of the PerClot® laparoscopic

Application Technique

1. Identify the bleeding lesion(s). Removing excess blood from the site of bleeding is essential to achieve maximum hemostatic efficacy.
2. Insert the applicator into the laparoscope and position its tip at the site of bleeding. Deliver the AMP® particles by deliberate pumping of the dispenser. Do not attempt to trim the applicator tip. In the event that the tip becomes occluded, use a new applicator.
3. If bleeding continues, remove excess AMP® particles and re-apply.
4. Once hemostasis is achieved, remove excess AMP® particles with irrigation and aspiration.
5. Remove the applicator.
6. Following the procedure, insure the laparoscope is completely cleaned by irrigation to avoid laparoscope channel occlusion.

CONTRAINDICATIONS

Do not apply PerClot® PHS into blood vessels as potential for embolization and death may exist.

PerClot® PHS is contraindicated in patients who are sensitive to starch or starch-derived materials.

WARNINGS

PerClot® PHS is not intended as a substitute for good surgical practice, and in particular, the proper use of conventional procedures (such as ligature) for hemostasis.

PerClot® PHS is not recommended when an infection is suspected. PerClot® PHS should be used with caution in contaminated areas. If signs of an infection develop in the site where PerClot® PHS has been used, surgery may be necessary to allow adequate drainage.

Combined use of PerClot® PHS with other topical hemostatic agents has not been studied in controlled clinical trials.

Remove excess AMP® particles once hemostasis is achieved. This removal of excess particles is

particularly important in and around the spinal cord, areas of bone confine, the optic nerve/chiasm, and foramina of bone because unsaturated particles may swell and compress the surrounding tissues.

PerClot® PHS should not be mixed with methylmethacrylate or other acrylic adhesives as it may reduce the adhesive strength and compromise the attachment of prosthetic devices to bone tissue. Excess particles should be fully removed from bony surfaces by irrigation prior to the use of adhesives.

Safety and effectiveness of PerClot® PHS have not been clinically evaluated in children and pregnant women.

When PerClot® PHS is used in the nasal cavity and laryngopharyngeal, PerClot® PHS should be used with caution to avoid the dry particles being drawn into the trachea or bronchi, which may form a gel that blocks the trachea and bronchi.

PerClot® PHS is a single use product. Do not use PerClot® PHS in more than a single surgical procedure.

PerClot® PHS should not be used for controlling post-partum bleeding or menorrhagia.

Safety and effectiveness in neurological and ophthalmic procedures has not been studied in controlled clinical trials.

PRECAUTIONS

PerClot® PHS is not recommended as a primary treatment for coagulation disorders.

PerClot® PHS is intended to be used in a dry state. Contact with fluids prior to application will result in the loss of hemostatic properties.

Do not apply more than 50g of PerClot® PHS in diabetic patients in case that excess of 50g could affect the glucose load.

When an extracorporeal cardiopulmonary bypass circuit or autologous blood salvage circuit is used in conjunction with PerClot® PHS, care must be exercised to prevent possible particle entry into the bypass circuit. Entry is prevented by using a 40µ cardiotomy reservoir, cell washing, and a 40µ transfusion filter (such as a LipiGuard®).

PerClot® PHS should not be left in bladder, ureteral lumen or renal pelvis to eliminate the potential foci for calculus formation.

Visualization of the bleeding site is critical during the application of PerClot® PHS. The bleeding site must be exposed to ensure the hemostatic particles contact with the bleeding site prior to achieving hemostasis, or else re-bleeding may occur. Especially for its application in myomectomy, it is hard for PerClot® PHS to reach the actual bleeding site, so the hemostasis is not

achieved.

ADVERSE REACTIONS

A total of seven adverse events have been reported for PerClot® PHS.

Five adverse events were reported during clinical use. Three were potential re-bleeding resulting from the unidentified bleeding source during myomectomy, emergency epistaxis and septoplasty. One adverse event was reported for aspiration of dry particles into the airway during tonsillectomy. One adverse event was regarding broken applicator.

Two adverse events occurred in a randomized prospective, concurrently controlled clinical trial of 288 patients. One patient had blood glucose increase and one patient had fever. None were determined to be related to PerClot® PHS.

ADVERSE REACTIONS THAT HAVE BEEN ATTRIBUTED TO OTHER STARCH DERIVED POLYSACCHARIDE HEMOSTATIC PARTICLES

The following adverse events have been reported for other starch derived polysaccharide hemostatic particles and may apply to the use of PerClot® PHS:

In laparoscopic or laparoscopic-assisted procedures, infection and bowel obstruction (ileus) resulting from excess and residual hemostatic particles have been observed.

In a randomized prospective, concurrently controlled clinical trial, it was reported for other starch derived polysaccharide hemostatic particles, the most common adverse events were pain related to surgery, anemia, nausea, and lab values out of normal range. Other adverse events included arrhythmia, constipation, respiratory dysfunction, hypotension, fever, pruritis, ecchymosis, tachycardia, edema, pain unrelated to surgery, hemorrhage, hypertension, paresthesia, cutaneous bleed, infection, seroma, confusion, renal insufficiency, heartburn, diarrhea, vertigo, hypovolemia, pneumonia, pleural effusion, paresis, dermal irritation, urinary dysfunction, muscle spasms, hematuria, ileus, coagulation, necrosis, hematoma, hypothermia, agitation, rash, hypoxaemia, myocardial infarction, hyperthermia, hypercapnia, clostridium difficile, eye irritation, xerostomia, nerve palsy, pericardial effusion, cardiac tamponade, excoriation, fatigue, flatus, unrelated illness, cellulitis, syncope, shivering, sore throat, alkalosis, heel ulcer, anastomotic leak, clot, gastritis, left ventricular fistula, liver insufficiency, adrenal insufficiency. None of the above adverse events that occurred were judged by the Data Safety Monitoring Board to be related to the use of the experimental product.

ADVERSE REACTIONS THAT HAVE BEEN ATTRIBUTED TO OTHER NON-STARCH DERIVED HEMOSTATIC AGENTS

The following adverse events have been reported for other non-starch derived hemostatic agents and may apply to the use of PerClot® PHS:

Paralysis and nerve damage have been reported when hemostatic agents are used in or in proximity to foramina in bone, areas of bone confine, the spinal cord, and/or the optic nerve and chiasm. While most of these reports have been in connection with laminectomy, reports of

paralysis have also been received in connection with other procedures.

Compression of the brain and spinal cord resulting from the accumulation of sterile fluid has been observed.

CLINICAL STUDIES

Objective

The objective of the study was to evaluate the safety and effectiveness of PerClot and SealFoam (a starch derived hemostatic sponge manufactured by Starch Medical) versus a commercially available starch derived polysaccharide hemostatic particles to control intraoperative bleeding in orthopedic surgery, general surgery and cardiac surgery.

Methods

This study was designed as a multi-center, randomized, non-inferiority, parallel controlled clinical study. After the investigators obtain the informed consent from subjects, subjects were randomized in a 1:1:1 allocation to experimental groups (PerClot as Group T¹ and SealFoam as Group T²) and the control group (as Group C). All subjects were evaluated through baseline assessment before surgeries, hemostatic efficacy during the surgeries, 3 days post-surgery or at discharge (whichever was earlier) and at 30 days post-surgery to undergo general physical examination and experimental examination, which checked the incidence of any adverse event.

Primary Endpoint

Success rate of achieving hemostasis after 5-mins: after applying PerClot or SealFoam, the lesions were evaluated at 1 minute intervals. If the bleeding stopped within 5 minutes, the result should be judged as effective; otherwise, the result should be judged as ineffective.

Success Rate = $N (\text{Successful cases}) / A (\text{total cases}) * 100\%$

Secondary Endpoint

To compare intraoperative transfusion volume, 24h post-surgery blood transfusion volume, 24h post-surgery drainage volume, intraoperative bleeding volume and hemostasis time.

Results

•Primary Endpoint

Observing the success rate of experimental group T¹, experimental group T², and control group C at 5 minutes after applying the material.

Compared Group T¹ with control group, the ratio of T¹'s subjects in FAS is 100%, control groups 100%. When comparing the ratio between two groups 5 minutes after application, the lower bound of 95% confidence interval is -2.06%, which is greater than the value of non-inferiority -10%. Hence, the comparison between T¹ and Control group is known as non-inferiority.

Compared Group T² with control group, the ratio of T²'s subjects in FAS is 100%, control groups 100%. When comparing the ratio between two groups at 5 minutes after application,

the lower bound of 95% confidence interval is -2.06%, which is greater than the non-inferiority critical value -10%. Hence, the comparison between T² and control group is known as non-inferiority.

Compared T¹, T² and control group respectively according to the data of three departments (General Surgery Department, Orthopedic Surgery Department, and Cardiac Surgery Department), the success ratios of FAS population of experimental groups and control group are 100%. The lower bound of 95% confidence interval of the efficiency ratio at 5 minutes after application is greater than the non-inferiority critical value -10%. Hence, the study is known as a non-inferiority trial.

•Secondary Endpoints

○Intraoperative bleeding volume

Compared T¹ with control group, T¹'s intraoperative bleeding volume is 325.85±460.17 ml, control group 371.40±474.46 ml, with p=0.345, which shows no statistical difference.

Compared T² with control group, T²'s intraoperative bleeding volume is 270.69±295.26 ml, control group 371.40±474.46 ml, with p=0.139, which shows no statistical difference.

○Intraoperative transfusion volume

Compared T¹ with control group, T¹'s intraoperative transfusion volume is 86.28±265.27 ml, control group 133.87±383.24 ml, with p=0.712, which shows no statistical difference.

Compared T² with control group, T²'s intraoperative transfusion volume is 60.00±218.11 ml, control group 133.87±383.24 ml, with p=0.224, which shows no statistical difference.

○24h post-surgery transfusion volume

Compared T¹ with control group, T¹'s 24h transfusion volume is 10.64±84.84 ml, control group 0.00±0.00 ml, with p=0.158, which shows no statistical difference.

Compared T² with control group, T²'s 24h transfusion volume is 4.26±41.26 ml, control group 0.00±0.00 ml, with p=0.320, which shows no statistical difference.

○24h post-surgery drainage volume

Compared T¹ with control group, T¹'s 24h post-surgery drainage volume is 225.47±268.69 ml, control group 185.27±180.10 ml, with p=0.488, which shows no statistical difference.

Compared T² with control group, T²'s 24h post-surgery drainage volume is 210.93±311.53 ml, control group 185.27±180.10 ml, with p=0.679, which shows no statistical difference.

○Hemostasis time

Compared T¹ with control group, T¹'s hemostasis time is 2.13±0.99 min, control group 2.40±1.13 min, with p=0.159, which shows no statistical difference.

Compared T² with control group, T²'s hemostasis time is 2.29±1.09 min, control group 2.40±1.13 min, with p=0.546, which shows no statistical difference.

ADMINISTRATION

Aseptic technique should always be used. A liberal amount of AMP® particles should be applied to the bleeding site until hemostasis is achieved. For profuse bleeding, apply pressure if necessary. After hemostasis is achieved, AMP® particles should be removed by irrigation and/or aspiration.

HOW SUPPLIED

PerClot® is available in 1g, 3g and 5g configurations.

PerClot® applicators are available in the following lengths: 90mm, 200mm and 380mm.

STERILIZING METHOD & EXPIRATION DATE

Contents of the PerClot® PHS package are sterilized by irradiation and should not be re-sterilized. Unused, open packages should be discarded properly.

If stored under the conditions specified in this manual (see STORAGE AND HANDLING), the unopened and undamaged product remains sterile for three (3) years from the date of sterilization.

STORAGE AND HANDLING

Do not store in extreme conditions, such as temperatures lower than -40°C (-40°F) or higher than 60°C (140°F). PerClot® PHS should be used immediately after the package is opened.

DISPOSAL

This product shall be disposed of in compliance with pertinent government regulations regarding medical devices.

LIMITED WARRANTY

Starch Medical Inc. warrants that this product is free from defects in workmanship and materials. Liability under this warranty is limited to refund or replacement of any product which has been found by Starch Medical Inc. to be defective in workmanship and materials. Starch Medical Inc. shall not be liable for damages arising from the use, misuse, or abuse of this product or its content in ways that are inconsistent with the specific indications described in these Instructions for Use. Damage to the product through misuse, alteration, improper storage, or improper handling shall void this limited warranty.

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authorities.

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TRADEMARKS

PerClot® and AMP® are registered trademarks of Starch Medical Inc.

LipiGuard® is a registered trademark of Haemonetics Puerto Rico LLC.



= Do not re-use



= Use-by date



= Catalogue number



= Sterilized using irradiation



= Batch code



= Date of manufacture



= Caution



= CE-mark and identification number of Notified Body.
Certified according with MDD (93/42/EEC)



= Manufacturer



= Authorized representative in the EC



= Temperature limitation



= Do not use if package is damaged



= Do not re-sterilize



= Consult instructions for use



Starch Medical Inc.

2150 Ringwood Ave. San Jose
California 95131 USA Tel: 408-428-9818

Fax: 408-383-9189

Email: info@starchmedical.com

www.starchmedical.com



ClotPlus Limited

Harcourt Centre, Block 4, Harcourt Road

Dublin 2, D02 HW77 Ireland

Tel: +353(0)1 477 3466

Fax: +353(0)1 402 9590

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