ARISTA™ AH

Absorbable Hemostatic Particles

Instructions for Use

DESCRIPTION

ARISTA™ AH is a medical device intended for application to surgical wound sites as an absorbable hemostat. This technology incorporates hydrophilic, flowable, microporous particles synthesized by cross-linking purified plant starch through a proprietary process; ARISTA™ AH is a 100% plant-based polysaccharide. ARISTA™ AH contains no animal or human components. ARISTA™ AH is a fine, dry, sterilized white powder that is biocompatible, non-pyrogenic, and is typically absorbed within 24 to 48 hours.

ACTION

ARISTA™ AH particles are hydrophilic molecular sieves that enhance natural hemostasis by concentrating blood solids such as platelets, red blood cells, and blood proteins on the particle surfaces to form a gelled matrix. The concentrated gel matrix provides a barrier to further blood loss and is formed regardless of the patient's coagulation status. The concentration of clotting factors and platelets in the gel serves to enhance normal clotting reactions and creates stable hemostatic plugs. The absorption process begins immediately and is dependent on several factors, including the amount applied and site of use.

INDICATIONS

ARISTA™ AH is indicated in surgical procedures (except neurological and ophthalmic) as an adjunctive hemostatic device to assist when control of capillary, venous, and arteriolar bleeding by pressure, ligature, and other conventional procedures is ineffective or impractical.

CONTRAINDICATIONS

Do not inject or place ARISTA™ AH into blood vessels as potential for embolization and death may exist.

WARNINGS

- ARISTA™ AH is not intended as a substitute for meticulous surgical technique and the proper application of ligatures or other conventional procedures for hemostasis.
- Once hemostasis is achieved, excess ARISTA™ AH should be removed from the site of application by irrigation and aspiration particularly when used in and around foramina of bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm. ARISTA™ AH swells to its maximum volume immediately upon contact with blood or other fluids. Dry, white ARISTA™ AH should be removed. The possibility of the product interfering with normal function and/or causing compression necrosis of surrounding tissues due to swelling is reduced by removal of excess dry material.
- Safety and effectiveness of ARISTA™ AH have not been clinically evaluated in children and pregnant women. Because there have been reports of decreased amylase activity in newborns up to 10 months, absorption rates of ARISTA™ AH in this population may be longer than 48 hours.
- ARISTA™ AH should be used with caution in the presence of infection or in contaminated areas of the body. If signs of infection or abscess develop where ARISTA™ AH has been applied, re-operation may be necessary in order to allow drainage.
- Safety and effectiveness in neurosurgical and ophthalmic procedures has not been established.
- ARISTA™ AH should not be used for controlling post-partum bleeding or menorrhagia.

PRECAUTIONS

- When ARISTA™ AH is used in conjunction with autologous blood salvage circuits, carefully follow instructions in the Administration section regarding proper filtration and cell washing.
- ARISTA™ AH is intended to be used in a dry state. Contact with saline or antibiotic solutions prior to achieving hemostasis will result in loss of hemostatic potential.
- ARISTA™ AH is not recommended for the primary treatment of coagulation disorders.
- No testing has been performed on the use of ARISTA™ AH on bone surfaces to which prosthetic materials are to be attached with adhesives and is therefore not recommended.
- ARISTA™ AH is supplied as a sterile product and cannot be resterilized. Unused, open containers of ARISTA™ AH should be discarded.
- Do not apply more than 50g of ARISTA™ AH in diabetic patients as it has been calculated that amounts in excess of 50g could affect the glucose load.
- In urological procedures, ARISTA™ AH should not be left in the renal pelvis or ureters to eliminate the potential foci for calculus formation.

ADVERSE REACTIONS

In a randomized prospective, concurrently controlled clinical trial, a total of 288 randomized patients received ARISTA™ AH or the Control (Gelatin Sponge with or without Thrombin). The most common recorded adverse events were pain related to surgery, anemia, nausea, and lab values out of normal range. The following is a complete list of adverse events reported in greater than 5% of the ARISTA™ AH treated patients. The corresponding adverse events for the Control group are listed for comparison. None of the adverse events that occurred were judged by the Data Safety Monitoring Board to be related to the use of ARISTA™ AH.

ADVERSE EVENTS REPORTED IN GREATER THAN 5% OF THE ARISTA™ AH TREATED PATIENTS

Adverse Events	ARISTA™ AH	Control
Pain related to surgery	140 (96.6%)	139 (97.2%)
Anemia	52 (35.9%)	49 (34.3%)
Nausea	44 (30.3%)	39 (27.3%)
Lab values out of normal range	26 (17.9%)	20 (14.0%)
Arrhythmia	24 (16.6%)	31 (21.7%)
Constipation	27 (18.6%)	12 (8.4%)
Respiratory Dysfunction	19 (13.1%)	18 (12.6%)
Hypotension	18 (12.4%)	18 (12.6%)
Fever	12 (8.3%)	15 (10.5%)
Pruritis	11 (7.6%)	12 (8.4%)
Ecchymosis	13 (9.0%)	8 (5.6%)
Tachycardia	10 (6.9%)	10 (7.0%)
Edema	9 (6.2%)	9 (6.3%)
Pain unrelated to surgery	9 (6.2%)	8 (5.6%)
Hemorrhage	9 (6.2%)	7 (4.9%)
Hypertension	8 (5.5%)	7 (4.9%)

Other adverse events reported in fewer than 5% of the ARISTA™ AH population included: Parethesia, Cutaneous Bleed, Infection, Seroma, Confusion, Renal Insufficiency, Heartburn, Diarrhea, Vertigo, Hypovolemia, Pneumonia, Pleural Effusion, Paresis, Dermal Irritation, Urinary Dysfunction, Muscle Spasms, Hematuria, Ileus, Coagulopathy, Pneumothorax, Dysphagia, Ischemia, Deep Vein Thrombosis, Gout, Inflammation, 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, Snycope, Shivering, Sore Throat, Alcalosis, Heel Ulcer, Anastomotic Leak, Clot, Gastritis, Left Ventricular Fistula, Liver Insufficiency, Adrenal Insufficiency.

ADVERSE REACTIONS THAT HAVE BEEN ATTRIBUTED TO OTHER ABSORBABLE HEMOSTATIC AGENTS

Note that ARISTA™ AH is a unique absorbable hemostatic agent consisting of 100% purified plant starch and it exhibits a faster absorption time (approximately 24 to 48 hours) compared to other absorbable hemostatic agents that absorb in 3 to 8 weeks. The following adverse events have been reported for other absorbable hemostatic agents and may apply to the use of ARISTA™ AH:

Paralysis and nerve damage have been reported when hemostatic agents are used in or in proximity to foramina in bone, areas of bony 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.

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CLINICAL STUDIES

Study Design and Objectives

A prospective, multi-center, multi-specialty, randomized, non-inferiority, controlled clinical trial was conducted. Two hundred eighty-eight (288) patients were randomized and treated at nine investigational centers. The objective of the study was to evaluate the safety and effectiveness of Arista™ AH versus a commercially available absorbable gelatin sponge used with or without Thrombin to control intraoperative bleeding in orthopedic, general, and cardiac surgeries.

Patients were randomized only after a lesion suitable for treatment with an adjunctive hemostatic device was identified. Complete hemostasis was defined as cessation of bleeding. The primary endpoint was complete hemostasis of the first treated lesion within 5 minutes (3 minutes for cardiac). Although multiple lesions in the same patient could be treated per the protocol, only the first treated lesion was used to determine the effectiveness as this was the only lesion that was truly randomized.

Primary Endpoint

For the primary endpoint, complete hemostasis of the first treated lesion within 5 minutes (3 minutes for cardiac) was achieved in 90.3% of the randomized and treated subjects in the Arista™ AH group and in 80.4% of the randomized and treated subjects in the control group. Arista™ AH was demonstrated to be non-inferior to the control ($p<0.0001$). The upper 95% limit on the difference in proportions (Control – Arista™ AH) was less than zero (-2.4%).

Primary endpoint data for the entire randomized and treated patient population as well as stratified by surgical specialty are summarized in the table below:

COMPLETE HEMOSTASIS OF FIRST TREATED LESION WITHIN 5 MINUTES (3 FOR CARDIAC)

Primary Efficacy Endpoint	Arista™ AH n/N (%)	Control n/N (%)
Hemostasis of First Treated Lesion	131/145 (90.3%)	115/143 (80.4%)
Surgical Application	**Arista™ AH n/N (%)**	**Control n/N (%)**
General (within 5 minutes)	68/72 (94.4%)	56/72 (77.8%)
Orthopedic (within 5 minutes)	33/35 (94.3%)	32/37 (86.5%)
Cardiac (within 3 minutes)	30/38 (78.9%)	27/34 (79.4%)

Secondary Endpoint

A secondary endpoint was time to hemostasis for the first treated lesion. The data for time to hemostasis are summarized below. The times to achieve complete hemostasis for the Arista™ AH and Control groups were statistically different using the chi square test ($p=0.003$).

CUMULATIVE PERCENT OF PATIENTS WITH COMPLETE HEMOSTASIS FIRST TREATED LESION

Time to Complete Hemostasis	Arista™ AH n/N (%)	Control n/N (%)
1 minute	73/145 (50.3%)	47/143 (32.9%)
2 minutes	96/145 (66.2%)	83/143 (58.0%)
3 minutes (Cardiac to 3 minutes only)	124/145 (85.5%)	103/143 (72.0%)
4 minutes	130/145 (89.6%)	111/143 (77.6%)
5 minutes	131/145 (90.3%)	115/143 (80.4%)

When data are stratified by surgical specialty, the median times to hemostasis were shorter for the Arista™ AH group than for the Control group. The median times are summarized in the table below. The median time to hemostasis for the Arista™ AH arm was statistically different from the Control arm using the non-parametric Wilcoxon sign-rank test ($p=0.002$). Note that one subject in the Arista™ AH arm had a time to complete hemostasis of 56.8 minutes and this value is considered an outlier.

COMPARISON OF TIME TO HEMOSTASIS – FIRST TREATED LESION

	Arista™ AH Median (n) (min, max)	Control Median (n) (min, max)
Median Time to Hemostasis (minutes)	1.0 (144) (1.0, 56.8)	2.0 (143) (1.0, 19.2)
General	2.0 (72) (1.0, 19.5)	2.0 (72) (1.0, 15.0)
Cardiac	2.0 (38) (1.0, 56.8)	3.5 (34) (1.0, 19.2)
Orthopedic	1.0 (34) (1.0, 6.2)	2.0 (37) (1.0, 7.0)

DIRECTIONS FOR USE

For open surgical procedures:

Inspect the integrity of the Arista™ AH packaging and applicator prior to use. If either is damaged, do not use.

Remove the applicator cap using a bending and twisting motion. For maximum benefit the following technique is recommended:

1. Blot, wipe, or suction the bleeding tissue. **It is important to remove excess blood so Arista™ AH may be applied immediately and directly to the site of active bleeding.**
2. Position the applicator tip as close to the source of bleeding as possible. Immediately apply a liberal amount of Arista™ AH at the site of bleeding within the wound, to completely cover the wound. Deep wounds may require equally deep application of Arista™ AH. To minimize occlusion of the tip, pressure should be applied to deliver Arista™ AH as the applicator enters the wound.
3. Quickly apply wound-appropriate, direct pressure over the treated site. Use of a non-adhering substrate to apply pressure may prevent adhesion of the formed clot to the surgical glove or other instrumentation. Amount and duration of pressure is wound dependent. For oozing, pressure may not be necessary. For more profusely bleeding wounds, pressure should be maintained longer.
4. If bleeding or oozing continues, remove excess Arista™ AH and reapply.
5. If any material other than the clot-bound Arista™ AH (i.e. surgical dressing) adheres to the wound site, irrigate the material with saline and carefully remove it from the treated site.
6. Immediately upon contact with blood or fluid, Arista™ AH will swell to approximately 5 times its original volume. Once hemostasis is achieved, excess Arista™ AH should be carefully removed by irrigation and aspiration. Avoid irrigation of direct suction of the formed blood clot.

When using Arista™ AH with extended applicators including endoscopic/laparoscopic applications, follow the instructions for use for the given applicator in order to appropriately apply Arista™ AH onto the wound site. The following applicators may be used with Arista™ AH:

Arista™ AH FlexiTip™ Applicator

Arista™ AH FlexiTip™ XL Applicator

Arista™ AH FlexiTip™ XL-R (rigid bodied) Applicator

For endoscopic / laparoscopic surgical procedures:

Follow all steps above for open surgical procedures. In addition to these steps:

- Setup the trocar prior to use. Carefully remove the FlexiTip™ XL-R Applicator from the trocar after use.
- Maintain direct visualization of the applicator tip at all times in order to minimize the potential for unintended contact with tissue, organs, or blood which may lead to occlusion of the tip.

If the FlexiTip™ XL-R Applicator becomes occluded during use, replace it with a new applicator.

ADMINISTRATION

Aseptic technique should always be used. A liberal amount of Arista™ AH should be applied to the bleeding site (see DIRECTIONS FOR USE) followed by pressure until hemostasis is achieved. After hemostasis is achieved, Arista™ AH should be removed by irrigation and/or aspiration. Opened containers of Arista™ AH should always be discarded.

Animal studies have indicated that Arista™ AH does not enhance infection of the wound site. Arista™ AH is rapidly degraded and cleared from the treatment site by endogenous alpha amylases. In an *in vivo* rat infection model, a specified amount of *E. coli* was inoculated into an induced abdominal wound followed by treatment with control (no hemostatic agent), positive control (absorbable gelatin sponge), and Arista™ AH. After 72 hours, animals were sacrificed and microbiology homogenate culture of the tissue removed found that there is no increase in the rate of *E. coli* infection in wounds treated with Arista™ AH [an average of 6.9×10^5 colony forming units (cfu) found after 72 hours] compared to the rate in wounds treated with no hemostatic agent (control) [average of 3×10^5 cfu after 72 hours] indicating that Arista™ AH is not a nidus for infection. The rate of infection in wounds treated with gelatin sponge [average of 2.4×10^7 cfu after 72 hours] was found to be significantly enhanced versus both the control and Arista™ AH.

When Arista™ AH is used in conjunction with autologous blood salvage circuits, a 40µ cardiotomy reservoir, cell washing, and 40µ transfusion filter, such as a LipiGuard™ or Pall filters, must be used.

HOW SUPPLIED

Arista™ AH is supplied in bellows applicators containing 1, 3, or 5 grams. In the Arista™ AH Trial, subjects in the Arista™ AH arm could have up to five (5) bleeding lesions treated with Arista™ AH. In the trial, surgeons used between approximately 1 to 9 g to treat these lesions. In the Arista™ AH Trial, the mean number of product applications onto the first treated lesion was 1.4 (range 1 to 5) and for control, the mean number of product applications was 1.4 (range 1 to 5).

STORAGE AND HANDLING

Arista™ AH should be stored to avoid temperature extremes (less than -40°C (-40°F) and greater than 60°C (140°F)). Once the applicator has been opened, contents are subject to contamination. It is recommended that Arista™ AH be used as soon as the applicator is opened and unused contents discarded.

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician or properly licensed practitioner.

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