FIBRIN SEALANT KIT I.P.

Fibroseal® 1.0 mL

DESCRIPTION

Fibroseal is a two-component Fibrin Sealant Kit essentially composed of purified Human Fibrinogen concentrate (Component 1) and purified Human Thrombin (Component 2). A fibrin clot is rapidly formed when the two reconstituted components are mixed simulating the final stage of the clotting cascade. No antimicrobial preservative is added.

The manufacturing process for Fibrinogen concentrate incorporates chromatography steps that removes Plasminogen from the preparation. **Fibroseal** is an Aprotinin-free Fibrin Sealant. By removal of Plasminogen, a product related impurity in Fibrinogen preparation of **Fibroseal**; the need for stabilization of the clot by Aprotinin is eliminated.

COMPOSITION

Fibroseal Kit Contains:

Component 1: 1 vial of lyophilized Human Fibrinogen Concentrate
1 mL of component 1 contains:
Fibrinogen Clottable protein: not less than 40 mg

Component 2: 1 vial of lyophilized Human Thrombin 500

1 mL of Thrombin 500 preparation contains: Thrombin 500 IU

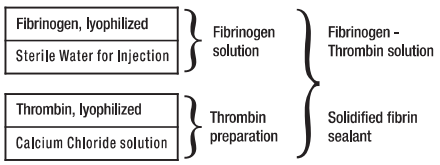
1 vial of 1 mL Calcium Chloride solution, 40 mmol/L

1 ampoule of 5 mL Sterile Water for Injection

Application device kit for reconstitution and application of two components.
1 Double syringe clip with plunger
2 Joining pieces
4x 2 mL Syringes
4 Needles (21G, 1.5 inch)
2 Blunt end needles (20G, 1 inch)

PROPERTIES AND EFFECT

Preparation of the two-component sealant using



Lyophilized Fibrinogen is reconstituted in 1.0 mL of Sterile Water for Injection to give the first component of the sealant. The lyophilized Thrombin is reconstituted in 1 mL of Calcium Chloride solution to give the second component. The two components are mixed during or immediately before application (refer Method of Application).

This results in a viscous Fibrinogen-Thrombin solution that quickly sets to form a white, elastic mass which firmly adheres to the tissue. This process simulates key features of the physiological coagulation process and is used to achieve hemostasis, to seal or glue tissue and to support wound healing.

In the course of wound healing the solidified fibrin sealant is completely absorbed.

VIRAL SAFETY

Human Fibrinogen and Human Thrombin are purified from a large pool of human plasma for fractionation using a series of chromatography based steps.

The pooled human plasma for fractionation conforms to the highest standards of quality as set forth by the regulatory authorities. In addition to serology based screening of plasma donor units and plasma pools for HBsAg, HCV, HIV 1&2 antibodies, minipools of plasma donor units and the manufacturing plasma pools are also tested negative for genomic materials of HIV 1&2, HCV and HBV using NAT approved by regulatory authorities.

The manufacturing process for Fibrinogen and Thrombin includes multiple dedicated orthogonal viral inactivation/removal steps ensuring viral safety of the product.
For Fibrinogen and Thrombin preparation, viral inactivation and removal is carried out by two orthogonal and dedicated steps in the purification process inclusive of solvent/detergent treatment.

INDICATIONS

Fibrin Sealant kit is used to achieve hemostasis, to seal or glue tissue and to support wound healing. In certain applications biocompatible material, such as collagen fleece, is used as a carrier substance or for reinforcement. Indications include any type of surgery in which hemostasis, sealing and gluing of tissue, or wound healing support is required. Examples of use are given below.

Hemostasis

Fibrin Sealant kit is used for hemostasis in diffuse bleedings, after joint and bone surgery, adenoidectomy and tonsillectomy as well as after maxillodental surgery in patients with bleeding disorders, sealing of the prostatic bed after prostatectomy.

Sealing

Coating and sealing of vascular prostheses, tympanoplasty, management of C.S.F. fistulae and dura lesions, treatment of premature rupture of the membranes in pregnancy by sealing of the lower amniotic region, air-tight sealing of sutures in lung parenchyma and pleura, of sutures in trachea, bronchus and oesophagus, management of malignant pleural effusion, sealing of the lens after injuries with perforations, sealing of suture lines to prevent leakage of intestinal anastomoses, additional sealing of sutured microvascular anastomoses etc.

Tissue gluing

Gluing of parenchyma in surgery on the kidney, liver, spleen and pancreas, spongiosa grafting when packing bone cavities and defects, pleurodesis in spontaneous pneumothorax, fixation of skin grafts and flaps, fixation of osteochondral fragments and implants, gluing of peripheral nerves, plastic surgery after opening of the maxillary sinus etc.

Support of Wound Healing

Skin grafting on devascularised and infected recipient sites, management of skin necrosis and mucosal ulcers, incorporation of homologous bone grafts.

DOSAGE AND CONCENTRATIONS, PREPARATION OF COMPONENTS, METHOD OF APPLICATION

1. Dosage and Concentrations

The required dose of Fibrinogen solution depends on the size of the surface to be sealed or coated or on the size of the defect to be packed. It is also dependent on the application methods chosen.

As a guideline for the gluing of surfaces, one (i.e. 1 mL Fibrinogen solution plus 1 mL Thrombin preparation) will be sufficient for an area of at least 10 cm^2.

When the sealant is applied by spray application the same quantity will be sufficient to coat an area of 25 cm^2 to 100 cm^3 depending on the specific indication and the individual case.

To avoid formation of excess granulation tissue and to ensure gradual absorption of the solidified Fibrin Sealant, only a thin layer of the

Fibrinogen-Thrombin solution should be applied. Gradual absorption of Fibrin Sealant is desirable as wound healing progresses.

The setting rate of the sealant depends on the concentration of the Thrombin solution used. The sealant takes few seconds to set with a Thrombin concentration of 500 IU/mL. The higher Thrombin. concentration is required in order to achieve hemostasis.

2. Preparation of Components

Prior to reconstitution of the sealant components, bring them to room temperature and disinfect the rubber stoppers of all vials to be used for preparation.

1. **Preparation of Fibrinogen solution (Component 1)**

   Lyophilized Fibrinogen Concentrate should be reconstituted with 1.0 mL of Sterile Water for Injection

   Always check that the lyophilized Fibrinogen Concentrate is fully reconstituted.

   Reconstitution is complete as soon as no undissolved particles are detectable when holding the vial against the light.

   Draw up the reconstituted Fibrinogen solution in a fresh sterile syringe using aseptic precautions.

II. **Preparation of Thrombin Solution (Component 2)**

   Transfer 1 mL of Calcium Chloride solution into the vial containing lyophilized Thrombin 500 IU (quick solidification).

   For preparing the Thrombin solution, use a fresh sterile syringe provided in the pack.

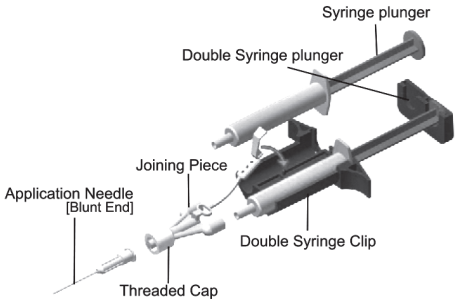
Note:

Do not expose to temperatures above 37°C.

Syringes and needles previously used for the reconstitution of Thrombin must not be reused for reconstitution of Fibrinogen Concentrate, as this would lead to premature setting of the Fibrin Sealant.

3. Method of Application

- Place the Syringes filled with Fibrinogen and Thrombin solutio ns into the double syringe clip. Both syringes should be filled with equal volumes and should not contain any air bubbles.
- Connect the nozzles of the two syringes to the joining piece ensuring that it is firmly fixed. Secure the joining piece by fastening the strap of the clip.
- Fit the application needle (Blunt end needle) onto the joining piece.
- **Do not expel any air remaining inside the joining piece or application needle as the aperture of the needle may clog before application of the sealant.**
- To ensure adequate mixing of the Fibrinogen protein component and the Thrombin component, the first few drops of the product from the application cannula should be expelled and discarded immediately before use.
- Apply sealant onto the recipient surface or surfaces of the parts to be sealed.



CONTRAINDICATIONS

Do not inject intravascularly.

Fibrin Sealant Kit is contraindicated in patients having known hypersensitivity to any constituent of the product.

Fibrin Sealant Kit alone is not indicated for the treatment of massive and brisk arterial or venous bleeding.

INTERACTIONS

Interactions are not known. The product may be denatured after exposure to solutions containing alcohol, iodine or heavy metals (e.g. antiseptic solutions). Such substances should be removed to the greatest possible extent before applying the product. Fibrin Sealant can even be applied in fully heparinized patients (e.g. extracorporeal circulation).

SPECIAL WARNINGS

When medicinal products prepared from human blood or plasma are administered, infectious diseases due to transmission of infective agents cannot be totally excluded.

For epilesional use only.

Fibrinogen Concentrate and/or Thrombin solution/s should not be injected. There is the risk of a possible anaphylactic reaction, and in intravascular administration there is also a risk of a thromboembolic event, both of which may be life-threatening. However, if in well-founded cases, the injection of Fibrinogen Concentrate and/or Thrombin solution/s into a tissue or vessel is indicated, careful risk/benefit analysis of the individual case is to be carried out. In the submucous injection of fibrin sealant into hollow ogans (stomach, duodenum), the following points are to be considered:

1. Insertion of the needle into the organ wall may result in accidental perforation, which in rare cases may injure adjoining organs or vessels.
2. No case of thromboembolic events following accidental vessel puncture and intra vascular injection of fibrin sealant has so far been observed in the treatment of ventricular or duodenal ulcers, but cannot be excluded with certainty.
3. Injection into the submucous membrane may cause a mechanical dissection between the tunica mucosa and the tunica muscularis propria, which in rare cases may lead to vessel injury or the formation of an intramural hematoma.

Fibrin Sealant must be applied with caution to minimize any risk of intravascular application, for example in coronary bypass surgery. Injection into the nasal mucosa must be avoided, as severe allergic-anaphylactoid reactions have been seen and thromboembolic events may occur.

Intravascular application might increase the likelihood and severity of acute hypersensitivity reactions in susceptible patients. 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.

PREGNANCY AND LACTATION

There are no adequate data from the use of Fibrin Sealant in pregnant or lactating women. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing Fibrin Sealant Kit.

STORAGE AND HANDLING

Store between 2°C and 8°C. Do not use after the expiry date indicated on the container and package labels.

Reconstituted Fibrinogen and Thrombin solutions must be used within 4 hours.

Do not refrigerate or freeze after reconstitution.

Store protected from light and moisture.

Keep out of reach of children.

Manufactured and Marketed by :

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