

**Synthetic hemostatic agents (Acceptable alternatives for Jehovah's Witnesses and those patients desiring not to receive whole blood or blood components)**

1. Desmopressin (DDAVP) and Vasopressin
  - These agents are synthetic forms of a naturally occurring hormone of the pituitary that promote clotting by increased plasma levels of factor VIII, von Willebrand and vascular constriction
  - They are used to treat acute bleeding and maintain hemostasis
  - Desmopressin can also be used to treat patients with mild Type 1 von Willebrand's disease and patients with mild/moderate Hemophilia A
  
2. Vitamin K (Phytonadione)
  - It is a synthetic form of vitamin K that is naturally produced by the body and is necessary for clotting due to Factor II, VII, IX, and X.
  - It is used to treat bleeding or coagulation disorders due vitamin K dependent clotting factors and reversal of over anticoagulation due to Warfarin
  
3. Helixate\*\*, Kogenate\*\*, Xyntha\*\*, and Advate\*\*
  - These agents are recombinant human factor VIII products and work by temporarily replacing the missing clotting factor VIII that is needed for effective hemostasis.
  - They are used to prevent and treat bleeding in patients with hemophilia A, perioperative management with patients with hemophilia A and routine prophylaxis to reduce the frequency of bleeding episodes in hemophilia A
  - These agents are made by cloning the gene for Factor VIII in culture media and then purifying by chromatographic process. Kogenate and Helixate are made in a culture media that contains human plasma protein solution (HPPS). No human or animal proteins are added during the purification process. Xyntha and Advate do not contain any material derived from human or animal sources.
  
4. BeneFix\*\*
  - BeneFix is recombinant human Factor IX that promotes hemostasis by temporarily replacing missing clotting factor IX.
  - It is used to treat and prevent bleeding in patients with Hemophilia B
  - It is made by cloning the gene for Factor IX in culture media and then purifying by chromatographic process. No human protein or serum is used in its production.
  
5. NovoSeven\*\*

- NovoSeven is recombinant human Factor VII and promotes hemostasis by activating the extrinsic pathway of the coagulation cascade
  - It is used to treat bleeding and/or prevent bleeding in surgery for patients with hemophilia A or B with inhibitors or congenital Factor VII deficiency
  - It is made by cloning the gene for Factor VII in culture media and then purifying by chromatographic process. No human protein or serum is used in its production
6.  $\epsilon$ -aminocaproic acid (Amicar) and Tranexamic acid (cylokapron)
- These agents are synthetic forms of a naturally occurring protein in the body that prevents fibrinolysis by inhibition of plasminogen activators
  - It is used to treat bleeding due to fibrinolysis

7. Topical hemostatic agents (Recothrom, Avitene, and Ferric subsulfate)
- (1) Recothrom is a topical thrombin that is used to aid in hemostasis by activation of platelets and conversion of fibrinogen to fibrin for oozing and minor bleeding when conventional surgical techniques (suture, ligature, and cautery) are ineffective or impractical.

Recothrom is available sterile recombinant topical thrombin lyophilized powder. When reconstituted as directed, the final solution contains 1000 units/mL of Recothrom. It can be topically applied onto the bleeding site directly using a spray applicator or may be used in conjunction with an absorbable gelatin sponge. Recothrom may cause thrombosis, so it should not be injected directly into the circulatory system and it is not used for the treatment of massive or brisk arterial bleeding.

It is not known whether Recothrom can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Recothrom should be given to a pregnant woman only if clearly needed. Safety and efficacy have also not been established in neonates.

Antibody formation to Recothrom occurred in <1% of patients. Hypersensitivity reactions, including anaphylaxis, may occur. Do not administer to patients with a history of hypersensitivity to Recothrom, any components of Recothrom or hamster proteins.

Recothrom is made by recombinant DNA technology in culture media and purified by chromatographic process. No human or animal materials are used in its production.

(2).Avitene is an active absorbable collagen hemostat that accelerates clot formation by enhancing platelet aggregation and release of proteins to form fibrin resulting in hemostasis.

Avitene is available in several forms. Avitene™ Microfibrillar Collagen Hemostat (MCH) can adhere to irregular spaces; Avitene™ Sheets (non-woven web) is ideal for use on flat surfaces or to wrap vessels and

anastomosis sites; and Avitene sponge (Ultrafoam) is used during surgical procedures. EndoAvitene and SyringeAvitene applicators are able to deliver Avitene to endoscopic or other active bleeding sites, respectively.

This line of products can be used for all surgical procedures but may create a dark gelatinous mass that may obscure the visual field during surgery.

Exposure Avitene to respiratory airway and eyes may produce bronchial and conjunctival irritation, respectively.

Avitene is derived from bovine collagen.

(3). Ferric subsulfate is an aqueous iron solution used for local hemostasis of superficial wounds or biopsies.

Ferric subsulfate should not be used in vesicular, bullous, or exudative (oozing) dermatoses because it may then cause permanent pigmentation on the skin.

Ferric subsulfate is for external use only and may be harmful if swallowed.

Ferric subsulfate is made from ferrous sulfate, sulfuric acid and nitric acid.

### **Plasma-derived hemostatic agents (Personal decision for Jehovah's Witnesses)**

#### **1. Humate-P\*\***

- Humate P is a factor VIII and von Willebrand factor concentrate product made from the purified cold insoluble fraction of pooled human fresh frozen plasma
- It is used to treat and prevent bleeding in patients with a history of hemophilia A; and treatment of trauma induced bleeding and perioperative bleeding in patients with von Willebrand disease

#### **2. Hemofil-M\*\* and Koate-DVI\*\***

- Hemofil-M and Koate-DVI are Factor VIII concentrates used to prevent and treat bleeding due to deficiency of the plasma clotting factor VIII such as patients with hemophilia A
- Hemofil-M is a monoclonal purified sterile nonpyrogenic Factor VIII concentrate made from pooled human plasma by immunoaffinity chromatography with a murine monoclonal antibody to Factor VIII followed by ion exchange chromatography for further purification
- Koate-DVI is a sterile purified Factor VIII concentrate prepared from the cold insoluble fraction of pooled human fresh frozen plasma

#### **3. Mononine\*\***

- Mononine is a Factor IX concentrate used to prevent and treat bleeding due to deficiency of the plasma clotting factor IX such as patients with hemophilia B

- Mononine is made from pooled human plasma and purified by immunoaffinity chromatography with a murine monoclonal antibody specific for Factor IX

#### 4. FEIBA\*\*

- FEIBA is a sterile human plasma fraction with Factor VIII inhibitor bypassing activity and contains factors II, VII, IX, and X
- It is made from pools of human plasma
- FEIBA is used to prevent and treat bleeding in patients with hemophilia A or B with inhibitors to factor VIII and IX

#### 5. Bebulin VH\*\* (3 factor PCC) and Kcentra (4 factor PCC)\*\*

- Kcentra is a prothrombin complex concentrate used to treat bleeding in patients with acquired coagulation factor deficiency induce by warfarin
- Bebulin is used to prevent and treat bleeding in patients with hemophilia B, congenital Factor IX deficiency or Christmas disease
- Kcentra contains factors II, VII, IX, and X and Protein C and S and Bebulin contains factors II, IX, and X
- Both Bebulin and Kcentra are made from pooled human plasma

#### 6. Riastap\*\*

- Riastap is a human fibrinogen concentrate made from pooled human plasma and used to replace low or missing fibrinogen protein
- Riastap is used to treat acute bleeding in patients with congenital fibrinogen deficiency

#### 7. Topical hemostatic agents (Tisseel)

- Tisseel is a fibrin sealant used as an adjunct to hemostasis in patients undergoing surgery when conventional surgical techniques (suture, ligature, and cautery) are ineffective or impractical
- Tisseel is made from human plasma

#### 8. Albumin

- Albumin is derived from human plasma with the function of regulating the colloidal osmotic pressure of blood
- Albumin may help to maintain blood pressure when other colloids, such as plasma can't be used

#### 9. Epoetin alfa (Epogen/Procrit)

- Epoetin alfa is human erythropoietin produced in mammalian cell culture using recombinant DNA technology and contains human albumin

- It is generally used in treating anemia resulting from chronic kidney disease and myelodysplasia, from the treatment of cancer (chemotherapy and radiation)

#### 10. Cryoprecipitate

- Cryoprecipitate is separated from human plasma and rich in several clotting factors, such as fibrinogen, factor VIII, XIII and von Willebrand factor
- It requires blood product transfusion consent prior to use

### **Others (Products may be utilized in the management of Jehovah's Witnesses with complicated bleeding and thrombosis conditions)**

#### 1. ATryn

- ATryn is a lyophilized recombinant antithrombin III concentrate. It is administered by dissolving the powder into solution for IV injection. ATryn is produced in the goat cells, therefore it is contraindicated in patients with known hypersensitivity to goat and goat milk proteins.
- Atryn is used in the prevention of perioperative and peripartum thromboembolic events in hereditary antithrombin deficient patients.

#### 2. Thrombate III

- Thrombate III is a lyophilized antithrombin III concentrate purified from human plasma. It is administered by dissolving the powder into solution for IV injection. It may contain infectious agents, such as viruses, potentially transmitting disease.
- Thrombate III is for the treatment of patients with hereditary antithrombin III deficiency in connection with surgical or obstetrical procedures or when they suffer from thromboembolism.

Asterisk (\*\*) denotes agents on the list requiring approval prior to dispensing by Miguel Escobar, M.D