

**BloodCenter of Wisconsin**

**2011 ADULT BLOOD UTILIZATION  
REVIEW GUIDELINES**

## **Introduction:**

This document is a revision of the 2007 Blood Utilization Guidelines. The purpose of these guidelines is twofold. The first is to provide practitioners and caregivers with an overview of evidence-based, suggested best practice for the appropriate utilization of blood and blood components to promote optimal transfusion therapy. Secondly, these guidelines also provide up to date references to support these practices. Selected references are listed under each blood component. The physicians and staff of the BloodCenter's Medical Science Institute have compiled these guidelines after review of the cited references. Further review and final approval was then completed by the Medical Advisory Committee.

These guidelines should be reviewed by each institution's medical staff in collaboration with the Transfusion Service Medical Director and modifications made that reflect the culture of the organization. After review and acceptance by the institution's Medical Executive Committee, the guidelines should be shared with all physicians and other practitioners who order blood and blood components. These guidelines may be used to establish audit criteria for blood ordering practice by hospital transfusion committee or quality improvement committee.

These guidelines are recommendations only. The decision to transfuse or not to transfuse should be made by the patient's physician only after a careful assessment of the patient's clinical condition and laboratory parameters. Documentation for transfusion of all blood and blood components should include the indication(s) for the transfusion; this is especially important if the circumstances/indication for the transfusion falls outside established guidelines for the institution.

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## RED BLOOD CELLS

**How Supplied:** All Red Blood Cell products supplied by BloodCenter of Wisconsin are leukocyte-reduced and 1 unit is approximately 300-350 mL.

### Utilization Review Guidelines:

Red cell transfusion may be appropriate to improve oxygen carrying capacity. Documentation of the indication(s) for transfusion and special circumstances for transfusion that take place outside these guidelines is recommended.

### Indications:

1. Acute Blood Loss: maintain circulating blood volume and hemoglobin concentration  $\geq 7$  g/dL in otherwise healthy patients;  $>8$ g/dL in elderly patients and those with known cardiac or respiratory disease.
  - 15-30% loss of blood volume: RBC transfusion likely not required
  - 30-40% loss of blood volume: RBC transfusion probably required
  - $>40\%$  loss of blood volume: RBC transfusion almost certainly required
2. Stable hospitalized patients including those in the critical care unit: hemoglobin  $\leq 7$ g/dL.
  - Patients with co-morbid conditions such as coronary artery disease, pulmonary disease, or evidence of acute MI have less tolerance for anemia
3. Peri-operative transfusions:
  - Hemoglobin concentration  $<7$  g/dL: RBC transfusion usually required
  - Hemoglobin concentration 7-10 g/dL: RBC transfusion may be appropriate if any of the following are present: organ ischemia, increased potential for or ongoing blood loss, volume status and risk factors for complications of inadequate oxygenation
  - Hemoglobin concentration  $>10$ g/dL: RBC transfusion usually unnecessary
4. Symptomatic anemia in a normovolemic patient (generally symptoms from anemia do not occur when Hgb  $\geq 10$ g/dL)
5. Outpatients with bone marrow failure may be prophylactically transfused to maintain Hgb  $>7$ g/dl

### Outcome Indicators:

- Improvement in clinical status of patient (relief of symptoms of decreased oxygen carrying capacity)
- Improvement in Hgb/Hct (one unit of red cells should raise the Hgb on average 1g/dL or Hct 3% in an adult). One hour post-transfusion Hgb is equivalent to one drawn within 24 hours of transfusion if there is no ongoing blood loss in a normovolemic patient.

### Comments:

- Transfusion of a **single** unit may be sufficient; transfusion of additional units should be based on **clinical assessment of patient**. Avoid transfusions based solely on Hgb or Hct value.
- Transfusions should be performed only after appropriate alternative therapies have been considered (e.g. iron, vitamin B12, folate and erythropoietin)

- Certain patient populations (e.g. patient with hemoglobinopathies) may tolerate lower hemoglobin thresholds and transfusions in such patients should not be based solely on hemoglobin values.

#### **WHOLE BLOOD:**

- **How supplied:** 1 unit contains approximately 550 ml; all whole blood units are leukocyte-reduced except autologous units. *Availability of whole blood is limited in this community.*
- **Indications:** For patients who require oxygen carrying capacity and volume replacement.

#### **References:**

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Nuttall GA et al. Practice Guidelines for Perioperative Blood Transfusion & Adjuvant Therapies: An Updated Report by the American Society of Anesthesiologists Task Force. *Anesthesiology* July 2006; 105(1):198-208.

Rao SV et al. Relationship of Blood Transfusion and Clinical Outcomes in Patients with Acute Coronary Disease. *JAMA* 2004; 292:1555-1562.

Vincent JL et al. Anemia and Blood Transfusion in Critically Ill Patients. *JAMA* 2002; 288(12): 1499-1507.

Wu Wen-Chih, Rathore S. et al. Blood Transfusion in Elderly Patients with Acute Myocardial Infarction. *N Engl J Med* 2001; 345:1230-1236.

### **AUTOLOGOUS AND DIRECTED UNITS - GENERAL COMMENTS:**

#### *Autologous Blood Usage:*

Preoperative autologous blood donation no longer represents a uniform standard of care. This practice, in general, is not cost-effective as the cost for transfused units is not fully reimbursed and is totally lost if the unit is not transfused. In the current era of improved viral testing for infectious diseases, the risk of transfusion-associated HIV and Hepatitis C is now approximately 1 in 2 million units transfused.

Despite the perceived safety of preoperative autologous blood collection and transfusion, there is the potential for transfusion errors and adverse reactions. Errors related to production and handling of autologous units are common (1 in 149 to 1 in 322 units collected) with one quarter of the errors related to autologous units not being available at the start of surgery. Other errors include the patient receiving allogeneic blood when their autologous blood is available or has expired – estimated error rate of 1 in 1500 to 5300. Any benefit from the autologous collection is then lost. Though adverse reactions to autologous blood are minor (febrile and allergic symptoms) the frequency is similar to allogeneic blood transfusions. Other risks associated with autologous blood transfusions

may include transfusion-associated bacterial contamination and incompatible transfusion due to mis-identification at time of sample collection or administration.

Use of preoperative autologous blood donation should be considered for patients with multiple RBC alloantibodies, for whom provision of appropriate antigen negative, crossmatch-compatible RBC units is limited.

**Autologous blood transfusion is not without risk and the criteria for transfusion of such products should be the same as that for allogeneic blood.**

*Comments:*

- In SE Wisconsin, 40-50% of preoperative autologous blood donation units collected are discarded. Autologous units cannot be transfused to anyone other than the person who donated the unit as the criteria for donation of autologous blood is not the same as that for allogeneic, volunteer donors.
- Preoperative autologous units are not leukoreduced
- Strong consideration should be given to the use of perioperative blood recovery and/or acute normovolemic hemodilution in place of preoperative autologous blood donation
- Preoperative donation is not recommended for procedures that generally do not require transfusion
- Iron replacement therapy should be considered to prevent pre-operative anemia that may develop as a result of donation if preoperative autologous blood collection is ordered
- Patient selection for autologous donation is determined by the patient's physician
- See [www.bcw.edu](http://www.bcw.edu) for additional information about autologous blood donation. Note that pre-surgical autologous donations must be made 7 or more days prior to date of surgery.

*Directed Donations:*

In general, blood that comes from directed donations offers no medical advantage over blood from the general volunteer inventory. The donor of a directed donation must qualify for donation using the same criteria as volunteer donors.

Also, the following general rules should be considered:

- Transfusion from a woman to her biologic children or the father of her biologic children should be avoided
- A woman should not receive a transfusion from a man or his blood relatives if she has had or is planning to have his children

**References:**

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Domen RE. Adverse reactions associated with autologous blood transfusion: evaluation and incidence at a large academic hospital. *Transfusion* 1998; 38:301-306.

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Guidelines for Autologous Blood Collection 2002. The Australian Society for Blood Transfusion Inc. April 2002; 9(2).

# PLATELETS

**How Supplied:** Only leukocyte-reduced single donor apheresis platelets are supplied by BloodCenter of Wisconsin.

## **Utilization Review Guidelines:**

Platelets are administered for the prevention and treatment of bleeding in patients with thrombocytopenia or platelet function defects. Documentation of the indication(s) for a transfusion episode and special circumstances for transfusion that take place outside these guidelines is recommended.

## **Indications:**

1. Active bleeding and platelet count  $<50,000/\mu\text{l}$  or platelet function defect
2. Prophylaxis treatment in hematology/oncology patients:
  - Platelet count  $<10,000/\mu\text{l}$  in stable patient
  - Platelet count  $<20,000/\mu\text{l}$  **and** presence of risk factor for bleeding (h/o bleeding, infection, Disseminated intravascular coagulopathy)
3. Surgical/invasive procedures:
  - Platelet count  $<50,000/\mu\text{l}$  for procedures with minimal bleeding risk
  - Platelet count  $<100,000/\mu\text{l}$  for CNS, eye, airway or other areas where microvascular bleeding is especially risky
  - Documented platelet function defect
  - Open heart surgery and:
    - a. microvascular bleeding **and** platelet count  $<100,000/\mu\text{l}$
    - b. microvascular bleeding **and** platelet function defect
    - c. microvascular bleeding **and** coagulation abnormality of unknown etiology (e.g. post-op chest tube drainage  $>500\text{ml}$  in 6 hours)
4. In the setting of massive blood transfusion early platelet support may be necessary to prevent or treat dilutional thrombocytopenia. Laboratory monitoring of coagulation studies is recommended.

## **Outcome Indicators:**

- Cessation or reduction of bleeding
- Rise in platelet count by 20,000-50,000/ $\mu\text{l}$  in a 70 kg recipient after transfusion of a single apheresis platelet unit

## **Comments:**

- Platelet function defect should be documented by abnormal laboratory assessment of platelet function; or presumed due to medications that inhibit platelet function, hypothermia, or mechanical devices that affect platelet function.
- Recommendations for stopping medication prior to invasive procedures vary with the medication and clinical situation. Platelet function tests may help assess the level of platelet inhibition and timing of surgical procedure. Platelet replacement of 1-2 units is usually adequate to control bleeding.
- Consider the administration of DDAVP, epsilon aminocaproic acid (Amicar) and tranexamic acid in addition to administration of platelets to control bleeding.

- Platelet transfusion is generally ineffective in thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, heparin-induced thrombocytopenia, and immune thrombocytopenia.
- Prophylactic platelet transfusions are generally not indicated for patients with chronic, stable, severe thrombocytopenia as in aplastic anemia or myelodysplasia. Platelet transfusions for bleeding episodes are more appropriate.

### References:

Circular of Information for the Use of Human Blood and Blood Components. AABB August 2009, revised December 2009.

Ferraris VA et al. Society of Thoracic Surgeons Blood Conservation Guideline Task Force. Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery. *Annals of Thoracic Surgery* 2011; 91(3): 944-982.

Slichter SJ et al. Dose of Prophylactic Platelet Transfusions and Prevention of Hemorrhage. *N Engl J Med* 2010; 362(7): 600-613.

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Vilahur G, Choi BG, Zafar Mu, et al. Normalization of Platelet Reactivity in Clogidogrel-Treated Subjects. *J Thrombosis and Hemostasis* 2007; 5(1):82-90.

# GRANULOCYTES

**How Supplied:** All requests for granulocytes are referred to a BloodCenter of Wisconsin physician for consultation with the ordering physician. Granulocytes are collected from G-CSF-stimulated donors with a typical course consisting of 5 daily collections. Each unit collected contains on average  $3-4 \times 10^{10}$  granulocytes.

## Utilization Review Guidelines:

Granulocytes can be administered for the treatment of severe neutropenia with the indications below. Documentation of the indication(s) for a transfusion episode and special circumstances for transfusion that take place outside these guidelines is recommended

## Indications:

- Severe neutropenia (absolute neutrophil count  $<500/\mu\text{l}$ ) with reversible marrow hypoplasia and documented bacterial or fungal infection unresponsive to 48 hours of appropriate antibiotic therapy
- Patients with severe neutrophil dysfunction and bacterial or fungal infection

## Outcome Indicators:

- Clinical resolution of infection
- Neutrophil count  $>500/\mu\text{l}$

## Comments:

- **Granulocytes must be irradiated before use**
- Granulocytes have a 24 hour shelf life but have best efficacy when transfused as soon as possible after collection
- Generally not for use in patients in whom marrow recovery is not anticipated
- Bedside leukoreduction filter should *not* be used in administration

## References:

Circular of Information for the Use of Human Blood and Blood Components. AABB August 2009, revised December 2009.

Joint UKBTS/NIBSC Professional Advisory Committee: Position Statement: Granulocyte Therapy; November 13, 2008 reconfirmed November 2009 by S. Stanworth, R. Cardigan & E. Massey.

Massey E et al. Granulocyte transfusions for preventing infections in patients with neutropenia or neutrophil dysfunction. *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD005341.

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Stanworth S et al. Granulocyte transfusions for treating infections in patients with neutropenia or neutrophil dysfunction. *Cochrane Database of Systemic Reviews* 2005, Issue 3. Art. No.:CD005339. (last assessed 6/30/2010)

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Einsele H, Northoff H, Neumeister B. Granulocyte Transfusion. *Vox Sang* 2004; 87(Suppl 2): 5205-5208.

Schiffer C. Granulocyte Transfusion Therapy 2006: The Comeback Kid. *Medical Mycology* 2006; 44: 5393-5386.

# PLASMA

## How Supplied:

### *Fresh Frozen Plasma/FP24*

- Plasma prepared from either a whole blood or apheresis collection and frozen either within 8 hours or 24 hours of collection
- Can be used interchangeably
- Contains similar levels of clotting factors
- Volume per unit is 250 – 330mL

### *Thawed plasma*

- Unit of FFP or FP24 that was thawed and stored at 1-6 °C for 1-5 days
- Use is determined by individual institutional policy
- Considered therapeutically equivalent to FFP/FP24.

### *Cryo-poor plasma*

- Prepared from FFP after cryoprecipitate is removed
- Contains limited or no factor VIII and XIII, vWF, fibrinogen, or fibronectin
- Used **solely** in the treatment of thrombotic thrombocytopenic purpura

## Utilization Review Guidelines:

Plasma transfusion therapy is indicated for treatment of documented coagulopathy, where the mechanism for coagulation defect is known, understood and attributable to coagulation factor deficiency and it is expected that replacement with plasma transfusion is the most efficient way to correct that deficiency. The PT and PTT are indicative of the severity of coagulation defect. Documentation of the indication(s) for a transfusion episode and special circumstances for transfusion that take place outside these guidelines is recommended.

## Indications:

1. Active bleeding and documented coagulopathy (INR >1.7 or PT and/or PTT greater than 1.5 times upper limit of normal range)  
Common settings include:
  - Liver disease with coagulopathy
  - Emergent reversal of warfarin effect
    - a. Co-administration of vitamin K should be considered
    - b. *If available, consider use of Prothrombin complex concentrates (PCC) for life-threatening bleed e.g. intracranial hemorrhage*
  - Disseminated Intravascular Coagulopathy (DIC)
    - a. Evaluate for hypofibrinogenemia; consider administration of cryoprecipitate
  - Dilutional coagulopathy/surgical bleeding
    - a. Best guided by timely coagulation testing
    - b. With massive transfusions in trauma patients, earlier use of plasma (FFP:RBC ratio 1:1 – 1:3) has been recommended in some guidelines
  - Replacement of single factor deficiencies for which no single factor concentrate product is available (e.g. factor XI, V deficiency)
2. Prophylaxis in patients undergoing surgery or invasive procedure and documented coagulopathy (INR>1.7; PT or PTT greater than 1.5 times upper limit of normal range).  
For non-urgent surgical procedures, Vitamin K should be used to reverse Warfarin effect

3. Replacement fluid in therapeutic plasma exchange when bleeding or additional bleeding risks are present.
4. Treatment of thrombotic thrombocytopenic purpura
  - FFP/FP24, Thawed plasma and cryo-poor plasma are all acceptable products

**Dosing:** 10-15ml/kg of body weight (3-4 units result in total volume to be infused of 800-1000ml)

A dose of 10 ml/kg will typically provide sufficient coagulation factors to achieve hemostasis. Factor levels in donor plasma are variable, but can be assumed to be approximately 1 U/ml. Post-transfusion recovery of transfused factors may be less than expected due to extravascular distribution or consumption.

**Outcome Indicators:**

- Improvement of INR, PT, PTT or specific coagulation factor assay
- Prevention and/or cessation of bleeding

**Comments:**

- Transfusion of a single unit of plasma for an average sized adult is considered under-dosing and is inadequate for the replacement of coagulation factors. Plasma should be administered in doses to achieve a minimum of 30% of plasma factor concentration which is usually achieved with administration of 10-15 ml/kg.
- If INR is between 1.4-1.7, treat underlying condition and provide supportive care including use of Vitamin K. Plasma is generally not required or effective.
- Plasma therapy will generally not bring INR value into a normal reference range.
- Vitamin K is the product of choice for warfarin reversal in non-bleeding patient; effects can be seen in 6-12 hours and preferred routes are oral or IV.
- In liver disease with prolonged PT/INR, plasma products may prevent bleeding but complete correction of INR is unlikely.
- Plasma products are contraindicated for volume expansion, nutritional supplementation and continued use in surgery without documented clotting deficiency, except in the setting of massive bleeding.
- Plasma products should not be used to reverse Heparin or Low Molecular Weight Heparin (LMWH).
- Isolated prolonged PTT is not an indication for plasma transfusion unless there is a known coagulation protein deficiency (such as factor XI deficiency). The most common causes of an isolated prolonged PTT include: heparin, lupus anticoagulants, factor VIII and IX deficiencies, and factor XII deficiency. In these clinical settings, plasma transfusion is not indicated.

**References:**

Circular of Information for the Use of Human Blood and Blood Components. AABB August 2009, revised December 2009.

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Roussiant R et al. Management of Bleeding Following Major Trauma: An Updated European Guidelines. *Crit Care* 2010; 14(2):R52-81

Segal, J. B. and Dzik, W. H. Paucity of Studies to Support that Abnormal Coagulation Test Results Predict Bleeding in the Setting of Invasive Procedures: an Evidenced-based Review. *Transfusion* 2005; 45:1413-1425.

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Wong MP et al. Guidelines for frozen plasma transfusion. *BC Med Journal* 2007; 49 (6): 311-319.

# CRYOPRECIPITATED AHF

**How Supplied:** Cryoprecipitate is distributed as a pool of 5 units or as single units.

## Utilization Review Guidelines:

Cryoprecipitated AHF contains factor VIII, von Willebrand factor, fibrinogen and factor XIII. Documentation of the indication(s) for a transfusion episode and special circumstances for transfusion that take place outside these guidelines is recommended.

## Indications:

1. Fibrinogen <100mg/dL, **with** bleeding or need for intervention
  - Common settings include:
    - a. Disseminated intravascular coagulopathy (DIC)
    - b. Liver disease
    - c. Massive transfusion
2. Liver disease with dysfibrinogenemia
3. Factor XIII deficiency

**Dosing:** 1 unit per 7-10 kg of body weight (generally 10 units in an adult)

## Outcome Indicators:

- Fibrinogen level >100 mg/dL
- Cessation of bleeding

## Comments:

- Not indicated in the absence of bleeding
- Use in hemophilia A or von Willebrand Disease (vWD) is NOT standard of care
- Fibrinogen threshold of 100 mg/dl is generally used, however, this value has not been rigorously defined in clinical trials
- In DIC, FFP and platelets, in addition to cryoprecipitate should be considered
- Use may be considered for control of uremic bleeding after other modalities have failed, but there is limited data to support routine use
- ABO-compatible cryoprecipitate is not required due to the small volume of plasma transfused. Rh compatibility need not be considered for transfusion
- In patients with congenital fibrinogen deficiency (afibrinogenemia, hypofibrinogenemia) with acute bleeding or surgery, consider fibrinogen concentrate ( RiaSTAP<sup>®</sup>) instead of cryoprecipitate

## References:

Callum, Jeannie L, Karkouti K & Lin Y. Cryoprecipitate: The Current State of Knowledge. *Transfusion Med Rev* July 2009; 23(3): 177-188.

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## **INDICATIONS FOR SPECIAL MODIFICATION OF BLOOD PRODUCTS**

### **LEUKOCYTE-REDUCED BLOOD PRODUCTS (Red Blood Cells, Platelets):**

#### **Indications:**

- Prevention of febrile non-hemolytic transfusion reactions
- Prevention of HLA alloimmunization to HLA antigens
- Prevention of cytomegalovirus infections in patients at risk for CMV transfusion-transmitted infection (leukocyte-reduced products are considered CMV-safe)

#### **Comments:**

- All blood products supplied by BloodCenter of Wisconsin are leukocyte-reduced except autologous whole blood/red cells.
- Guidelines from AABB require that a leukocyte-reduced blood product contain fewer than  $5 \times 10^6$  leukocytes to prevent non-hemolytic febrile transfusion reactions, and for other indications. At BloodCenter of Wisconsin, both leukocyte-reduced red cells and leukocyte-reduced platelets generally contain  $<1 \times 10^6$  leukocytes.
- There is insufficient evidence of the role of leukocyte reduction in the prevention of transfusion-related immune modulation.

### **WASHED Red Blood Cells or Platelets:**

#### **Indications:**

- History of anaphylactic reaction to blood components
- IgA deficiency with documented IgA antibody
- Recurrent severe or allergic reactions not prevented with appropriate premedication
- Severe hyperkalemia (e.g. neonates)

### **CYTOMEGALOVIRUS SERONEGATIVE (CMV NEGATIVE) CELLULAR PRODUCTS (Red Blood Cells, Platelets)**

#### **Indications:**

- Newborns weighing  $<1500$  grams
- Any intrauterine transfusion
- Allogeneic peripheral stem cell or bone marrow transplant patients or candidates who are CMV seronegative or of unknown CMV serostatus
- CMV seronegative bone marrow transplant donors who require homologous products
- Known or suspected congenital immunodeficiency due to T-cell defects (DiGeorge syndrome, etc.) or other severe immune deficiencies who are CMV seronegative

**Potential Indications upon Physician Request:**

- Pregnant women
- CMV-seronegative patients with HIV
- Heart and lung transplant patients who are CMV seronegative
- CMV-seronegative autologous stem cell transplant patients
- Any patient for whom the physician, in consultation with the Transfusion Service physician, determines may be at risk for serious post-transfusion CMV infection

**Comments:**

- Leukocyte-reduced blood products are considered a safe alternative for CMV seronegative patients if CMV seronegative products are unavailable.
- Some institutions or physicians may choose to use leukoreduction as the sole means of prevention of transfusion-transmitted CMV disease
- CMV seronegative products are not required for patients who are CMV seropositive
- CMV serostatus does not need to be considered for fresh frozen plasma or cryoprecipitated AHF because these products are relatively acellular.

**IRRADIATED BLOOD PRODUCTS**

**Purpose:** Prevention of transfusion-associated graft vs. host disease (TA-GVHD)

**Indications:**

- Intrauterine transfusions
- Infants  $\leq$ 12 months of age
- Donation from blood relatives
- HLA-matched platelets
- Granulocyte transfusions
- Recipients of allogeneic or autologous bone marrow/hematopoietic progenitor cell transplants.
- Patients with hematological malignancies
- Patients with Hodgkin's lymphoma
- Patients with other malignant diseases (see comment below)
- Known or suspected congenital immunodeficiency due to T-cell defects (e.g. DiGeorge syndrome, SCID)
- Patients who have received purine analogue drugs (such as fludarabine, cladribine) or other related chemotherapeutic drugs
- Patients who are receiving alemtuzumab (anti-CD52 monoclonal antibody CAMPATH-1H),
- Aplastic anemia patients who are receiving anti-thymocyte globulin (Rabbit derived) ATG medications.
- Patients with neoplastic disease considered to be at high risk for TA-GVHD by their physician

**Comments:**

- Irradiation of the product should be completed as close as possible to time of planned transfusion
- Irradiation is not required for previously frozen products (FFP/FP24, cryoprecipitate AHF)
- Unused previously irradiated products may be used for patients who do not require irradiated products
- There is no indication for irradiation of red blood cells or platelets for patients who are HIV positive or have AIDS
- Use of irradiated blood components is not routinely required for solid organ transplant patients

**References:**

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## FACTOR CONCENTRATES

### **Recombinant or plasma-derived Factor VIII**

In patients with *moderate to severe factor VIII deficiency (hemophilia A) or with mild factor VIII deficiency unresponsive to DDAVP*:

- Before and after an invasive procedure
- During and after acute bleeding
- After trauma
- For prevention of chronic joint disease
- To prevent bleeding
- In patients with mild factor VIII deficiency responsive to DDAVP, when there is severe or life-threatening bleeding (such as intracranial hemorrhage) or high-risk surgery

### **Intermediate-purity plasma-derived Factor VIII (Humate-P, Alphanate)**

1. In patients with *von Willebrand disease*
  - Who are unresponsive to DDAVP:
    - a. Before and after an invasive procedure
    - b. During and after acute bleeding
  - For severe, life-threatening bleeding
2. Immune tolerance therapy in selected factor VIII-deficient patients with inhibitors

### **Recombinant or plasma-derived Factor IX (Benefix)**

In patients with *factor IX deficiency (hemophilia B)*:

- Before and after an invasive procedure
- During and after acute bleeding
- After trauma
- For prevention of chronic joint disease
- Prophylaxis to prevent bleeding
- Immune tolerance therapy in factor IX-deficient patients with inhibitor

### **Activated Prothrombin Complex Concentrates (FEIBA, Autoplex)**

- Bleeding episodes or surgical procedures in patients with hemophilia A or B with inhibitors
- Non-hemophiliac patients with acquired inhibitors to coagulation factors

### **Prothrombin Complex Concentrate (PCC) (Profilnine SD, Bebulin VH)**

- For urgent reversal of warfarin in life-threatening bleeding (Although this is an off-label indication, use of PCC is recognized in such clinical situations and recommended by multiple practice guidelines).
- Other off-label uses: deficiency of other vitamin K-dependent factors in settings where no other concentrate is available (factor X and factor II deficiency)

### **Recombinant Factor VIIa (Novoseven)**

- Bleeding and surgical procedures in patients with factor VIII or IX deficiency and inhibitors
- Bleeding and surgical procedures in selected patients with congenital factor VII deficiency
- Bleeding in patients with acquired hemophilia
- Examples of non FDA-approved use include:
  - a. Bleeding in patients with Glanzmann's thrombasthenia
  - b. Uncontrolled hemorrhage in on-pump cardiac surgery or extracorporeal membrane oxygenation (ECMO)
  - c. Emergent reversal of warfarin
  - d. Rescue therapy of trauma patients with massive transfusion

### **Antithrombin III (AT III) Concentrate**

- In patients with congenital antithrombin deficiency for:
  - a. Prophylaxis for obstetric or surgical procedures
  - b. Thromboembolism
- Non-FDA-approved use must be based on individual institution policy. AT III has been used in patients with documented acquired antithrombin deficiency in:
  - a. Venous or arterial thrombosis with associated heparin resistance
  - b. Bone marrow transplantation with associated veno-occlusive disease
  - c. Cardiopulmonary bypass or ECMO and heparin resistance
  - d. Disseminated intravascular coagulation with severe AT deficiency

### **Fibrinogen Concentrate (Human; RiaSTAP<sup>®</sup>)**

- Indicated for the treatment of acute bleeding in patients with *congenital fibrinogen deficiency (CFD)*, including afibrinogenemia and hypofibrinogenemia.
- RiaSTAP<sup>®</sup> is not indicated for dysfibrinogenemia

### **Factor Concentrate Comments:**

- All patients treated with plasma derived concentrates should have demonstrated immunity to hepatitis B.
- Consultation with hematologist for treatment options and dosing is highly recommended.
- Any off label use of factor concentrates must be based on individual institutional policy.

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