Plasma

How Supplied:

Fresh Frozen Plasma (FFP) or Plasma Frozen Within 24 Hours After Phlebotomy (PF24)

- Plasma prepared from either a whole blood or apheresis collection and frozen within 8 hours (FFP) or 24 hours (PF24) of collection.
- FFP and PF24 once thawed are stored at 1-6°C for 24 hours unless converted and relabeled as *Thawed Plasma.*
- Contain similar levels of clotting factors and can be used interchangeably[1].
- Volume is specified on product label and generally ranges from 200-310 mL.

Thawed Plasma

- Unit of FFP or PF24 that ***is thawed at hospital*** *a*nd then relabeled as *Thawed Plasma.*
- Stored at 1-6°C for up to 5 days from date FFP or PF24 thawed.
- Use is determined by individual hospital policy.
- Considered therapeutically equivalent to FFP/PF24.[1]

Plasma Cryoprecipitate Reduced

- Prepared from FFP or PF24 after cryoprecipitate is removed.
- Once thawed, store at 1-6°C for 24 hours; unless relabeled as *Thawed Plasma Cryoprecipitate Reduced* and then may be stored for up to 5 days from date product thawed.[1]
- Contains limited levels of factor VIII, factor XIII, vWF, fibrinogen, and fibronectin.
- **Limited Use:** Indicated for use in the treatment of thrombotic thrombocytopenic purpura (TTP).
- Should not be used as a substitute for FFP, PF24 or thawed plasma.[1]

Liquid Plasma

- Plasma prepared from a whole blood collection and stored at 1 to 6°C (never frozen).
- When stored at 1-6°C, expiration is 5 days after the expiration date of the whole blood product. At Versiti, liquid plasma is prepared from Group A CPD whole blood and has an expiration date of 26 days.[1]
- Clotting potential of liquid plasma at day 26 is similar to thawed plasma at day 5.[2,3]
- Component is irradiated prior to distribution from Versiti since it contains viable lymphocytes and can theoretically cause transfusion-associated graft-versus-host disease (TA-GVHD) in susceptible individuals.
- **Limited Use:** Specifically approved for the initial treatment of patients undergoing massive transfusion because of life-threatening trauma/hemorrhage and who have clinically significant coagulation deficiencies.[1]
- Liquid plasma is a "**special order**" and requires coordination with Versiti. All requests must be coordinated with your Hospital Relations Specialist.

Utilization Review Guidelines:

Plasma transfusion therapy is indicated for treatment of coagulopathy attributable to coagulation factor deficiency where it is expected that replacement with plasma transfusion is the most efficient way to correct that deficiency. Documentation of the indication(s) for a transfusion episode and special circumstances for transfusion that take place outside these guidelines is recommended.

Best Practice:

- Abnormal coagulation test results ***do not*** predict the risk of bleeding during invasive procedures. Transfusion of plasma prior to a procedure for correction of mildly elevated test results neither corrects the abnormality nor reduces the perceived bleeding risk.[4-6]
- If medically necessary, transfuse plasma no sooner than 5 to 6 hours prior to a procedure for maximum effect.
- Plasma should not be used for reversal of vitamin K antagonists in patients without severe bleeding.[7-11]

Indications:

1. Active bleeding ***and*** documented coagulopathy (INR ≥1.8 or PT and/or aPTT greater than 1.5 times upper limit of normal range). Common settings include:
    - Liver disease with coagulopathy.
    - Emergent/urgent reversal of warfarin effect when Prothrombin Complex Concentrate (PCC) is not available.
    - Disseminated Intravascular Coagulopathy (DIC)
        - Evaluate for hypofibrinogenemia; consider administration of cryoprecipitate.
    - Dilutional coagulopathy/surgical bleeding
        - Best guided by timely coagulation testing.
        - With massive transfusion and damage control resuscitation for trauma patients, early and balanced use of plasma (e.g., RBC:FFP ratio 1:1 to 2:1) is recommended.[12]
    - Replacement of single factor deficiencies for which no single factor concentrate product is available (e.g., factor XI or V deficiency).
2. Prophylaxis in patients undergoing surgery or invasive procedure and documented coagulopathy (INR ≥1.8; PT or aPTT greater than 1.5 times upper limit of normal range).
3. Replacement fluid in therapeutic plasma exchange (TPE) when bleeding or additional bleeding risks are present.
4. Treatment of thrombotic thrombocytopenic purpura (TTP):
    - FFP/PF24, Thawed Plasma and cryo-poor plasma are all acceptable products.
5. Treatment of patients who have acute onset of angioedema related to ACE inhibitors or in hereditary angioedema (C1 esterase inhibitor deficiency) and who are refractory to standard of care.[13,14]

Dosing Recommendations:

- Dose of 10-20 mL/kg body weight will typically provide appropriate procoagulant factors.
- Transfusion of a single unit of plasma for an average sized adult is inadequate for the replacement of coagulation factors.
- Factor levels in donor plasma are variable but can be assumed to be approximately 1 U/mL or 1%/mL.

Expected Outcomes:

1. Each dose (10-20 mL/kg) increases patient's coagulation factor levels by 30-40%. Coagulation factor levels of approximately 30% are required for hemostasis.
2. Post-transfusion recovery of transfused factors may be less than expected due to extravascular distribution or consumption.

Comments:

- Recommendation for patients on warfarin[7,8]

  Elevated INR Without Bleeding
  - Plasma is not indicated in these clinical situations.
  - Holding or lowering of next warfarin dose is generally effective.
  - Vitamin K (low dose) may be indicated based on degree of INR elevation.

  Elevated INR With Major Bleeding[15-17]
  - Co-administration of 4-factor Prothrombin Complex Concentrate (4-F PCC, e.g., Kcentra®) and slow IV infusion of Vitamin K should be considered.
  - 4-F PCC is preferred to FFP because the coagulopathy correction will be significantly faster.

  Elevated INR and Invasive Procedure/Surgical Patients[18-20]
  - For Non-Urgent Surgical Procedures:
    - Holding warfarin and/or use of Vitamin K should be considered based on timing of surgical procedure.
  - For Urgent/Emergent Procedures:
    - If the procedure will occur within 6 hours, plasma or 4-F PCC to replace clotting factors and help control bleeding is recommended. If sustained reversal is needed Vitamin K must be administered.
    - If procedure will occur after 6-24 hours, Vitamin K should be considered as first line treatment. Preferred routes of Vitamin K are oral or IV. Full effect can be seen in 6-12 hours with IV or in 24 hours with oral route. Subcutaneous Vitamin K should not be used because of erratic absorption.[17,20,21]

- Interventional Radiology (IR) procedure considerations[22]
  - Consider use of an algorithm to assess patients on anticoagulant therapy and needing IR procedure:
    - Assess bleeding risk of procedure and patient.
    - Is procedure emergent?
    - Does patient have high thrombotic risk? Consider bridge therapy.
    - If emergent with high risk of bleeding, consider reversal of anticoagulant.

  - For low bleeding risk procedures (e.g., non-tunneled or tunneled venous catheter placement and removal, paracentesis, thoracentesis), the following parameters are recommended:
    - Correct INR to range within ≤2.0-3.0
    - Correct platelet count to >20,000/µL
  - For high bleeding risk procedures (e.g., solid organ biopsies, gastrostomy or gastrojejunostomy tube placement, epidural injections, nephrostomy tube placement, transjugular intrahepatic shunt placement), the following parameters are recommended:
    - Correct INR to range within ≤1.5-1.8
    - Correct platelet count to >50,000/µL

- Most studies to date have failed to show a relationship between preprocedural mild to moderate abnormal coagulation tests and increased bleeding complications in patients undergoing interventional radiology (IR) procedures. In a single center retrospective study, the use of prophylactic plasma transfusion prior to invasive IR procedures in patients with INR ≥1.5 was not associated with decreased RBC transfusion rates or improved patient outcomes.[23]

- Plasma therapy is not indicated for a mildly elevated INR value, or if given, will not bring the INR into the normal reference range in such cases.[24] For an elevated INR (i.e. <1.8), treat underlying condition and provide supportive care including use of Vitamin K in the settings of warfarin therapy or Vitamin K deficiency.

- Plasma products are not indicated for volume expansion, nutritional supplementation, or if the PT/INR and aPTT are normal.[1]

- Given the complex coagulopathy in liver disease, the commonly utilized thresholds for INR do not correlate with bleeding risk and should not be used. In patients with cirrhosis or advanced liver disease with an elevated INR, transfusion of plasma (and platelets) prior to low-risk therapeutic procedures (e.g., paracentesis, thoracentesis and routine endoscopic variceal band ligation) is generally not indicated. For management of active bleeding or high-risk procedures, transfusions to maintain hematocrit ≥25%, platelet count >50,000/µL, and fibrinogen >120 mg/dL may better optimize clot formation.[25]

- During resuscitation for massively bleeding trauma patients, a high transfusion ratio of RBC to plasma (1:1 or 2:1) and earlier administration of plasma has been found to improve outcomes. Once stabilized, individualized component therapy based on laboratory or point-of-care testing is preferable over massive transfusion protocols.[26-28]

- Plasma products should not be used to reverse unfractionated Heparin or Low Molecular Weight Heparin (LMWH). Protamine is recommended for reversal of unfractionated heparin. While not fully effective (60% reversal), protamine is recommended for bleeding patients on LMWH.[17]

- Plasma will not reverse the direct oral anticoagulants (i.e., dabigatran, rivaroxaban, apixaban or edoxaban).[17] Antidotes for direct oral anticoagulants are available. See **Factor Concentrate Products** section for additional information.

- Isolated prolongation of aPTT is not an indication for plasma transfusion unless there is a known coagulation protein deficiency and the presence of bleeding or impending invasive procedure. The most common causes of an isolated prolonged aPTT include heparin, lupus anticoagulants, factor VIII and IX deficiencies, and factor XII deficiency. In these clinical settings, plasma transfusion is not indicated.

- Liquid plasma retains more than 85% of the initial clotting factor and inhibitor activities through day 26 of storage.[2,3] This results in sufficient factor levels for coagulation and clot formation as evidenced by in vitro functional parameter studies. Fibrinogen levels are stable up to 40 days post collection when liquid plasma is manufactured from CPDA-1 whole blood.[3]

- Liquid plasma can be considered as an alternative to thawed plasma for massive transfusion protocols.

- Liquid plasma is easier to store and prepare for prehospital transfusion and can have important benefits when considering it as an alternative to crystalloid.[3]

- Liquid Plasma should not be used as the treatment for coagulation factor deficiencies when plasma products with higher clotting factor concentrations are available.[1]

- For additional information on best practices for plasma transfusion see *TxMD ™ Myths and Realities of Plasma Use*.

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Additional Resources:

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