

# **Cryoprecipitated AHF**

## **How Supplied:**

Cryoprecipitated AHF contains fibrinogen, factor VIII, von Willebrand factor, factor XIII, and fibronectin.

Cryoprecipitate for neonatal and pediatric transfusion is typically distributed as either a single donor unit or a pool of 5 donor units by Versiti.

At Versiti, a single unit of cryoprecipitate contains on average 500 mg (±130 mg) of fibrinogen. Estimated average level of fibrinogen in 5-pool Cryo is 1800 mg (± 330 mg).

## **Utilization Review Guidelines:**

Cryoprecipitate is mainly administered for the treatment of bleeding in patients with acquired deficiency of fibrinogen or dysfunctional fibrinogen. Documentation of the indication(s) for a transfusion episode and special circumstances for transfusion that take place outside these guidelines is recommended.

## **Transfusion May be Considered For:**

- 1. Hypofibrinogenemia (fibrinogen <150 mg/dL) or dysfibrinogenemia (regardless of mg/dL) *with* active bleeding or undergoing an invasive procedure.
- 2. Replacement therapy in congenital Factor XIII deficiency with active bleeding or undergoing an invasive procedure when Factor XIII concentrate is unavailable.
- 3. Extracorporeal membrane oxygenation (ECMO) or perioperative/postoperative bleeding and fibrinogen <150 mg/dL.
- 4. Massive bleeding/trauma; target fibrinogen level >150-200 mg/dL.
- 5. When fibrinogen is <100mg/dL and patient has multiple risk factors for bleeding [lack of synthesis (liver disease), consumption (DIC), intermittent bleeding].

#### **Dosing Recommendations:**

• Dosing for Cryopreciptate is best done when calculated using child's weight, their total blood volume, desired increase in fibrinogen level and average fibrinogen content in a single unit.<sup>1</sup>

Example Calculation:

Dose (units) = <u>Desired fibrinogen increment (mg/dL) x Patient's plasma volume (dL)</u> Fibrinogen content of 1 unit (e.g. 400mg/1 unit)

Patient's plasma volume (dL) = [(Body wt in kg) x (blood volume mL/kg\*) x (1-Hct)] / 100mL

\*Full term neonate: 80-90 mL/kg; Infant: 70-80 mL/kg; Child: 70-75 mL/kg

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- For ease in ordering, the following dosing parameters are suggested:
  - For neonates, give a single donor unit of cryoprecipitate<sup>2</sup>
  - For infants weighing up to 10 kg, start with a single donor unit of cryoprecipitate and reassess.
  - For pediatric patients weighing more than 10 kg, give 1 unit cryoprecipitate for every 10 kg of body weight to maximum of 10 units (2 bags 5-pool).
- ABO-specific or compatible cryoprecipitate should be given to neonates and infants due to their small blood volume. Rh compatibility need not be considered for transfusion.<sup>3</sup>

# **Outcome Indicators:**

- Transfusion of one (1) unit of cryoprecipitate per 10 kg body weight should raise the fibrinogen by approximately 50-75 mg/dL.<sup>4</sup>
- Recovery of transfused fibrinogen is about 50-60%. With certain underlying clinical conditions, (i.e. bleeding or DIC), recovery may vary. Check pre and post-transfusion fibrinogen levels to best monitor for desired outcome.<sup>4</sup>

#### **Comments:**

- Transfusion thresholds for cryoprecipitate remain controversial, although recommended fibrinogen levels range from 100 mg/dL (traditionally indicated for congenital hypofibrinogenemia) up to 150 to 200 mg/dL for acquired deficiency secondary to trauma or cardiovascular surgery.<sup>5</sup>
- The much smaller relative volume of cryoprecipitate (20–25 mL per unit vs 200–250 mL per unit of plasma) allows for delivery of a concentrated equivalent dose when fibrinogen is needed and is an important consideration when transfusing pediatric patients.
- The transfusion of one (1) single donor unit of cryoprecipitate for a neonate rather than weightbased dosing (i.e., 10 mL/kg) adequately increases the fibrinogen level by 150 mg/dL or more while limiting donor exposure and decreasing costs.<sup>2</sup>
- The risk of severe bleeding in children with liver disease and acquired hypofibrinogenemia seems to be less than what is seen in adults. Prophylactic fibrinogen replacement is not recommended in children.<sup>6</sup>
- Use of cryoprecipitate in hemophilia A or von Willebrand disease (vWD) is NOT standard of care. Use factor concentrates as first line therapy. Only in rare situations when the specific factor concentrate is not available and there would be delay in care should cryoprecipitate be used.<sup>7</sup>
- For treatment of patients with congenital fibrinogen deficiency or Factor XIII deficiency, fibrinogen concentrate or Factor XIII concentrate (Corifact®) is available. (See <u>Factor</u> <u>Concentrates</u> section at <u>https://versiti.org/education/txmd-transfusion-medicine-resources</u> under *Blood Utilization Guidelines - Adult* for more information.)
- Human-derived fibrinogen concentrate is increasingly being used as an alternative to cryoprecipitate for acquired deficiencies when cryoprecipitate is in short supply or unavailable.

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Several randomized controlled trials (RCTs) have found fibrinogen concentrate to be equally effective in treating hypofibrinogenemia-related bleeding following cardiac surgery in infants and children.<sup>5,7</sup>

- Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PRCFC) is a 4-pool product (prepared from 8 whole blood-derived plasma units) with 5-day postthaw storage and similar indications as conventional cryoprecipitate. Each 4-pool PRCFC contains an average fibrinogen concentrate of 2900mg. While studies of this product have not been conducted in pregnant women or pediatric patients, PRCFC is produced from INTERCEPT processed plasma and no unexpected adverse events with transfusion of INTERCEPT processed plasma to pregnant women or children have been reported.<sup>8</sup>
- Commercially available fibrin sealants now supercedes the use of cryoprecipitate for topical applications during surgery. Commercially available, virally inactivated concentrates have a higher fibrinogen concentration and are preferred for this purpose.

#### **References:**

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- Tkach EK, Mackley A., Brooks A., Kessler J. and Paul DA. Cryoprecipitate transfusions in the neonatal intensive care unit: a performance improvement study to decrease donor exposure. *Transfusion* 2018;58: 1206-1209. <u>https://doi.org/10.1111/trf.14555</u>
- 3. Chiofolo J (chair). Guidelines for Transfusion of Pediatric Patients. New York State Council on Human Blood and Transfusion Services. 2016.
- 4. Circular of Information for the Use of Human Blood and Blood Components. AABB, America's Blood Centers, ARC, Army Services Blood Program, December 2021.
- 5. Mo YD and Delaney M. Transfusion in pediatric patients; Review of evidence-based guidelines. *Clin Lab Med* 2021;41:1-14.
- 6. Crighton GL and Huisman EJ. Pediatric Fibrinogen Part II:-Overview of indications for fibrinogen use in critically ill children. *Front. Pediatr*:2021; 9:647680. Doi:10.3389/fped.2021.647680.
- 7. Roseff SD, Wong ECC, editors. Pediatric Transfusion: A Handbook. 5<sup>th</sup> edition. AABB, Bethesda, MD 2020; pp 29-32.
- INTERCEPT<sup>®</sup> Blood System for Cryoprecipitation Package Insert for the manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex <u>https://intercept-cryoprecipitation.com/wpcontent/uploads/sites/2/2021/02/SPC-00910-AW-v3.0.pdf</u>

# **Additional Resources:**

- 9. Tirotta CF, Lagueruela RG, Madril D, et al. Use of human fibrinogen concentrate in pediatric cardiac surgery patients. Int J Anesthetic Anesthesiol 2015;2:037. doi.org/10.23937/2377-4630/2/4/1037.
- 10. Callum JL, Karkouti K, Lin Y. Cryoprecipitate: the current state of knowledge. Transfusion Med Rev. 2009; 23(3);177-188.
- 11. Callum J, Farkouh ME, Scales DC et al. Effect of fibrinogen concentrate vs. Cryoprecipitate on blood component transfusions after cardic surgery. *JAMA* 2019; 322(20):1966-1976.
- 12. Davenport P and Sola-Visner M. Hemostatic challenges in neonates. Front. Pediatr. 2021;9:627715. Doi:10.3389/fped.2021.627715.
- Wicklund, BM. Bleeding and Clotting Disorders in Pediatric Liver Disease. Hematology Am Soc Hematol Educ Program 2011 (1): 170–177. <u>https://doi.org/10.1182/asheducation-2011.1.170</u>
- 14. Nellis ME, Karam O, Valentine SL, Bateman ST, et al. Pediatric Critical Care Transfusion and Anemia Expertise Initiative—Control/Avoidance of Bleeding (TAXI-CAB), in collaboration with the Pediatric Critical Care Blood Research Network (BloodNet), and the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Executive summary of recommendations and expert consensus for plasma and platelet transfusion practice in critically ill children: From the transfusion and anemia expertise initiative-control/avoidance of bleeding (TAXI-CAB). Pediatr Crit Care Med. 2022;23(1):34-51. doi: 10.1097/PCC.00000000002851. PMID: 34989711; PMCID: PMC8820267.