

Transfusion of Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PRCFC)

produced from the
INTERCEPT® Blood System



Overview of Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PRCFC)

What is PRCFC?

- PRCFC is a highly-processed, pathogen reduced product optimized to provide a concentrated source of fibrinogen to treat massive bleeding associated with fibrinogen deficiency.
- PRCFC does not contain the same levels of other blood clotting factors found in traditional cryoprecipitate antihemophilic factor (AHF) (“cryoprecipitate”) and cannot be described by traditional cryoprecipitate codes.

What is the U.S. regulatory status for PRCFC?

- PRCFC was cleared for marketing on November 24, 2020 by the FDA for:
 - Treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency.
 - Control of bleeding when recombinant and/or specific virally inactivated preparations of factor XIII or von Willebrand factor (vWF) are not available.
 - Second-line therapy for von Willebrand disease (vWD).
 - Control of uremic bleeding after other treatment modalities have failed.
- PRCFC was also awarded Breakthrough Device designation by FDA for control of massive bleeding associated with fibrinogen deficiency.

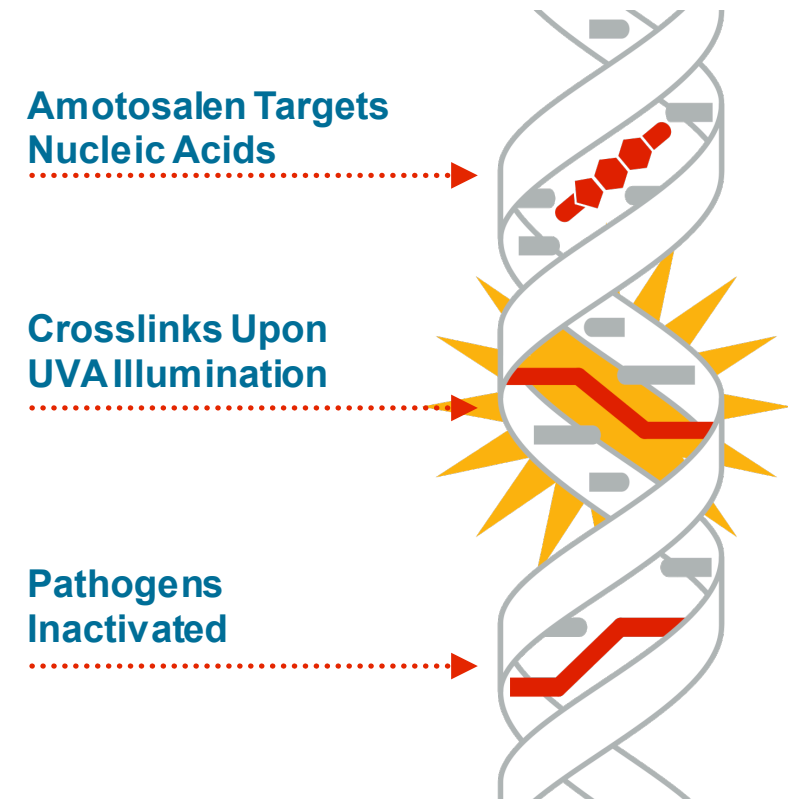
Pathogen Inactivation Reduces Transfusion-Transmitted Infection (TTI) Risk & Enables Five-Day Post-Thaw Shelf Life for PRCFC

- PRCFC is produced from plasma treated by the INTERCEPT Blood System which uses amotosalen and UVA light to inactivate pathogens.
- The INTERCEPT Blood System process enables a broad spectrum TTI* risk reduction, including viruses, bacteria, and other pathogens^{1,2}
- Due to pathogen inactivation, PRCFC:
 - Has a 5-day post-thaw shelf life, while traditional cryoprecipitate has only a 4 to 6 hour shelf life.
 - Can be stored thawed in the OR or ED for immediate use without concerns about excess wastage.

INTERCEPT-treated plasma has 20 years of clinical and post-market surveillance experience.

*There is no pathogen inactivation process that has been shown to eliminate all pathogens. Certain non-enveloped viruses (e.g., HAV, HEV, B19 and poliovirus) and Bacillus cereus spores have demonstrated resistance to the INTERCEPT process. For a full list of pathogens, please refer to package inserts.

INTERCEPT® Blood System Mechanism of Action



Upon UVA illumination, amotosalen crosslinks nucleic acids to block replication and inactivates pathogens.

1. INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA, Cerus Corporation. May 1, 2020.

2. INTERCEPT Blood System for Cryoprecipitation for the manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex [Package Insert]. Concord, CA, Cerus Corporation. November 24, 2020.

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What does PRCFC do?

- PRCFC replaces the fibrinogen and other clotting factors that bleeding patients have lost due to excessive bleeding in order to add the clotting strength needed to achieve stable clot formation and restore hemostasis.
- After thawing, PRCFC has a five-day shelf life at room temperature and therefore is immediately available in a ready-to-transfuse form as a fibrinogen source, thereby providing a significant benefit for patients with massive hemorrhage in a real time-critical fashion that is not achievable with existing fibrinogen replacement today.

How is PRCFC used?

- In practice, we expect that the vast majority of the PRCFC used in a hospital will be administered for the treatment of massive hemorrhage. The availability of specific factor XIII and vWF products suggests that PRCFC would be used rarely for patients requiring these specific factors.

Where is PRCFC used?

- Once marketed, PRCFC will be used in all settings where massive hemorrhage is being treated. These settings could include: ED, operating room, labor and delivery suite, regular ward, ICU.

Effective Treatment of Hemorrhage: Restore Fibrinogen and Other Clotting Factors

- Fibrinogen decreases rapidly and significantly in hemorrhage^{1,2}
- Fibrinogen level in the low 200's is an independent risk factor for severe hemorrhage³⁻⁵

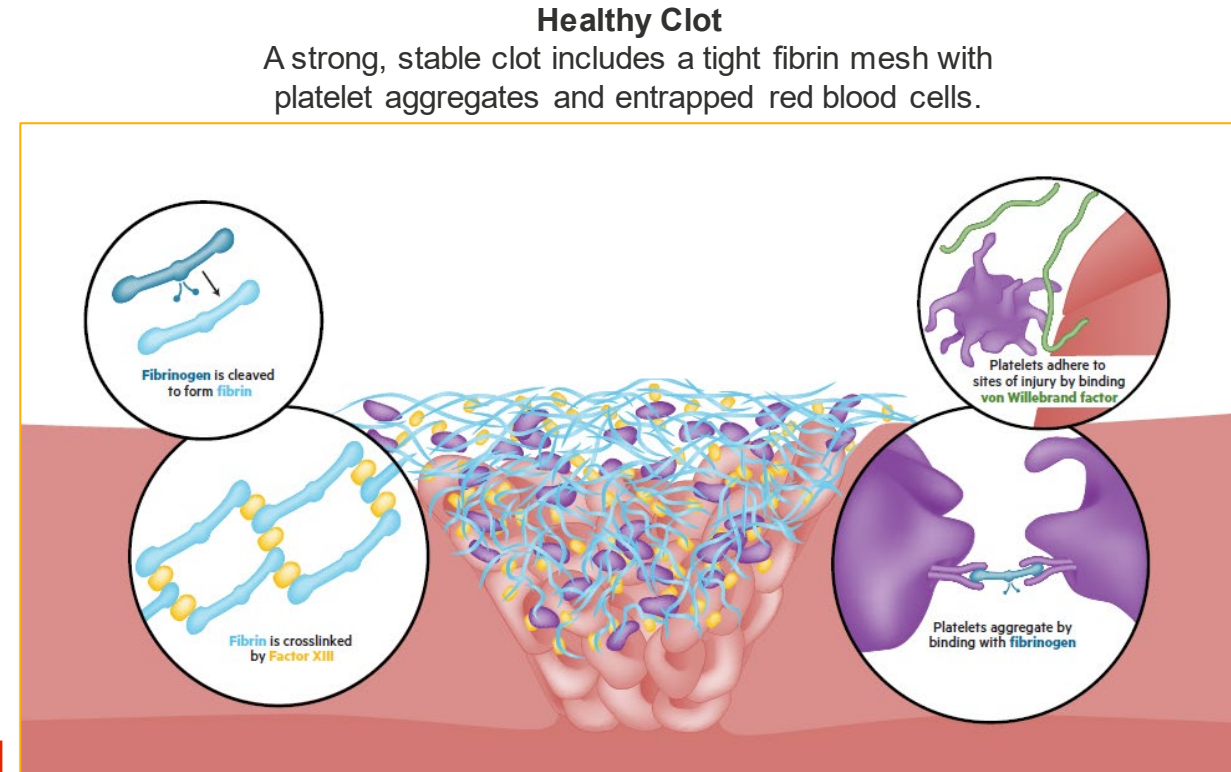
Fibrinogen (Fb)

- Most critical protein needed for stable clot formation and hemostasis^{1,6}

FXIII

- Adds strength and stability to clot formation^{7,8}

Early fibrinogen supplementation restores clot strength, reduces blood loss, and lowers mortality¹



Fibrinogen, Factor XIII and von Willebrand factor add the clotting strength needed to achieve stable clot formation and restore hemostasis.

1. Rourke C et al. Journal of thrombosis and haemostasis: JTH 2012;10:1342-51; 2. Hiippala ST et al. Anesthesia and analgesia 1995;81:360-5; 3. Charbit B et al. JTH 2007;5:266-73; 4. Ranucci M et al. The Annals of Thoracic Surgery 2016;102:78-85; 5. Hagemo JS et al. Critical care 2014;18:R52; 6. Levy JH et al. Anesthesia and analgesia. 2012;114:261-74; 7. von Rappard et al. Transfus Med Hemother 2017;44:85-92; 8. Rijken DC et al. Biomed Res Int 2017;2017:1209676.

Hemorrhage is a Leading Cause of Preventable Death¹

- Median time to death from exsanguination: **1.6 hours**²
- Leading cause of death in the first hours of arrival to a trauma center³
- Increases mortality in:
 - Trauma^{4,5}
 - Cardiac (CV) surgery⁶
 - Postpartum hemorrhage⁷
 - Combat^{8,9}



Trauma #1 cause of death in adults <45 years old¹⁰
~ 40% of trauma deaths are the result of bleeding¹⁰

36% of U.S. trauma deaths may have been preventable after injury with optimal trauma care¹

1. Drake SA et al. Annals of surgery 2018; 2. Cripps et al. The journal of trauma and acute care surgery 2013;75:S255-62; 3. Fox EE et al. Shock 2017;47:567-73; 4. Stanworth SJ et al. The British journal of surgery 2016;103:357-65; 5. Rourke et al. Journal of thrombosis and haemostasis: JTH 2012;10:1342-51; 6. Görlinger K et al. J Cardiothorac Vasc Anesth 2013;27:S20-34; 7. Butwick AJ, et al. Current opinion in anaesthesiology 2015;28:275-84; 8. Stinger HK, Spinella PC, Perkins JG, et al. J Trauma. 2008;64:S79-S85; 9. Joint Trauma System, Damage Control Resuscitation Clinical Practice Guideline, 12 July 2019; 10. Callcut RA et al. The journal of trauma and acute care surgery 2019;86:864-70.

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What are the procedural steps involved?

- PRCFC is stored frozen.
- Once thawed, PRCFC can be kept on a shelf at room temperature for five days.
- Cerus expects that trauma centers and cardiac operating rooms will maintain a stock of thawed PRCFC available for immediate and rapid use in massive hemorrhage.
- To use PRCFC, clinicians determine the desired dose of fibrinogen required to treat the patient and use the requisite number of PRCFC units to create the desired dose.
- No ABO or other pre-administration testing is required before using PRCFC.

Is PRCFC only used for the inpatient setting or is it also used in the outpatient setting?

- PRCFC will be used in a variety of settings but the vast majority of the use will be in inpatients.
- Note that some hemorrhage patients may be stabilized in the ED and then transferred to another facility. In these instances, the use of PRCFC in the ED could be considered “outpatient.”

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What diagnoses are associated with or indicated for use of PRCFC?

- PRCFC is indicated for treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency. There are no specific ICD-10-CM codes for massive hemorrhage. Data analysis suggests that patients undergoing cardiac surgeries, experiencing trauma, hemorrhaging post delivery, or experiencing a gastrointestinal hemorrhage are the most likely to also be at risk for massive hemorrhage and thus may be administered PRCFC.
- PRCFC is also indicated for additional uses (control of bleeding when recombinant and/or specific virally inactivated preparations of factor XIII or von Willebrand factor (vWF) are not available; second-line therapy for von Willebrand disease (vWD), control of uremic bleeding after other treatment modalities have failed). However in practice, we expect that the vast majority of the PRCFC used in a hospital will be administered for the treatment of massive hemorrhage.

Where would PRCFC be documented in the medical record for individuals (e.g. medical coders) to identify?

- Cerus anticipates that PRCFC usage will be recorded in the “Transfusion plan” section within the “Treatment” module of the medical record.

Overview of Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PRCFC)

What are the different naming conventions for PRCFC?

- PRCFC is produced by the INTERCEPT Blood System for Cryoprecipitation. PRCFC may also be referred to as:
 - INTERCEPT Blood System for Plasma Pathogen Reduced Cryoprecipitated Fibrinogen Complex
 - INTERCEPT Fibrinogen Complex

What is the route of administration for PRCFC?

- PRCFC is administered by intravenous infusion.

If the technology is a device or implant, is only one device/implant routinely inserted or can multiple devices/implants be utilized?

- The amount of PRCFC provided is directly related to the fibrinogen deficiency being experienced by the patient. A study of cardiac patients with hemorrhage found that patients required a dose of 5.2 grams of fibrinogen for stabilization.
- PRCFC will be provided in several package sizes, each containing a different amount of fibrinogen allowing providers to choose the fibrinogen dose most appropriate for each patient.

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If the technology involves a device or implant, is the device considered permanent?

- PRCFC is not permanent as the fibrinogen and other clotting factors provided will eventually be degraded by the body.

Is the procedure/technology performed in conjunction with another procedure/technology or is it considered a standalone procedure/technology?

- The use of PRCFC is not a standalone technology but is part of the stabilization for patients experiencing massive hemorrhage.

Have there been any associated complications/sequela/adverse events? If yes, how many and what did they consist of?

- No complications, sequela, or adverse events have been reported for PRCFC.

How Does PRCFC Differ from Traditional Cryoprecipitate?

PRCFC differs from traditional cryoprecipitate in the following ways:

PRCFC is a highly-processed product that has

- Been optimized to provide the fibrinogen required to treat massive bleeding associated with fibrinogen deficiency.
- Undergone pathogen inactivation, which
 - Reduces the risk of transfusion-transmitted infection (TTI).
 - Enables PRCFC to be stored at room temperature for up to five days after thaw, allowing for immediate infusion.
 - Traditional cryoprecipitate must be discarded if not used after four to six hours post-thaw.
- Different levels of other blood clotting factors compared to traditional cryoprecipitate.

Summary

- Massive bleeding with fibrinogen deficiency is a common life-threatening condition.
- Traditional cryoprecipitate is of limited usefulness to treat massive hemorrhage due to concerns about availability at the point of patient care, the speed with which it can be ready (takes some time to thaw), lack of pathogen inactivation, and potential for wastage if it is not used within 4 to 6 hours of thaw.
- PRCFC, a highly-processed product optimized to provide fibrinogen and other clotting factors, is FDA-approved for the treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency.
- Because PRCFC is produced from plasma that has been pathogen reduced with the FDA-approved INTERCEPT Blood System to reduce the risk of transfusion-transmitted infection (TTI), PRCFC can be stored at room temperature for up to 5 days after thawing, thereby enabling stocking at the point of patient care and rapid administration to the bleeding patient.
- PRCFC has been granted FDA Breakthrough Device designation on the basis of improved treatment of massive hemorrhage, a life-threatening medical condition.
- There are no existing ICD-10-PCS codes that appropriately describe the administration of PRCFC.