ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Beriplex® P/N
Prothrombin Complex Concentrate

APPLICABILITY: This document applies to all APL, AHS, Covenant Health, and all other health care professionals involved in the transfusion of blood components and products in Alberta.	***Other Names:*** *Prothrombin Complex Concentrate, PCC* ***Company:*** *CSL Behring* ***Class:*** *Manufactured blood product, derived from human plasma*

	INTRAVENOUS			OTHER		
ROUTES	**DIRECT IV**	**IV Infusion**	**Continuous Infusion**	**SC**	**IM**	**OTHER**
Acceptable Routes*	Yes**	Yes	No	No	No	N/A

* Administration of blood components and blood products is a restricted activity. For specific conditions that apply to a profession's authorization to administer blood components and blood products, consult the applicable discipline-specific regulation under the Health Professions Act (Alberta). Health care professionals with this authorization require the applicable education, training, and competency.

** Direct IV administration of blood products may be performed by health care professionals that have authorization of administration of blood products within their scope of practice.

DESCRIPTION

- Beriplex® is a lyophilized, manufactured prothrombin complex concentrate (PCC) derived from human plasma.
- Contains vitamin K dependent coagulation factors (Factors II, VII, IX, X) and the thrombo-inhibitor proteins C and S. See product insert for actual amounts.
- Pathogen inactivation/removal steps include pasteurization, ammonium sulphate precipitation, calcium phosphate adsorption, and nanofiltration.
- Available in 500 IU and 1000 IU vials packaged with 20 mL and 40 mL sterile water for injection respectively.
- Factor IX is used to determine the concentration of the product.
- Also contains heparin, sodium citrate, sodium chloride, HCl or NaOH, human antithrombin III and albumin.
- The lyophilized powder is white or slightly coloured, and the reconstituted solution is clear or slightly opalescent.
- Preservative free.
- Latex free.

AVAILABILITY

- Supplied by Canadian Blood Services.
- Contact your local laboratory/transfusion service regarding stock availability on site.
- Note: Sites in Alberta may stock Beriplex® and/or Octaplex®. The two brands of PCCs are considered interchangeable in practice.

INDICATIONS

APPROVED PCC INDICATIONS

Clinical Indication	And	Dosing Recommendations
• Vitamin K Antagonist (VKA) reversal • Vitamin K dependent factor deficiency	• Major bleeding, or • Urgent surgical or invasive procedure required (within 6 hours)	• Adults - INR based • Pediatrics - Weight and INR based Monitor with repeat INR. No wait time required to draw INR after giving PCC.
• Coagulopathy • Liver dysfunction	Plasma is contraindicated or refused (e.g. patient high risk for fluid overload, Jehovah's witness accepting of derivatives).	• 25 IU/kg to a maximum of 3000 IU
Major bleeding	Plasma not available, contraindicated, or refused	• Adults - 2000 IU • Pediatrics - 25 IU/kg • Consider Fibrinogen Concentrate if available.
Cardiovascular Surgery	Coagulation Defects or Bleeding	• 25 - 50 IU/kg • Consider Fibrinogen Concentrate if available.
Severe or life-threatening bleeding in patient on direct factor Xa inhibitor (e.g. rivaroxaban, apixaban, edoxaban)	Specific reversal agents are not currently available in Canada.	• 2000 IU fixed dose, or • 25 - 50 IU/kg to max 3000 IU • Consider holding other anti-clotting and anti-platelet agents. • Consider tranexamic acid.

NOT APPROVED PCC INDICATIONS (TM Physician Consult Required)

Clinical Indication	Recommended Alternatives to PCC
VKA reversal when • Non-urgent surgery or invasive procedure is planned. • Surgery or invasive procedure has low risk of bleeding.	• Discontinue VKA • Consider Vitamin K
Elevated INR in the absence of bleeding or need for surgical intervention.	• Consider Vitamin K

Treatment of bleeding in patient on direct thrombin inhibitor (e.g. Dabigatran).	• Specific reversal agents (pharmacy)
	DOAC: Dabigatran — Reversal Agent: Idarucizumab (Praxbind™)
	• PCCs:
	  ○ only in severe or life-threatening bleeding if above options are not available.
	  ○ 50IU/kg to max 3000 IU.
	• Activated PCCs (FEIBA) may be considered in consultation with a TM physician if available on site.

CONTRAINDICATIONS:

- Patients who are hypersensitive to this product, or any ingredient in the formulation or component of the container.
- Patients with a history of heparin induced thrombocytopenia (HIT).
- Patients with recent history of disseminated intravascular coagulation (DIC), thrombosis, or myocardial infarction.

WARNINGS:

- The use of prothrombin complex concentrates is associated with the risk of thrombosis.
- Use with caution in patients with recent thrombotic events, history of coronary heart disease or myocardial infarction, patients with liver disease, pre- and post -operative patients, neonates, and patients at risk of thromboembolic events, DIC, or simultaneous inhibitor deficiency.
- Replacement therapy may lead to the formation of circulating antibodies inhibiting one or more of the human prothrombin complex factors.

DOSE:

- **VKA Reversal - Adult**
  - Dosing should be based on INR.
  - If major bleeding is present and INR is unknown, recommended dose is 80 mL (2000 IU).
  - Vitamin K 10 (mg IV) co-administration strongly recommended if reversal is required for longer than 6 hours.

	INR less than 3.0	INR 3.0 - 5.0	INR greater than 5.0
PCC dose	• 40 mL (1000 IU) • 60 mL (1500 IU) if intracranial hemorrhage or epidural / spinal anesthesia required	80 mL (2000 IU)	120 mL (3000 IU)

- **VKA Reversal - Pediatric**
  - Dosing should be based on weight and INR

Patient Weight	INR less than 3	INR 3.0 or higher
Less than 10 kg	10 mL (250 IU)	20 mL (500 IU)
10 – 25 kg	20 mL (500 IU)	30 mL (750 IU)
25 – 50 kg	30 mL (750 IU)	40 mL (1000 IU)

- **Bleeding Management with DOAC treatment**
  - Recommended dose: 2000 IU fixed dose or 25-50 IU/kg to a max of 3000 IU (120mL)
- If time permits, reassessment of INR at 10 - 30 minutes post dose is recommended, with additional PCC provided if the INR remains greater than 1.5 and bleeding continues. In the event sufficient product is not available to meet the above recommendations, the maximum dose available should be given with consideration for transferring the patient to another facility for additional treatment.
- Maximum total dose = 120 mL (3000 IU).

ADMINISTRATION:

Confirm written (signed) consent has been obtained and documented prior to requesting blood product from lab/transfusion service where possible.

Pre-Infusion:

- Ensure recent patient weight is on file
- Ensure pertinent labs are ordered if required and time allows. (i.e. INR)
- Ensure any ordered premedications have been given (antihistamines, antipyretics prn).
- Perform pre-transfusion checks per AHS Transfusion Policy.
- Report any new onset acute illness to the authorized prescriber prior to commencing infusion.

Access:

- Beriplex® can be given via CVAD or peripheral venous line.

Reconstitution:

- Refer to Mix2Vial reconstitution instructions
- Do not dilute further.
- Beriplex® should be administered immediately (maximum 3 hours) after reconstitution.
- Do not refrigerate after reconstitution.

Compatible IV Solutions:

- Normal saline should be used to prime and flush the line.
- Do not mix with other products, medications, or solutions.

Administration Supplies:

- Direct IV:
  - Sterile plastic Luer lock syringe (large enough to contain dose)
- IV Infusion:
  - IV administration set (either a buretrol, infusion set for syringe pump or minibag with regular infusion set)
  - IV pump or syringe pump (if required)

Administration:

- The amount of product received for administration may be 10% lower or higher than the actual dose
- ordered. Administer the entire dose. Visually inspect the product prior to administration. Do not use products that are cloudy or contain particulates.
- No other drugs or IV solutions can be co-administered in the same line while Beriplex® is being infused.
- Administration rate should be specified by the MRHP after patient assessment.
- Use a 15-micron filter or larger if required for administration (e.g.for patients with orders for a filtered administration set due to their condition such as patent foramen ovale, Hereditary Hemorrhagic Telangiectasia [HHT], etc.)
- **Options for Administration:**
  - **Regular IV set:** Empty IV bag and inject reconstituted Beriplex® into the empty bag. Prime line with Beriplex®. Infuse Beriplex®. Flush line with 35 mL normal saline at the end of Beriplex® infusion.
  - **Buretrol:** (In-line or 'add-a-line')
    - **Option 1:** Attach 500-mL NS bag to buretrol line. Prime tubing with 35 mL NS **(leave chamber empty)** and close clamp between normal saline and buretrol. Add Beriplex® to chamber for infusion. Flush line at same rate with 35 mL normal saline at the end of Beriplex® infusion to ensure entire dose has been administered.
    - **Option 2:** Prime buretrol line with product (similar to tPA process). Infuse product. Flush line at the same rate with 35 mL normal saline at the end of infusion.
  - **Direct IV:** Not to exceed 8 mL/min (480 mL/h or 1000IU/5 min)
  - **Syringe pump:** microbore tubing required. Not to exceed 8 mL/min (480 mL/h).
- **Administration Rate:** Do not exceed 8 mL/min (480 mL/h).

NURSING IMPLICATIONS:

Patient Monitoring:

- Vital Signs: Pre-administration**,** on completion of dose, and as patient condition requires.
- Patients should be monitored for signs and symptoms of thromboembolic events.

Patients receiving blood product transfusions must be observed closely for signs of any unexpected or untoward reactions. These reactions may occur during or after the infusion of blood or blood products. For follow up instructions to a transfusion reaction, go to: http://www.albertahealthservices.ca/lab/page4240.aspx.

Documentation:

- Ensure documentation is completed as per the *AHS Transfusion of Blood Components and Products Policy.*
- Patient tolerability should be documented in appropriate flow chart or clinical record (electronic or paper).
- Document vital signs as required in the appropriate flow chart or clinical record (electronic or paper).
- Provide patient notification documentation as required.

Laboratory Monitoring:

- INR should be performed pre-administration along with other indicated blood work, and 10-30 minutes post-administration.
- Beriplex® contains heparin, and therefore may interfere with clotting tests which are sensitive to heparin (e.g. aPTT).

POTENTIAL HAZARDS WITH PARENTERAL ADMINISTRATION:

- Potential adverse events related to a blood product transfusion range in severity from minor with no sequelae to life-threatening.
- All adverse events occurring during a transfusion should be evaluated to determine whether the transfusion can be safely continued/restarted.
- All adverse events suspected to be related to a product transfusion (whether during or after a transfusion) must be reported to your local transfusion service.
- The most common adverse events associated with Beriplex® are thromboembolic events, headache, and body temperature increase.
- Beriplex® has been rarely associated with immediate allergic or thrombotic complications.

Side Effects - Flushing - Headache - Nausea - Itching and redness at the venipuncture site	→	**Action:** Slow rate of infusion
Potential Allergic Reaction - Stuffy nose - Hives/severe itching - Cough - Chest pain - Wheezing - Facial swelling - Fainting	→	**Action:** **STOP** infusion **IMMEDIATELY** and contact physician

STORAGE & STABILITY:

- Store at 2-25°C until expiry (up to 36 months from date of manufacture).
- Stable up to 3 hours at room temperature once reconstituted.
- Do not refrigerate after reconstitution.
- Do not freeze.
- Do not use expired product.

CONTACT INFORMATION:

Approved By: APL Transfusion Medicine Discipline Council
For questions or comments please contact: Transfusion.SafetyTeam@aplabs.ca

REFERENCES:

CSL Behring Canada Inc., 23 Oct 2019, Beriplex® P/N 500 / Beriplex® P/N 1000 Package Insert. Submission Control No: 221855 [Accessed 2021Oct26] https://labeling.cslbehring.ca/PM/CA/Beriplex-PN/EN/Beriplex-PN-Product-Monograph.pdf

Recommendations for Use of Prothrombin Complex Concentrates in Canada. 2022 update http://www.nacblood.ca PCC Recommendations Revision Feb 2022