Beriplex® AU (4-factor Prothrombin Complex Concentrate [PCC])

Beriplex® AU (4-factor PCC) has replaced the previously available 3-factor concentrate Prothrombinex-VF.

	Active ingredients content per vial comparison	
	Beriplex® AU 500	**Prothrombinex-VF**
Factor II	400-960 IU	~ 500 IU
Factor IX	400-620 IU	500 IU
Factor X	440-1200 IU	~ 500 IU
Factor VII	200-500 IU	
Protein C	300-900 IU	
Protein S	240-760 IU	

The CSL Product Information (PI) states that Beriplex® AU is indicated for:

- Treatment of bleeding due to acquired deficiency of the prothrombin complex coagulation factors (II, VII, IX and X).
- Reversal of vitamin K antagonists (e.g., warfarin) when rapid reversal required in perioperative setting or bleeding context.
- Treatment of vitamin K antagonist overdose

The CSL Beriplex® AU PI states:

The safety and efficacy of Beriplex® AU in the paediatric population has not been established in clinical studies.

Due to the need to provide some pragmatic guidance to paediatric clinicians, the following warfarin reversal guidance is provided.

Beriplex® AU	Details
Additional RCH indications	• Emergency DOAC reversal • Cardiopulmonary bypass bleeding • Vitamin K deficiency bleeding of newborn • Patient/family refusing whole blood products
Pharmacokinetics	• Peak plasma concentrations occur within five minutes of infusion • Elimination half-life of coagulation factors: factor II - 60 hours, factor VII - 4.2 hours, factor IX - 17 hours, and factor X - 31 hours
Contraindications	• Hypersensitivity to any components of the product. • History of Heparin Induced Thrombocytopenia (HIT). Beriplex® AU contains Heparin. • In DIC, Beriplex® AU should only be considered after resolution of the consumptive state.

Cautions	• Children with a history of thrombosis • Prothrombotic state at increased risk of thrombosis • Patients with liver disease, patients in active DIC, the presence of a CVAD and neonates
Consent	• Blood transfusion consent should be sought (where possible)
Presentation	• 500 IU vials with 20 mL water for injection
Ordering and approval	• Requires Haematologist approval • Prescribe via the EMR
Dosing	• Based on weight up to but not exceeding 100kg • >15 kg round to the nearest vial size • ≤15 kg consider rounding to nearest 25 IU or 50 IU • Consider the clinical indication, current INR, target INR, need for re-anticoagulation and patient weight
Administration	• Reconstitute using diluent provided and according to the product instructions including **Mix2Vial™** • If multiple vials of Beriplex® are required they may be pooled into a single infusion. • Do not further dilute Beriplex® AU. • Slow IV push, do not exceed 3 IU/kg body weight/minute, maximum 210 IU/minute, approximately 8 mL/minute. • Do not mix with other medicinal products, administer via a separate IV line.
Stability	• Store below 25°C • Beriplex does not contain antimicrobial preservative. • CSL recommends using immediately after reconstitution.
Monitoring	• INR check within 30 minutes post warfarin reversal

Beriplex® AU – warfarin reversal dosing guidance		
	Pre-treatment INR	**Beriplex® AU dose IU/kg**
Major bleeding *that is critical organ or life threatening*	Any INR ≥1.5 or recent dose of Warfarin even if INR <1.5	50 IU/kg (Maximum 5000 IU)

Urgent peri-operative reversal **Or** **Major bleeding *on Warfarin***	INR 2.0 – 3.9	25 IU/kg (Maximum 2500 IU)
	INR 4.0 – 6.0	35 IU/kg (Maximum 3500 IU)
	INR ≥6.0	50 IU/kg (Maximum 5000 IU)

Where Beriplex® AU is administered in the context of Warfarin reversal and major bleeding, vitamin K should be considered.

Vitamin K dosing for warfarin reversal		
	Type of warfarin reversal	**Vitamin K dose**
Major bleeding irrespective of INR	Complete	300 mcg/kg PO Or IV (max 10 mg)

Please see attached background document, for other paediatric indications for Beriplex® AU specific to RCH, e.g., dosing for emergency direct oral anticoagulant reversal.