Whittington Health NHS

Use of Prothrombin Complex Concentrate

Subject:	Use of prothrombin complex concentrate (PCC)
Policy Number	N/A
Ratified By:	Dr F Shah – Consultant Haematology
Date Ratified:	July 23 2013
Version:	3.0
Policy Executive Owner:	Dr R Jennings
Designation of Author:	Dr Chew - SpR Haematology
Name of Assurance Committee:	Hospital Transfusion Team
Date Issued:	July 2013
Review Date:	July 2016
Target Audience:	Haematologist, A/E, Intensivists, Anaesthetists, Obstetrics
Key Words:	PCC, Beriplex® P/N, warfarin reversal, life-threatening bleeding

Version Control Sheet

Version	Date	Author	Status	Comment
1				
2	2011	Dr Roddie	SpR Haematology	
3	July 2013	Dr Chew	SpR Haematology	Minor amendment P3, Indication for Use - removal of wording *non-life threatening*

Key words: PCC, Beriplex® P/N, warfarin reversal, life-threatening bleeding

➢ Criteria for use

For use by haematologists in non-contraindicated patients for short-term reversal of warfarin in cases of major, life-threatening haemorrhage and intracranial bleeding.

➢ Background/ introduction

• Prothrombin Complex Concentrate (PCC) (Beriplex®, P/N (CSL Behring) is a plasma-derived concentrate of the Vitamin K dependent coagulation **factors II, VII, IX, X, Protein C and Protein S.**
• The concentrate is dual virally inactivated and available in lyophilized powder form, which is reconstituted in sterile water immediately prior to administration.
• PCC is produced by fractionation of pooled plasma from non- UK donors.
• It is **NOT** blood group specific

• It usually reverses warfarin anticoagulation within 10-30 minutes.

➢ Indication for use

•PCC allows **rapid reversal of warfarin in the context of major or lifethreatening bleeding (including intracranial bleeding)** within 10-30 minutes, but has a transient effect related to the half-life of the factors. Complete longer-term reversal of warfarin requires vitamin K *(see warfarin guideline).*
• Other indications for use of PCC should be discussed with a consultant haematologist and include:
o Reversal of anticoagulation with anti-thrombin agents
o Reversal of non-life threatening bleeding in patients who cannot tolerate FFP volumes
o Reversal of anticoagulation prior to urgent surgery

o Use in patients who refuse blood products and are bleeding- however it is still a blood product and therefore unacceptable to some, e.g. jehova's witnesses.

➢ Risks associated with PCC treatment

• Hypersensitivity/allergic reactions- **discontinue PCC immediately**
• Thrombosis (arterial and venous)
• Angina Pectoris
• Disseminated intravascular coagulation
• Transfusion transmitted infection (mainly viral)
• Heparin induced thrombocytopenia (HIT)

• Development of antibodies to one/several of the factors in PCC

Contraindications and side effects of PCC

Absolute contraindications

• Patients with known hypersensitivity to any of the product components eg: heparin (which is present in the concentrate)
• History of heparin induced thrombocytopenia (HIT)
- Active disseminated intravascular coagulation- until the consumptive state has been stopped.

• The product has traces of IgA and should not be used in patients with IgA deficiency.

In these groups, recombinant VIIa can be considered for life threatening bleeding.

Relative contraindications:
• Recent thrombosis or angina pectoris
• Recent myocardial infarction *(exception: life-threatening haemorrhage following overdosage of oral anticoagulants, and before induction of fibrinolytic therapy).*
These patients will have a higher risk of a post treatment thrombotic event.

Unknown:
• The safety of PCC (Beriplex® P/N) for use in human pregnancy and lactation has not been established hence it should only be used if clearly indicated following discussion with a haematologist.

➢ Contacts (inside and outside the Trust including out-of-hours contacts)

The need for PCC (Beriplex® P/N) **MUST** be discussed with the consultant supervising the care of the patient PRIOR to discussion with the consultant haematologist, who will then authorise PCC release **(and dose**) from Blood Bank.

➢ Storage

PCC (Beriplex® P/N) is to be stored in Blood Bank. **The product will be issued on a named patient basis only.** Patient details (identification and indication for treatment) need to be recorded in the Beriplex record folder kept in Blood Bank before the drug will be released.

Dosing and administration

• **Consent form required in ALL patients prior to use of PCC.**
• PCC doses between 25 IU/kg and 50 IU/kg have been used. The average starting dose is 25 IU/kg and a **repeat clotting test should be taken to the laboratory 30 minutes post dosing to verify degree of correction of INR.**
• Reversal of anticoagulation is rapid, but due to the short half-life of Factor VII (6 hours), **it is essential to give intravenous vitamin K simultaneously.**
• The concentrates, available in lyophilised powder form, are reconstituted in sterile water immediately prior to administration.
• They are **NOT** blood group specific.

Body weight (kg)	Total Dose in IU if 25 IU/Kg used	No of vials of 500iu	mls	Duration of infusion
50-60	1500	3	60	7 minutes
61-80	2000	4	80	10 minutes
81-100	2500	5	100	12 minutes
101-120	3000	6	120	14 minutes

• Beriplex® P/N should be administered intravenously at no more than 3 IU/kg/min (max 210 IU/min). A syringe driver should be used if available.

• **The maximum single dose should NOT exceed 5000 IU factor XI.**

➢ Efficacy monitoring

Primary measure of haemostatic efficacy is correction of INR.

➢ Laboratory tests

Blood must be taken for full blood count, activated partial thromboplastin time (APTT), prothrombin time (PT), international normalised ratio (INR) and fibrinogen pre- and 30 minutes post PCC and then dependent on
the clinical situation. The PT will shorten dramatically and the APTT may also shorten post dose.

PCC has a reasonably short half-life so these effects will not be long lasting: it is vital to also give intravenous Vitamin K for a more long-term effect. Regular monitoring of INR and clotting studies will be required if bleeding reoccurs or continues.

Record of PCC use- audit

The batch number, vial size and number of vials issued will be recorded on the blood transfusion computer system, with details issued with the product to be stored in the patient's notes. Usage will be documented at Transfusion team meetings.

- The consultants responsible for administration will be expected to present a case study at a clinical audit meeting.
- The consultants responsible for administration will be expected to record and feedback the dose level at which haemostasis improved to help update the protocol.
- The use of Beriplex® will be audited annually and reported to the Hospital Transfusion Committee.

References

1. Evans G, Luddington R and Baglin T. Beriplex P/N reverses severe warfarin-induced overanticoagulation immediately and completely in patients presenting with major bleeding. British Journal of Haematology 2001; 115:998-1001.

2. Pabinger I, Brenner B, Kalina U, Knaub S, Nagy A, Ostermann H. for the Beriplex® P/N anticoagulation reversal study group. Prothrombin complex concentrate (Beriplex® P/N) for emergency anticoagulation reversal: a prospective multinational clinical trial. Journal of Thrombosis and Haemostasis 2007;6:622-631.

3. Bruce D and Noakes T.J.C. Prothrombin complex concentrate (Beriplex P/N) in severe bleeding: experience in a large tertiary hospital. http://ccforum.com/content/12/4/R105.

4. Beriplex® P/N Product Monograph, CSL Behring, April 2008.

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	Yes/No	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to support the monitoring of compliance with and	Yes	

	Title of document being reviewed:	Yes/No	Comments
	effectiveness of the document?		
	Is there a plan to review or audit compliance with the document?	Yes	
10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			
Relevant Committee Approval			
The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name	Dr Shah	Date	23/07/2013
Name of Committee	Hospital Transfusion Committee	Name & role of Committee Chair	Dr F Shah Consultant Haematologist
Signature			

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	Who will lead on this aspect of monitoring? Name the lead and what is the role of the multidisciplinary team or others if any.	What tool will be used to monitor/check/observe/Assess/inspect/ authenticate that everything is working according to this key element from the approved policy?	How often is the need to monitor each element? How often is the need complete a report ? How often is the need to share the report?	What committee will the completed report go to?
Element to be monitored	**Lead**	**Tool**	**Frequency**	**Reporting arrangements**
Transfusion of Prothrombin Complex Concentrate (PCC)	**Abdul Adamu – Hospital Transfusion Practitioner**	**Case studies of all patients transfused PCC**	**Annually**	**Hospital Transfusion Committee**