***CAUTION**: You must refer to the intranet for the most recent version of this policy.*

Guidelines on the use of OCTAPLEX® (Prothrombin complex concentrate/PCC) for rapid reversal of warfarin in association with life threatening bleeding.

SharePoint Location	General Policies and Guidelines
SharePoint Index Directory	Cancer and Specialist Care
Sub Area	Haematology and Blood Transfusion
Key words *(for search purposes)*	Transfusion, warfarin reversal, PCC
Central Index No	0254
Endorsing Body	Hospital Transfusion Committee
Endorsement Date	Jan 2011
Review Date	Jan 2014
Lead author and designation	Dr Kanchan Rege Consultant Haematologist
(if under review) Review led by	Dr Kanchan Rege Consultant Haematologist

KEY POINTS: - This document

1. Provides guidance for clinicians on rapid reversal of warfarin therapy in cases of life threatening bleeding.

2. Outlines the indications and contraindications for the use of Octaplex (Prothrombin Complex Concentrate)

Background
Octaplex /PCC:-

- Contains freeze dried human derived Factors II, VII, IX, X and Proteins S and C
- Provides very effective, rapid reversal of warfarin
- Is potentially thrombogenic and may provoke arterial or venous thrombosis
- Should be used when the thrombotic risks are relatively less than the risk of continued bleeding - its use should therefore be restricted to life threatening situations
- Is licensed in the UK for treatment of bleeding disorders including reversal of oral anticoagulation.

Although the risk of bleeding on warfarin increases when INR>4.5 most bleeds (including intracranial bleeds) occur with the INR in the therapeutic range

Purpose and scope of policy
These guidelines have been produced to ensure that Octaplex® is used appropriately when clinically indicated, in cases of life threatening bleeding.

They should be referred to by all staff responsible for requesting, prescribing, and administering Octaplex, and are based on British Committee for standards in Haematology guidelines.

1 Definition of Terms
Octaplex Prothrombin Complex Concentrate (PCC) contains freeze dried human derived Factors II, VII, IX, X and Proteins S and C

2.1 Process
The request, prescription and administration of Octaplex PCC.

2.2 Content

2.2.1. Indications for use
- Life threatening haemorrhage
- Intracranial haemorrhage (this carries a 50% mortality in patients on warfarin)
- Prior to emergency surgery in patients on Warfarin (if delaying surgery plus giving vitamin K is not clinically reasonable)
- May not be suitable for treatment of Jehovah's Witnesses as it contains human material

It is not indicated for less serious bleeding or for preparation for elective surgery

2.2.2. Dose
Each box contains 500 IU. Max single dose 3000 IU (6 Boxes)

Wt/kg	INR 2-2.5	INR 2.5-3	INR 3-3.5	INR >3.5
50	1500iu	2000iu	2500iu	2500iu
60	2000iu	2000iu	2500iu	3000iu
70	2500iu	2500iu	3000iu	3000iu
80	2500iu	3000iu	3000iu	3000iu
90	2500iu	3000iu	3000iu	3000iu
100	3000iu	3000iu	3000iu	3000iu

Once a vial is reconstituted please use complete vial. DO NOT discard part used vials

2.2.3 Contraindications
- Known hypersensitivity to plasma proteins
- Disseminated Intravascular Coagulation
- Recent arterial thrombosis
- Previous history of heparin associated thrombocytopenia type II
- Uncompensated liver disease

2.2.4 Relative contraindications
- Patients with history of Ischaemic Heart Disease
- Liver disease
- Safety in pregnancy not established

2.2.5 Risks
- Thrombosis (arterial and venous) and may provoke DIC
- Anaphylaxis
- Viral transmission

2.2.6 Consequences of not administering the drug
Fresh frozen plasma may also be used for the same indication as Octaplex. It, however, is associated with the risk of transfusion transmitted infection, anaphylaxis, Transfusion Related Acute Lung Injury, volume overload and other potential hazards of transfusion. It is also likely to correct the INR more slowly and less predictably. The British Committee for Standards in Haematology (2005) recommend that complete and rapid reversal of over-anticoagulation is more readily achieved with a factor concentrate than with FFP.

2.2.7 Reconstitution and administration
The clinical decision to use Octaplex should be approved by a Haematology Consultant. It should then be administered as soon as possible.

Octaplex is stocked in the Transfusion Laboratory, and should be collected as soon as it is available after being requested.

Octaplex is provided as a dried powder (available vial size is 500 IU /vial) along with sterile water and special transfer needle. It will need to be reconstituted in the clinical area by the nurse or doctor responsible for the patient.

One box of Octaplex contains:-

- Octaplex 500IU powder in a vial with a stopper and flip off cap
- 20ml Water for injection with a stopper and flip off cap
- A transfer set (1 double ended needle and 1 filter needle)

Multiple boxes will be issued to provide the correct dose.

Octaplex is stored refrigerated. The vials will need to be warmed (by the nurse or doctor gently rolling the bottle in their hands) prior to administration

To reconstitute, follow the instructions provided in the pack - i.e.

- Remove the caps from the powder vial and the water vial and clean the rubber stoppers with an alcohol swab.
- Remove the protective cover from the short end of the double-ended needle, making sure not to touch the exposed tip of the needle. Then perforate the centre of the water vial rubber stopper with the vertically held needle.
- In order to withdraw the fluid from the water vial completely, the needle must be introduced into the rubber stopper in such a way that it just penetrates the stopper and is visible in the vial.
- Remove the protective cover from the other (long) end of the double-ended needle, making sure not to touch the exposed tip of the needle.
- Hold the water vial upside-down above the upright powder vial and quickly perforate the centre of the powder vial rubber stopper with the needle. The vacuum inside the powder vial draws in the water.
- Remove the double-ended needle with the empty water vial from the powder vial, and then slowly rotate the powder vial until it is completely dissolved.
- Octaplex dissolves quickly at room temperature to a colourless / slightly opalescent solution. If the powder fails to dissolve completely or a deposit is formed, do not use the preparation.
- The total number of vials required to give the final dose can be reconstituted at the same time.

2.2.8 Administration

- After the powder has been reconstituted in the manner described above, draw the preparation up into a syringe using the filter needle. The filter needle is for single use only.
- Attach a 60 ml syringe to the needle. Remove the protective cover from the filter needle and perforate the rubber stopper of the reconstituted solution.
- Turn the vial with the attached syringe upside-down and draw up the solution into the syringe. Under most circumstances, two 60 ml syringes will be required to administer the total dose, up to a maximum of 120ml. The syringes must be clearly labelled with the name and strength of the drug.
- Administer the reconstituted Octaplex solution by the intravenous route at a rate of 10ml/minute, using a syringe driver. The recommended administration rate is much slower (2-3mls/minute) but relates to treatment in non-emergency

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situations when immediate reversal is unnecessary - this is not practical in cases of life threatening haemorrhage.

- There is a small risk of allergic reactions – if these occur the infusion should be stopped immediately and standard allergy/anaphylaxis therapy should be instituted. As a precautionary measure, the patients pulse rate should be measured before and during the infusion. If a marked increase in the pulse rate occurs the infusion speed must be reduced or the administration must be interrupted
- No blood must flow into the syringe due to the risk of formation of fibrin clots.
- Once reconstituted, the solution should be used immediately.

2.2.9 Post administration

- Repeat PT/INR 30-60 minutes post administration and at 6hours + 18 hours (may need further therapy).
- Monitor clinical response and for evidence of DIC/thrombosis
- Daily FBC and INR/clotting screens required for 2-3 days
- Some severely over anticoagulated patients may need further doses of Vitamin K if clinical need to maintain complete reversal
- Once acute event treated and patient stable it may be appropriate to consider prophylactic heparin in some situations e.g.: mechanical heart valves
  Record efficacy of Octaplex in patient notes

2.3 Endorsement

The policy will be approved by the Hospital Transfusion Committee

2.4 Distribution

The policy will be recorded on SharePoint.
Staff will be made aware of the policy during induction and clinical update sessions, and via e Brief.

3. Implementation

The policy will be reviewed every three years or sooner if required in light of new evidence or statutory requirements.
The use of Octaplex will be audited annually, see Appendix A
If there is any deviation from this policy, an incident form will be raised via DATIX, and the incident investigated by the transfusion operational management team and corrective and preventative actions implemented. If appropriate, a report will be made to SHOT and SABRE.

Glossary of Terms

PCC	Prothrombin Complex Concentrate
IU	International Unit
DATIX	Electronic Adverse event and near miss reporting form
SHOT	Serious Hazards of Transfusion - UK wide reporting system for adverse transfusion events and ‘near misses’
SABRE	Serious Adverse Blood Reactions and Events This system allows reporters to electronically submit reports of serious adverse events or serious adverse reactions directly to the Medicines and Healthcare Products Regulatory Agency (MHRA)

References

British Committee for Standards in Haematology (2005) Guidelines on oral anticoagulation (warfarin): third edition –
2005 update Available:
http://www.bcshguidelines.com/documents/oralanticoagulation_update_bjh_2005.pdf

Octaplex (human Prothrombin complex) - Summary of Product Characteristics (UK Specific) 2010. Octapharma Ltd.

Appendix A
Compliance Monitoring

Process to be monitored	How will compliance with the outlined process be monitored?	Frequency	By who?	If compliance gaps have been identified, who is responsible for creating an action plan, and ensuring implementation of required changes?
Appropriate use of Octaplex	Review of patient records	Annually	Transfusion coordinator	Hospital Transfusion Team

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Summary and Audit Trail

Development process Title:								
Guidelines on the use of OCTAPLEX (Prothrombin complex concentrate/PCC) for rapid reversal of warfarin in association with life threatening bleeding.	Trustwide & Healthcare Economy		Trustwide	X	CBU		Dept	
	Multidisciplinary		Medical Staff	X	Allied Health Professionals		Nursing/ Midwifery	X

Reason for Development: (eg planned review of existing document, patient complaint, critical incident, publication of new evidence, inconsistent practice, NICE Guidance)
Planned review of existing document

Development Lead:	Dr Kanchan Rege Consultant Haematologist		
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Development Team Members:
Kaye Bowen -Transfusion Coordinator
Martin Drury- Transfusion Laboratory Manager

Key sources of evidence used in the development of the document or the method of achieving consensus where evidence is not available:
Guidelines from:-
British Committee for Standards in Haematology

Consultation Process

Please list key Staff Members and Groups/Committees involved in the Consultation Process:
Hospital Transfusion Team

Please identify committee(s) which will approve the policy (see flow chart for development) **:**
Hospital Transfusion Committee

Once this form has been completed it should be sent to the Compliance Officer with the final copy of the policy