Bedfordshire Hospitals NHS Foundation Trust

CLINICAL PROCEDURAL DOCUMENTS

Document Title: Guidelines on the use of Octaplex (Prothrombin complex concentrate/PCC) for rapid reversal of Warfarin in cases of major haemorrhage or emergency surgery

This document is relevant for staff at: *(please indicate)*	Luton Hospital site X	Bedford Hospital site	Both Hospital sites
Document Type: **Clinical Guideline**	**Clinical Guideline** **X**	**PGD**	**Integrated Care Pathway**

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If the document is not merged cross site, please provide an explanation:
Bedford do not use Octaplex

Signature of Clinical Lead of the CSL:	Date:

Is this document new or revised / or has minor amendments? Reason for minor amendments? Please highlight all amendments in your document.
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Target Audience/Scope: Doctors, nurses, Blood Transfusion staff, Haematology Department

Associated Trust Documents:
CG375 - Major Haemorrhage Protocol in Adults, Children and Neonates and Procedure for Obtaining Blood and Blood Products in an Emergency
CG436 - Reversal of anticoagulation and management of bleeding in adult patients on either warfarin, non-Vitamin K oral anticoagulants (NOACs) or heparin

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	Jogesh Kapadia	5th May 2021

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Guidelines on the use of Octaplex (Prothrombin complex concentrate/PCC) for rapid reversal of Warfarin in cases of major haemorrhage or emergency surgery

1. Introduction

Octaplex is a prothrombin complex concentrate (PCC). It contains the clotting factors II, VII, IX and X (the Vitamin K dependent clotting factors).

Octaplex should be used for the rapid reversal of warfarin or other vitamin K antagonists (e.g. phenindione, acenocoumarol) in cases of life, limb or sight-threatening haemorrhage or prior to emergency surgery with high risk of bleeding.

2. Purpose and scope

These guidelines are for the use of staff responsible for requesting, prescribing, and administering Octaplex and to ensure that Octaplex is used appropriately when clinically indicated, in cases of life threatening bleeding.

3. Indications for use of Octaplex

- **Life-threatening haemorrhage** e.g. intracerebral bleed (preferably demonstrated on CT scan), intra-ocular bleed, retroperitoneal haemorrhage, muscle bleed with compartment syndrome, massive gastrointestinal haemorrhage or uncompensated bleeding from any orifice with developing shock, in a patient on warfarin or other vitamin K antagonist.
- **Reversal of warfarin for emergency surgery** i.e. within 6 hours (please discuss with on-call Consultant Haematologist).
- **Head injury in patients on warfarin** – Patients on warfarin presenting with head injury should have their INR measured as soon as possible with a lower threshold for performing a head CT scan. Patients on warfarin with a strong suspicion of intracerebral haematoma after a clear head injury should have their anticoagulation reversed immediately and before results of investigations are available.

For other indications, discussion with a Haematologist is required to authorise Octaplex.

The clinical decision to use Octaplex to reverse warfarin in cases of major haemorrhage should be approved by either the Consultant in charge of the patient or a Consultant Haematologist.

If Octaplex is to be administered for an indication other than major haemorrhage on a vitamin K antagonist, then the patient must be discussed with the Consultant Haematologist on-call. PCC should not be used to enable elective or non-urgent surgery.

Please seek advice from the Consultant Haematologist on-call if there is any doubt regarding its use.

Fresh frozen plasma (FFP) is not indicated for reversal of oral anticoagulation and should be used only if Octaplex or other PCC is not available.

4. Contraindications to Octaplex

- Hypersensitivity to the active substance or to any of the excipients.
- Known allergy to heparin or history of heparin-induced thrombocytopenia.
- Individuals who have IgA deficiency with known antibodies against IgA.

5. Cautions and warnings

All decisions for using Octaplex should be made on an individual basis balancing the risks of continued bleeding against the prothombotic effects of PCCs.

There is a risk of thrombosis or disseminated intravascular coagulation (DIC) when patients are treated with PCC particularly with repeated dosing. Because of the risk of thromboembolic complications, caution should be exercised when administering PCC to patients with a history of coronary heart disease, liver disease, pre- or post-operative patients, or patients at risk of thromboembolic events or DIC. In each of these situations, the potential benefit of treatment should always be weighed against the risk of these complications.

If in doubt, seek advice from the Consultant Haematologist on-call.

6. Availability and product location

Octaplex is available from the Blood Transfusion laboratory on telephone extension 7217 or on-call bleep 553 during out-of-hours.

7. Dose

Octaplex contains clotting factors II, VII, IX, X, protein S and protein C. The product also contains heparin. Each vial of Octaplex contains 500 units factor IX. The dose is conventionally calculated on the desired rise of factor IX.

Octaplex when made up according to the instructions has a concentration of 25 units/ml (500 units in 20ml). The doses in the chart below are suggested in the SPC. The dose should be rounded up or down to the nearest multiple of 500 units (20 ml vial). Dose of a single infusion should not exceed 3000 units (120 ml).

Initial INR	Approximate dose* in ml/kg	Approximate equivalent dose* in units/kg
2 – 2.5	0.9 –1.3	22.5 – 32.5
2.5 – 3	1.3 – 1.6	32.5 – 40
3 – 3.5	1.6 – 1.9	40 – 47.5
> 3.5	> 1.9	50

*** Dose of a single infusion should not exceed 3000 units (120 ml).**

8. Reconstitution

Follow instructions on product package insert supplied for reconstitution of Octaplex.

Draw up diluted product into a 50ml syringe and administer via syringe pump (see section 9 for administration details). Administer immediately after reconstitution.

9. Administration

Octaplex should be given by slow IV infusion with a syringe pump, starting at a rate of 1 ml/minute (60ml/hour) for 5 minutes, increasing to maximum 3 ml/minute (180ml/hour) as tolerated (see Appendix B).

Octaplex will have immediate effect in reversal of warfarin but as the half-life of factor VII is only 6 hours, Vitamin K 5 - 10mg IV should also be given with the Octaplex. This will allow synthesis of active coagulation factors to give a sustained response and avoid the need for a second dose of Octaplex.

10. Monitoring

Recovery and the duration of effect may vary, therefore monitoring of INR during treatment is mandatory. The INR should be checked before administration, and then again immediately after completion of infusion, and at 6 hours.

11. Side effects

- **Thromboembolic complications**: Octaplex should only be used for the reversal of life, limb or sight- threatening haemorrhage. When the acute situation has resolved, consider thromboprophylaxis, e.g. anti-embolism stockings, heparin prophylaxis. The risk is higher in patients with liver disease.
- **Allergic-anaphylactic reactions** can very rarely occur; the infusion must be discontinued immediately and appropriate treatment initiated.
- **Viral transmission.** Octaplex is a blood product, therefore infectious diseases due to the transmission of infective agents cannot be totally excluded despite viral inactivation steps in preparation.
- Headache and transient increase in liver transaminases may rarely occur.

12. Documentation

The product must be prescribed as for any blood product and the batch number recorded on the prescription chart.

13. Process for monitoring compliance

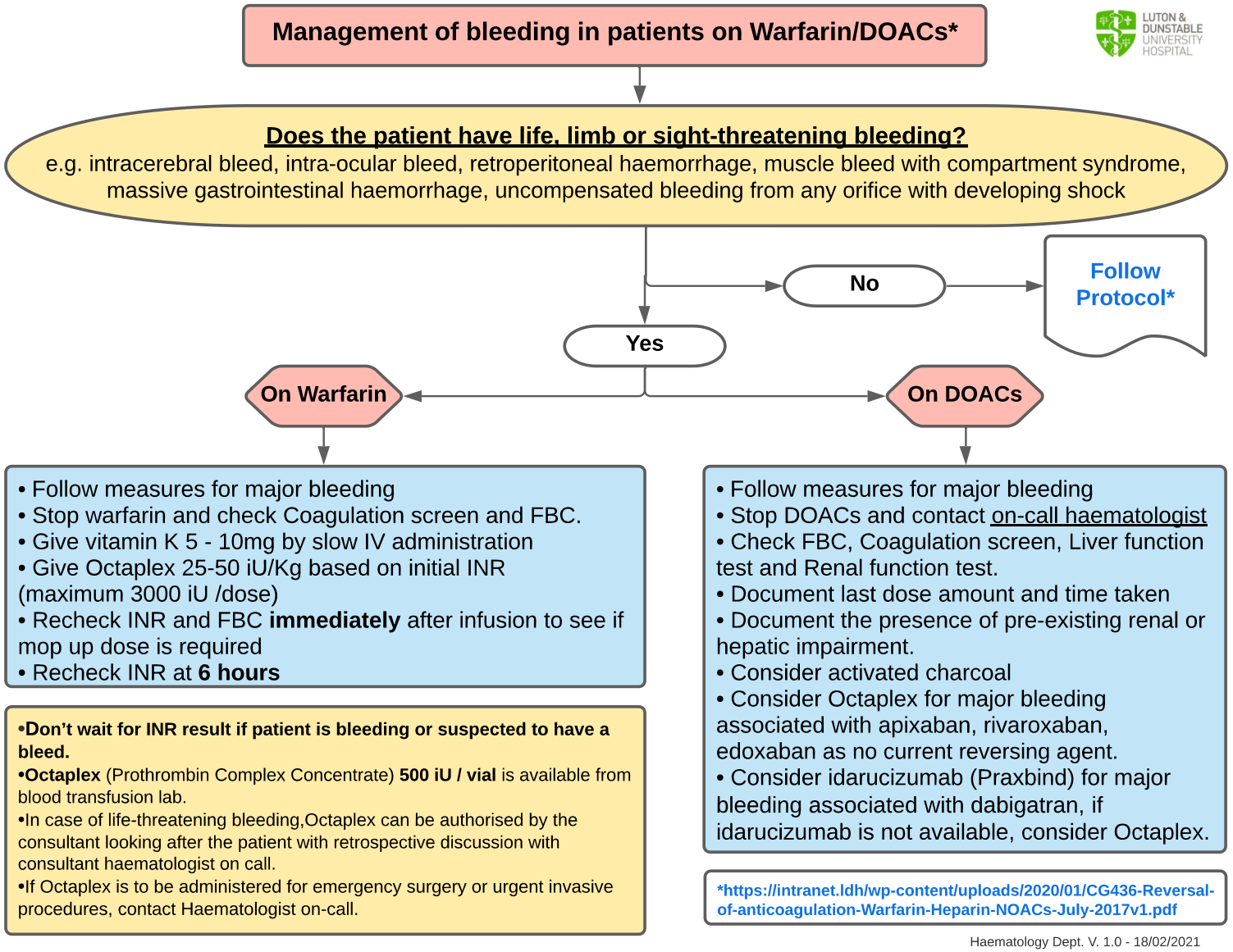
Audit criteria	Time frame/ Format /how often	How/Method	Reviewed and action plan development by who/which group	Action Plans monitored by and how often
Appropriate use of Octaplex	Annually	By Transfusion Practitioner	Hospital Transfusion Team (HTT), Hospital Transfusion Committee (HTC)	Hospital Transfusion Team (HTT), Hospital Transfusion Committee (HTC)

14. References

Keeling D, Baglin T, Tait C, Watson H, Perry D, Baglin C, Kitchen S, Makris M; British Committee for Standards in Haematology. Guidelines on oral anticoagulation with warfarin - fourth edition. *British Journal of Haematology,* 2011 Aug; **154** (3):311-24. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2011.08753.x/full

Octaplex - Summary of Product Characteristics (SPC). Accessed on 13/03/21 via https://www.medicines.org.uk/emc/product/6566/smpc

Appendix A: Flowchart on management of bleeding



Haematology Dept. V. 1.0 - 18/02/2021

Appendix B: Octaplex Administration Guide

Octaplex Administration Guide					
Dose prescribed in Factor IX International Units	1000 units	1500 units	2000 units	2500 units	3000 units (maximum single dose)
Number of vials of Octaplex to be given	2	3	4	5	6
Approximate total volume to be given	40 ml	60 ml	80 ml	100 ml	120 ml
Administration	Ensure product is at room temperature before reconstituting. Follow instructions on product package insert supplied for reconstitution of Octaplex. Draw up diluted product into a 50ml Syringe and administer via syringe pump. Use appropriate giving line to infuse.				
Rate of infusion	60 ml/hour for 5 min then increase to maximum of 180ml/hr if tolerated				
Monitoring	TPR/BP before starting, at 5 min, 15 min and completion of infusion. If a marked increase in pulse rate occurs stop infusion and seek medical advice. PT/INR should be monitored immediately post infusion and at 6 hours to assess efficacy and the need for further dosing.				
Documentation	100% Traceability required - peel off batch number from Trace Safe label and add against Octaplex prescription				