Octaplex - Full Clinical Guideline

Reference No:CG-T/2014/076

Protocol for the use of Octaplex in the reversal of Vitamin K antagonists (VKAs) or direct-acting oral anticoagulants (DOACs) in life, limb or sight threatening bleeding, or emergency surgery. Octaplex use for the reversal of DOACs should be discussed with haematology first.

Background

- The immediate reversal of vitamin K antagonists (VKA) or direct-acting oral anticoagulants (DOACs) is sometimes necessary in the case of life, limb or sight threatening bleeding, or if requiring emergency surgery.
- Other measures[1]
    - For the reversal of prolonged INR due to VKA:
        - Giving vitamin K and /or stopping VKA takes 6 hours – 4 days to take effect.
        - When reversing warfarin, intravenous vitamin K works in approximately 6-12 hours[2]. In the case of emergency surgery where there is no bleeding this is the best option if surgery can be deferred for a few hours.
    - For reversal of DOACs:
        - When possible, surgery should be delayed for 12 – 24 hours to allow the plasma level of the drug to fall.
- Fresh Frozen Plasma (FFP) should not be used as reversal of anticoagulation can be incomplete despite apparent correction of the INR[3]. FFP produces suboptimal anticoagulation reversal and should only be used if prothrombin complex concentrate (PCC) is not available.
- PCCs which contain coagulation factors II, VII, IX, and X have been shown to be superior to FFP in the context of intracranial haemorrhage[4].
- Octaplex is an available PCC in this Trust.
- IV Vitamin K 5mg must also be given alongside Octaplex for a sustained response[2].
- Tranexamic acid is a safe and effective adjunct and should be considered for all patients on a DOAC prior to and following emergency surgery[1]. It can be administered intravenously (IV) or orally (PO) (usual dose 1g three times a day).
- Octaplex supply:
    - Burton: Supply is made from blood bank after approval through haematologist.
    - Derby: Supplied from pharmacy (bleep ward pharmacist or 88364 for out-of-hours supply). A+E have the resources to make their own Octaplex.
- NOTE: **Andexanet alfa (Ondexxya)** is available as an option for reversal of apixaban or rivaroxaban in life-threatening or uncontrolled bleeding in the **gastrointestinal tract**. Discuss with haematology for further advice and see separate Trust guideline on andexanet alfa for further details.
  Note that there is lack of data to support the combined use of Andexanet alfa and Octaplex for the same bleeding episode.

Indications[2,5]:

- Life, limb or sight threatening bleeding in patients who are anticoagulated with either:
  - A VKA and who require urgent reversal of the INR or;
  - A DOAC (apixaban, rivaroxaban or edoxaban). [unlicensed use – discuss with haematologist] Note that idaruciumab (Praxbind) is available for the rapid reversal of dabigatran.
- Emergency surgery which cannot wait for either:
  - 6-12 hours for intravenous vitamin K to work to reverse VKA or;
  - 12 – 24 hours to allow the plasma level of the DOAC (apixaban, rivaroxaban or edoxaban) to fall [unlicensed use – discuss with haematologist]. Note that idarucizumab (Praxbind) is available for the rapid reversal of dabigatran.
- If Octaplex is to be administered for an indication other than the above, then the patient must be discussed with the Consultant Haematologist on-call via Switchboard. PCC should not be used to enable elective or non-urgent surgery.

Contraindications[2]:

- Previous history of heparin induced thrombocytopenia or allergy to heparin.
- Individuals who have IgA deficiency with known antibodies against IgA

Cautions[2]:

- DIC
- Severe Liver disease (risk of DIC).
- Perioperative period
- History of thrombosis (venous or arterial).
- History of myocardial infarction or coronary heart disease
- Vaccination against hepatitis A and hepatitis B may be required

Complications:

- Common: Thrombosis (arterial and venous); Embolism
- Frequency not known: DIC, HIT

Baseline tests:

- INR, APTT, Fibrinogen, FBC, LFT

Dose:

For reversal of prolonged INR due to VKA, the dose depends on INR before treatment and the patient's weight. The following table gives approximate doses required (units/kg reconstituted product per actual body weight).

Initial INR	≤ 4.5	INR >4.5
Approximate dose (unit/kg)	25	35

For reversal of DOACs (Apixaban, Rivaroxban, Edoxaban) [Unlicensed use]
Note idarucizumab (Praxbind) is a specific reversal agent available for dabigatran.

The following table gives approximate dose required for DOAC patient has been administered (units/kg reconstituted product per actual body weight).

DOAC	Apixaban, Rivaroxban,	Edoxaban	Dabigatran
Approximate dose (unit/kg)	30 (unless life-threatening GI bleed – use andexanet)	30	Not recommended (Use idaracizumab)

- Round to the nearest 500 unit vial. The maximum single dose should not exceed more than 3000 units.
- Vitamin K (phytomenadione) 5mg IV must also be given for a sustained effect on VKAs.
- Patients on a DOAC: can also consider tranexamic acid IV or PO 1g TDS

Administration[6]:

- Reconstituted in pharmacy, except A&E where this is made by nursing staff
- Give the whole dose up to 10mL per minute or 15 minutes via syringe pump.
- Octaplex should not be mixed with any other medicinal products and should be administered using a separate infusion line.
- Care should be taken to ensure that no blood enters the syringe when connecting, as there is the risk that the blood coagulates in the syringe and fibrin clots are administered to the patient.

Repeat blood tests (30 mins, and next day post administration): INR, APTT, Fibrinogen, FBC, LFT

References.

[1]UKCPA. The Handbook of Perioperative Medicines. Available at: www.ukcpa-periophandbook.co.uk. Accessed July 2021

[2]Summary of Product Characteristics. Octaplex (Octapharma Limited). Last updated July 2020. Available at www.medicines.org.uk/emc/product/7958/smpc. Accessed July 2021.

[3]Makris, M., Greaves, M., Phillips, W.S., Kitchen, S., Rosendaal, F.R. & Preston, E.F. (1997) Emergency oral anticoagulant reversal: the relative efficacy of infusions of fresh frozen plasma and clotting factor concentrate on correction of the coagulopathy. *Thrombosis and Haemostasis*, **77**, 477–480.

[4]Yasaka, M., Minematsu, K., Naritomi, H., Sakata, T. & Yamaguchi, T. (2003) Predisposing factors for enlargement of intracerebral hemorrhage in patients treated with warfarin. *Thrombosis and Haemostasis*, **89**, 278–283.

[5]Keeling D, Campbell Tait R, Watson H on behalf of the British Committee for Standards in Haematology. Peri-operative management of anticoagulation and antiplatelet therapy. British Journal of Haematology. 2016; 175:602-612

[6]NHS Injectable Medicines Guide. Available at: medusa.wales.nhs.uk. Accessed: July 2021

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	Clinical Pharmacy Team
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