Direct-acting oral anticoagulants (DOACs)

This guideline details management of acute overdose of the direct thrombin inhibitor (dabigatran), and Factor Xa inhibitors (rivaroxaban and apixaban)

Toxicity / Risk Assessment

- *Single-dose ingestions in naïve individuals or double dose ingestions in those on therapy are benign and do not require investigations or monitoring.*
- *Coagulation studies and anti-Xa concentration do NOT reliably predict risk of haemorrhage following exposure to DOACs.*
- *Risk factors for increased toxicity: renal failure, uncontrolled hypertension, concomitant use of p-glycoprotein inhibitors with Factor Xa inhibitors e.g. verapamil, ketoconazole.*
- *Elderly or disabled patients are at increased risk of complications from falls.*

Clinical features:

- Usually asymptomatic
- Haemorrhage is rare even in massive overdose

Management: Prevention of secondary risk factors for haemorrhage (falls or ↑BP) is the mainstay of treatment

Decontamination: 50g activated charcoal (paediatric: 1g/kg) within 2 hours of overdose

Management of life-threatening haemorrhage, or haemodynamic instability:

- Resuscitate and administer – **Prothrombinex** 50 IU/kg intravenously, and two units of fresh frozen plasma (**FFP**)
- **Tranexamic acid** 1g IV followed by 1g IV over 8 hours. Urgent haematology consult +/- massive transfusion protocol
- Vitamin K is **NOT** effective in the management of haemorrhage caused by DOAC overdose
- Whilst dabigatran is dialysable, the risks of bleeding versus benefit should be carefully considered
- There is **no** role for dialysis in Factor Xa inhibitor overdose
- Idarucizumab (for dabigatran reversal) should be administered to patients with severe life-threatening haemorrhage associated with dabigatran overdose. Dose: 5g intravenously as single dose (discuss with haematologist)
- Reversal agents for Factor Xa inhibitors (rivaroxaban and apixaban) are not routinely available

Management of patients without active bleeding (the majority):

- Check Thrombin Time (TT) for dabigatran or anti-Xa concentration for Xa inhibitors at time of presentation

(NOTE: anti-Xa concentration interpretation is dependent on individual DOAC/assay: discuss with local laboratory service)

- Repeat TT (for dabigatran) and anti-Xa concentration (for rivaroxaban and apixaban) at 6 hourly intervals

Disposition:

- Minor accidental exposure does not require admission or investigation. Well patients with normal TT and anti-Xa concentrations at 12 hours post overdose can be discharged with advice to avoid activity with high risk of injury
- Patients with abnormal coagulation studies or anti-Xa concentration should be admitted
- Patients normally receiving a DOAC therapeutically can be discharged once the TT/anti-Xa conc. is within safe range