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):

- Following dabigatran or rivaroxaban exposures, APTT / INR / PT will be deranged if there is significant coagulopathy
- Following apixaban exposures, some patients may benefit from measurement of Apixaban-Anti-Xa concentration (discuss with a clinical toxicologist)

Disposition:

- Minor accidental exposures do not require admission or investigation.
- **Dabigatran:** discharge pending mental health assessment if no bleeding + normal APTT at 12 hours
- **Rivaroxaban:** discharge pending mental health assessment if no bleeding + normal INR at 12 hours
- **Apixaban:** discharge pending mental health assessment if no bleeding + falling Anti-Xa conc. at 12 hours (Anti-Xa concentration available) OR no bleeding + normal APPT / INR/PT at 24 hours (Anti-Xa concentration NOT available)