

## Management of Bleeding in Patients Taking Oral Anticoagulants

### Vitamin K antagonists:

Warfarin (half-life 40h)  
Acenocoumarol  
Phenindione

### Direct thrombin inhibitors:

**Dabigatran** – Half-life 12-14 hours,  
or 27h if Creat.Clearance<30ml/min

### Factor Xa inhibitors:

**Rivaroxaban** (half-life 5-9 hours, 11-13h in the elderly)  
**Apixaban** (half-life 12 hours)  
**Edoxaban** (half-life 10-14 hours)

#### Minor Bleeding

1. Stop Warfarin and check INR.
2. If INR >5, give 1-3mg Vitamin K IV (Konakion MM 2mg in 0.2mL ampoules). Repeat dose at 24h if INR still too high. Restart when INR<5.0 and happy bleeding improving
3. If INR<5 consider Vitamin K

#### Minor Bleeding

Consider oral activated charcoal if dabigatran or apixaban taken < 2 hrs ago

1. Local haemostatic measures.
2. Mechanical compression.
3. Tranexamic acid topically or orally (1g tds orally, or 1.5g tds if weight>100kg. Reduce in renal impairment)
4. Delay next dose or discontinue treatment as appropriate.

#### Moderate to Severe Bleeding

1. Stop Warfarin and check INR.
2. Give vitamin K 5 to 10mg by slow intravenous injection (over at least 30 seconds). May alternatively be given by i.v. infusion (draw up 0.5 to 1 ml of Konakion MM and add to a 50ml bag of Glucose 5%). Consider re-checking INR after 6 hrs if response inadequate; dose may be repeated.
3. If major bleeding, Senior clinician to consider prothrombin complex concentrate (Beriplex® 25-50 IU/kg i.v.). Recheck INR ten minutes after administration (consider further dose). Obtain from Transfusion.
4. Advice available to Senior Clinician from on-call Consultant Haematologist, if required.

#### Moderate to Severe Bleeding

Give oral activated charcoal if dabigatran or apixaban taken < 2 hrs ago.  
If rapidly deployable, haemodialysis/haemofiltration offers the possibility of enhanced dabigatran clearance.

1. Control haemorrhage:
  - Local haemostatic measures
  - Mechanical compression
  - Consider surgical intervention, wound packing or interventional radiology.
  - Tranexamic acid 1g by slow i.v. injection over 10 mins followed by 1g tds by slow i.v. infusion over 8 hrs.
  - In Dabigatran-treated patients consider PRAXBIND (reversal agent) for severe or life-threatening bleeding. If out-of-hours, obtain from on-call pharmacist via switchboard. 5g dose, follow product insert. (No indication Beriplex/PCC)
2. Fluid replacement. Maintain good urine output.
3. Maintain tissue oxygenation – oxygen and red cell transfusion (aim for Hb > 70g/L).
4. Consider platelets if level less than 70 to 80 x 10<sup>9</sup>/L or patient on concomitant antiplatelet therapy.

**Ongoing life-threatening bleeding.** Consider use of Prothrombin Complex Concentrate. No evidence that this reverses effect of these drugs in-vivo/improves outcomes, but in absence of specific antidote is sometimes considered. Consider time since last dose and drug half-life. Advice available to Senior Clinician from on-call Haematology Consultant.

#### Moderate to Severe Bleeding

## Additional Notes:

### **Bleeding Classification**

Moderate to Severe Bleeding:

- A clinically overt bleed causing Hb to fall > 20g/L or a bleed requiring transfusion of  $\geq 2$  units packed red cells, or
- Symptomatic bleeding into a critical area or organ (i.e. intracerebral, intraocular, intraspinal, intraabdominal, retroperitoneal)

Life-threatening Bleeding:

- Symptomatic intracranial bleed,
- Hb fall of > 50g/L, bleed that requires  $\geq 5$  units of packed red cells
- Hypotension requiring inotropic agents or an organ related bleed requiring urgent surgical intervention

**Rivaroxaban, apixaban and edoxaban do not currently have a specific reversal agent** and their anticoagulant effect cannot be reversed by administration of vitamin K or plasma infusion.

### **Blood Tests**

- Check coagulation screen including prothrombin time (PT), activated partial thrombin time (aPTT) and fibrinogen assay
- Check FBC, electrolytes including calcium, renal function, and LFTs. The latter is to consider if other causes of coagulopathy may be present
- Indicate time of last dose of dabigatran, rivaroxaban, apixaban and edoxaban when requesting tests

NB half-lives are:

- Warfarin (40 hours)
- Acenocoumarol (8-11 hours)
- Phenindione (5-6 hours)
- Dabigatran (12-14 hours – 27 hours if CrCl < 30ml/min)
- Rivaroxaban (5-9 hours – 11-13 hours in the elderly)
- Apixaban (12 hours)
- Edoxaban (10-14 hours)

Authors: Dr Phil Robson / Marcus Jones

Approved by Drug & Therapeutics Committee December 2018

Review December 2021

References:

1. Makris M, Van Veen J, Tait C, et al. British Committee for Standards in Haematology: Guideline on the management of bleeding in patients on antithrombotic agents. *British Journal of Haematology*, 2012, 160, 35–46
2. Summary of Product Characteristics for Konakion MM. Last updated on the eMC: 05/10/2016. Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)
3. Summary of Product Characteristics for Pradaxa® (dabigatran) . Last updated on the eMC: 09/07/2018 Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)
4. Summary of Product Characteristics for Xarelto® (rivaroxaban) . Last updated on the eMC: 29/08/2018. Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)
5. Summary of Product Characteristics for Eliquis® (apixaban). Last updated on the eMC: 16/08/2018. Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)
6. Summary of Product Characteristics for Lixiana®(edoxaban). Last updated on the eMC: 10/08/2018. Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)
7. Summary of Product Characteristics for Marevan® (warfarin) . Last updated on the eMC: 16/04/2018. Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)
8. Summary of Product Characteristics for Sinthrome® (acenocoumarol). Last updated on the eMC: 05/04/2016. Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)
9. Summary of Product Characteristics for phenindione (Concordia brand). Last updated on the eMC: 28/07/2017. Electronic Medicines Compendium. [www.medicines.org.uk](http://www.medicines.org.uk)