Guidelines for Management of Patients on Rivaroxaban (Xarelto) or Apixaban (Eliquis)

Conversion to or from parental anticoagulants

For patients currently receiving a parenteral anticoagulant (eg LMWH), start rivaroxaban or apixaban 0 to 2 hours before the time that the next dose of the parenteral drug was to have been administered or at the time of discontinuation of a continuously administered parenteral drug (e.g. intravenous unfractionated heparin).

For patients currently taking rivaroxaban or apixaban, the first dose of the parenteral anticoagulant should be given at the time that the next dose of rivaroxaban or apixaban would be given.

Conversion to or from warfarin

When converting patients with atrial fibrillation from warfarin therapy to rivaroxaban, or apixaban discontinue warfarin and start rivaroxaban or apixaban when the international normalized ratio (INR) is below 2.0 (If the INR is above 2.0 this usually occurs 3-5 days after discontinuing warfarin).

For patients currently taking rivaroxaban or apixaban, warfarin therapy can be introduced at the time that the next dose of rivaroxaban or apixaban would be given. The requirement for LMWH during warfarin initiation, and whether rapid or slow warfarin initiation is appropriate will depend on clinical circumstances.

INR measurement is not appropriate to measure the anticoagulant activity of rivaroxaban or apixaban and it should not be used for these purposes. Patients on rivaroxaban or apixaban do **not** require routine coagulation monitoring.

Management of Bleeding

There is no antidote to rivaroxaban or apixaban.

In the event of serious haemorrhagic complications:

- Discontinue treatment with rivaroxaban or apixaban (half life around 9 hours for both with normal renal function).
- Consult the on call haematologist/blood transfusion.
- Initiate appropriate clinical support, e.g. surgical or local hemostasis, transfusion of red cells, volume substitution, intropic drugs.
- Consider administration of platelet concentrates in case where thrombocytopenia is present or long acting antiplatelet drugs have been used.
- Investigate the source of bleeding.

Unlike dabigatran where 85% of clearance is renal, only around 1/3 of rivaroxaban/apixaban undergoes renal clearance. Due to high plasma protein binding, rivaroxaban/apixaban is not expected to be dialysable.

There is some experimental evidence from normal volunteers to support the role of activated prothrombin complex concentrates. However, their usefulness in clinical settings has not been evaluated and therefore these alternatives cannot be relied upon.

Overdose

Due to limited absorption a ceiling effect with no further increase in average plasma exposure is expected at supra-therapeutic doses of 50mg of rivaroxaban and above. The use of activated charcoal to reduce absorption in cases of overdose may be considered.

Discontinuation before surgery

The half life of rivaroxaban and apixaban is around 9 hours. If an invasive procedure or surgical intervention is required, rivaroxaban or apixaban should be stopped at least 24 hours before the procedure where possible. If the procedure cannot be delayed the increased bleeding due to rivaroxaban or apixaban should be assessed against the urgency of the procedure. As above there is no reversal agent.

Rivaroxaban or apixaban can be restarted after the procedure when the clinician carrying out the procedure is happy that adequate haemostasis has been achieved. In most cases this is likely to be the day after the procedure.

Monitoring

No routine coagulation test monitoring is required.
Rivaroxaban and apixaban will lead to mild prolongation of the APTT and PT but these can not be reliably used to confirm or exclude a rivaroxaban or apixaban anticoagulant effect. Rarely there may be a role for using specific anti-Xa assays to assess the anticoagulant effect but evidence is limited – discuss with on call haematologist.

More information can be obtained from the rivaroxaban summary of product characteristics http://www.medicines.org.uk/EMC/medicine/25586/SPC/Xarelto+20mg+film-coated+tablets/ or the apixaban summary of product characteristics http://www.medicines.org.uk/emc/medicine/24988

For any queries please contact Dr Ron Kerr Consultant Haematologist (bleep 4874). If not available in an emergency contact the on call haematologist.