NHS Tayside Drug & Therapeutics Committee

Local Treatment Protocol for rivaroxaban 10mg tablets
(Xarelto®)▼

1.	**New medicine name:** Rivaroxaban 10mg film- coated tablets (Xarelto®)
2.	**Licensed indication(s):** Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.
3.	**Scottish Medicines Consortium advice:** Rivaroxaban is accepted for use in the above indications and in three large phase III trials was superior to low molecular weight heparins (LMWH) in reducing VTE and all cause mortality whilst having a similar incidence of bleeding events. **Medicines Advisory Group advice:** ***(to be completed by MAG following receipt of protocol)*** ***Hospital only for the prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.***
4.*	**Prescriber details:** **Hospital Only – Orthopaedics.** **Note-** The full course will be supplied by the hospital pharmacy prior to discharge**.**
5.*	**Criteria for patient selection:** 1st line in adult patients undergoing elective hip or knee replacement surgery.
6.	**Administration details:** The dose of rivaroxaban is 10mg orally once daily starting 6 to 10 hours after surgery. <u>Duration of therapy:</u> Knee Surgery patients – 14 days. Hip Surgery patients – 35 days. **Patients on Anti-platelet therapy:** Stop prior to admission as per current NHS Tayside guidelines. *Currently being updated.* **Patients on combination anti-platelet therapy and / or at very high risk of cardiovascular events (eg recent coronary intervention or angioplasty) will be assessed in pre-admission by a consultant anaesthetist and an individual management plan formed and documented in consultation with a cardiologist if required.** Patients already on warfarin should not be given rivaroxaban and should be treated as per current guideline or be referred to anaesthetic pre-assessment clinic and an individual management plan formed and documented.

Anti-platelets should routinely be re-started the day after the rivaroxaban has been stopped. The patient and GP should be informed of this through pre-admission clinics and immediate discharge letters respectively.

7. Contra-indications:

Hepatic disease associated with coagulopathy and clinically relevant bleeding risk.
Clinically significant active bleeding.
Renal impairment – Creatinine Clearance < 15ml/min.

8. Side-effects/cautions:

Common (>1/100) adverse events include bleeding, anaemia, nausea and increased liver transaminases and GGT.

Due to the mode of action the most pertinent side-effect to be monitored is occult or overt bleeding. Any such new bleeding must urgently be assessed by medical personnel.

Patients with liver or renal impairment should be closely monitored for signs of bleeding.

As with other anti-coagulants caution should be exercised with patients at increased bleeding risk from other causes

<u>Spinal/Epidural Anaesthesia or Puncture:</u>

Such patients should be monitored frequently for signs of neurological impairment as would be the case with other anti-coagulants. Usual postoperative observations in patients with epidural or spinal anaesthesia apply.

<u>Removal of peripheral nerve or epidural catheters</u>

Peripheral nerve catheters or epidural catheters are not to be removed earlier than 18 hours after the last administration of rivaroxaban. After catheter removal the next rivaroxaban dose must not be administered until at least 6 hours have elapsed.

As rivaroxaban is a black triangle new drug then any adverse events should be reported to the MHRA via the yellow card reporting system.

9.* Monitoring - response to treatment:

There is no monitoring required during treatment.
INR measurements have no value in assessing efficacy of treatment or potency of effect.

10.* Monitoring – treatment safety:

Patients will require monitoring for signs and symptoms of bleeding throughout the duration of treatment and for 48 hours post treatment as with other anti-coagulants. Patients should be counselled on the symptoms and signs of bleeding prior to discharge and an information leaflet supplied. This is particularly important for the at risk patient groups highlighted above.

Overdose:

Maximum plasma concentration is 2-4 hours post dose
Half life is 7-11 hours (drug eliminated after 5 half lives 35-55 hours)
There is no specific antidote.

Bleeding should be managed in a supportive manner, severe bleeding would warrant urgent haematology referral.

11. Drug Interactions

Rivaroxaban use is contra-indicated with azole-antimycotics (ketoconazole, itraconazole, voriconazole and posiconazole) as well as HIV protease inhibitors (for example ritonavir). These drugs may increase rivaroxaban plasma concentrations to a clinically significant level and lead to an increased bleeding risk. Interaction with fluconazole or macrolide antibiotics however is not deemed clinically significant. They can be co-administered with caution but they may increase the anticoagulant effect of rivaroxaban

Co-administration of strong CYP3A4 inducers such as rifampicin, carbamazepine, phenytoin, phenobarbital or St John's Wort can significantly reduce plasma concentrations of rivaroxaban therefore caution should be exercised as the anti-coagulant effect will be reduced.

Due to increased risk of bleeding caution should be exercised in the combined use of rivaroxaban with NSAIDS, anti-platelet agents or other anti-coagulants.

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Date: 15/01/09

13.* Review date: January 2010

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