MEMO

TO: WakeMed Department of Pharmacy
FROM: Cardiology Core Team
DATE: December 12, 2011
SUBJECT: New drug update: Xarelto® (rivaroxaban)

General information: rivaroxaban is an oral factor Xa inhibitor with two FDA approved indications:
- To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation
- For DVT prophylaxis in patients who have undergone knee or hip replacement surgery

Black Box Warnings

A: Discontinuation of Xarelto in patients with nonvalvular atrial fibrillation puts them at risk of thrombotic events. If Xarelto must be discontinued for reasons other than pathological bleeding, recommend administering another anticoagulant in place of Xarelto.

B: Epidural or spinal hematomas have occurred in patients on Xarelto who are receiving neuraxial anesthesia or undergoing spinal puncture (see package insert/comparison chart for further details)
- An epidural catheter should not be removed earlier than 18 hours after last administration of rivaroxaban. The next dose of rivaroxaban is not to be administered earlier than 6 hours after removal of catheter.

Contraindications for use: rivaroxaban is contraindicated in patients with active pathological bleeding

Warnings/Precautions:
- Hepatic impairment (for both nonvalvular atrial fibrillation and DVT prophylaxis): Avoid in patients with moderate-to-severe hepatic impairment (Child-Pugh classes B/C) or in patients with any hepatic disease associated with coagulopathy

Dosing:

Nonvalvular Atrial Fibrillation:

| CrCl > 50 ml/min | 20 mg once daily with the evening meal |
| CrCl 15 – 50 ml/min | 15 mg once daily with the evening meal |
| CrCl <15 ml/min | **avoid use** |

DVT prophylaxis: *do not initiate until at least 6-10 hours after surgery (once hemostasis established)

| Knee Replacement | 10 mg once daily with or without food | 12-14 day duration of therapy |
| Hip Replacement | 10 mg once daily with or without food | 35 days of therapy recommended |
| CrCl <30ml/min | **avoid use** |

Administration:
- May be crushed and given via a feeding tube gastric placement of the tube should be confirmed since absorption is decreased in the small intestine
- Please ensure the times for administration are followed in the Siemen’s PCO
  - Nonvalvular Atrial Fibrillation: 20 mg once daily at 18:00
    - Renal Dose: 15 mg once daily at 18:00
  - DVT Prophylaxis in Orthopedic Patients: 10 mg once daily at 09:00
    - No renal dose
Monitoring:
- In the major clinical trials for rivaroxaban monitoring of PT, PT/INR and anti Xa did NOT occur.
- Certain patient populations (renal insufficiency, hepatic impairment, low body weight or obesity) may benefit from PT monitoring, which correlates well with rivaroxaban concentrations; however, the PT time available at WakeMed is not reliable for monitoring. The PT must be specific to rivaroxaban which we do not have.
- PT time, INR and aPTT are all elevated in a dose-dependent fashion. Anti-factor Xa activity is also augmented by rivaroxaban.

Common adverse effects:
- Bleeding (>5%)

Perioperative dosing: Discontinue rivaroxaban 24 hours prior to surgical procedure. Re-start as soon as adequate hemostasis established. Consider transition to parenteral anticoagulant if patient unable to take oral.

Transition between rivaroxiban and other anticoagulants:
- SC anticoagulant (i.e. fondaparinux, enoxaparin) to rivaroxaban:
  - Initiate rivaroxaban 2 hours prior to the next scheduled dose of the SC anticoagulant
- IV anticoagulant (i.e. heparin) to rivaroxiban:
  - Initiate rivaroxaban when heparin infusion stopped
- Rivaroxaban to IV or SC anticoagulant:
  - Initiate IV or SC anticoagulant 12 hours after the last dose of rivaroxaban; 24 hours if CrCl<30 ml/min
- Warfarin to rivaroxaban:
  - Discontinue warfarin and immediately start rivaroxaban when the patient’s INR drops below 3.0

Toxicology: There is no specific reversal agent for rivaroxaban and it is not expected to be dialyzable. Overdose is expected to result in bleeding – if this occurs appropriate supportive measures should be taken. Anecdotal reports of prothrombin complex concentrate (PCC) have been reported to be successful.

Pharmacist Role:
- Counseling:
  - Any patient receiving rivaroxaban as a new initiation or continuation of a home medication at WakeMed will need counseling by pharmacy.
- Monitoring:
  - All rivaroxaban patients should be monitored on the anticoagulation monitoring form for SCr, CBC, and platelets every 72 hours.

If you need additional information, please contact Erin Allender, PharmD at eallender@wakemed.org or 795.3789 or Jenna Huggins, PharmD at jhuggins@wakemed.org or 539.0471.