Xarelto® *(Rivaroxaban)*

Category[1] Anticoagulant (Factor Xa Inhibitor)

Mechanism of Action[2]

Rivaroxaban is a direct, selective, and reversible factor Xa inhibitor in both the intrinsic and extrinsic coagulation pathways.

Indications[1]

Rivaroxaban is indicated for the prevention of venous thromboembolic events (VTE) in patients who have undergone elective total hip replacement or total knee replacement surgery.

Dosing[1]

- 10 mg po once daily.
- The initial dose should be taken 6-10 hours after surgery if hemostasis is established. (Delay treatment if hemostasis has not been established).

Treatment Duration[1]: Total hip replacement: 35 days
Total knee replacement: 14 days

Contraindications[1,2]

- Hepatic disease associated with coagulopathy and a clinically relevant bleeding risk.
- Clinically significant active bleeding (hemorrhagic manifestations & bleeding diathesis)
- Lesions at increased risk of clinically significant bleeding such as hemorrhagic or ischemic cerebral infarction within the last 6 months or patients with spontaneous impairment of hemostasis
- Concomitant **systemic** treatment with strong inhibitors of both *CYP3A4* & P-glycoprotein
- Pregnancy or Lactation

Warnings/Precautions[2]

- Bleeding is the most common complication and should be monitored
- Due to an increased risk of bleeding, avoid use with direct thrombin inhibitors, unfractionated heparin or heparin derivatives, low molecular weight heparins, aspirin, coumarin derivatives, and sulfinpyrazone.
- Use caution with NSAIDs and other platelet aggregation inhibitors
- Formulation contains lactose; use is not recommended in patients with lactose or galactose
- Avoid removal of epidural catheter for at least 18 hours following last rivaroxaban dose and avoid rivaroxaban administration for at least 6 hours following epidural catheter removal. (Risk of hematomas occurring)

Adverse Effects[2]

- Nausea (1%)
- Major bleeding: (<1% - 2%)
- Nonmajor Bleeding: (4% to 7%)
- Anemia (1%)
- Increased transaminases (2%)

Drug Interactions[2]

Rivaroxaban may increase levels/effects of: Anticoagulants, Ibritumomab, Tositumomab & Iodine I 131 Tositumomab

Rivaroxaban levels/effects may be increased by: Antiplatelet agents, CYP3A4 inhibitors, Dasatinib, Erythromycin, Herbs (anticoagulant/antiplatelet), Metronidazole systemic, NSAIDs, Pentosan polysulfate sodium, P-glycoprotein inhibitors, Prostacyclin analogues, Salicylates, Thrombolytic agents

Rivaroxaban levels/effects may be decreased by: CYP 3A4 inducers (strong), Deferasirox, Herbs (CYP3A4 inducers), P-glycoprotein inducers

Pharmacokinetics[2]

Bioavailability: ~100%
Half-life elimination: 5-9 hours (Young individual); 11-13 hours (Elderly)

Special Populations[1]

- *Renal Impairment:* Use not recommended in patients with severe renal impairment. Caution should be used in those with moderate renal impairment (Cl_{cr} 30-49mL/min)
- *Body Weight:* Use caution with patients weighing <50kg or >120kg.
- *Pediatrics:* Use of rivaroxaban not recommended in children <18 years old

Efficacy[3]

According to several studies, rivaroxaban appears slightly more effective than enoxaparin at preventing VTE post-knee/hip replacement surgery.

Safety[3]

Bleeding rates do not appear statistically significant between rivaroxaban and enoxaparin (0.3% vs. 0.2%). Rivaroxaban is otherwise well tolerated.

Advantages of Rivaroxaban[3]

- Oral administration
- Once daily dosing
- Minimal dose adjustments
- No INR monitoring
- Immediate onset of anticoagulation
- Has EDS status in the Saskatchewan Formulary

Available Products / Costs[4]

10mg Tablet: $474 (50 tablets)

EDS Criteria for Rivaroxaban[5]

(a) For prophylaxis following total knee arthroplasty for up to 14 days following the procedure.
(b) For prophylaxis in patients undergoing total hip replacement for up to 14 days following the procedure.

References

1. Bayer Inc. Xarelto (rivaroxaban). [Product Monograph] Toronto ON. September 10, 2008. <http://www.bayer.ca/files/XARELTO-PM-ENG-10SEP2008-119111.pdf>
2. Lexi-Drugs Online. Rivaroxaban. [Product Monograph] Lexi-Comp Inc. c2010. <http://online.lexi.com.cyber.usask.ca/crlsql/servlet/crlonline?siteid =293>
3. Saskatchewan Drug Information Services. New Oral Anticoagulants. Saskatoon SK 27(1): February 2010. <www.druginfo.usask.ca/pdf/New_Oral _Anticoagulants.pdf>
4. McKesson Canada. PharmaClik: Xarelto. Saint-Laurent, QB; C2005. Accessed March 15, 2010. <http://clients.mckesson.ca>
5. Government of Saskatchewan: Drug Plan and Extended Benefits Branch; Online Formulary. Appendix A: Exception Drug Status Program; Rivaroxaban. Regina SK; c2000. Accessed March 15, 2010. <http://formulary.drugplan. health.gov.sk.ca/publications/APPENDIX%20A.pdf>