

NOVEL ORAL ANTICOAGULANTS (May 2013) – SFVA Anticoagulation and Thrombosis Service

	Dabigatran (PRADAXA[®] 1,2	Rivaroxaban (XARELTO[®] 3,4,5,6	Apixaban (ELIQUIS[®] 7
Mechanism	Oral direct thrombin inhibitor	Oral direct Factor Xa inhibitor	Oral direct Factor Xa inhibitor
Approved Uses	AFIB	AFIB VTE treatment and secondary prevention VTE prophylaxis post-hip/knee replacement	AFIB
Frequency of dosing	BID	Daily/BID	BID
Dosing	<p>AFIB CrCl > 30 mL/min: 150 mg PO BID CrCl 30-50 mL/min and co-administered with dronedarone or ketoconazole: 75 mg PO BID CrCl < 30 mL/min: NOT RECOMMENDED</p>	<p>AFIB CrCl > 50 mL/min: 20 mg PO Daily CrCl 30-50 mL/min: 15 mg PO Daily CrCl < 30 mL/min: NOT RECOMMENDED VTE Treatment and secondary prevention 15 mg PO BID for 21 days, then 20 mg Daily CrCl < 30 mL/min: NOT RECOMMENDED VTE prevention s/p hip/knee replacement 10 mg PO Daily w/ or w/o food for 35 days (hip) or 12 days (knee), starting 6-10 hrs post-op, after hemostasis achieved CrCl < 30 mL/min: NOT RECOMMENDED</p>	<p>AFIB 5 mg PO BID 2.5 mg PO BID if 2 or more of the following: >80yo, <60kg, SCr >1.5mg/dL 2.5 mg PO BID if co-administered with strong 3A4/P-gp dual inhibitors CrCl < 25 mL/min: NOT RECOMMENDED</p>
Food	w/ or w/o food	w/food (for 15 and 20 mg tablets)	w/ or w/o food
Crushable?	No	Can crush; do not administer via J tube	Can crush and administer orally or via NG tube
Renal adj?	Yes	Yes	Yes
Kinetics	t ½=12-17 hours; tmax=2 hours	t ½=5-9 hours; tmax=3 hours	t ½=12 hours; tmax=3 hours
Influences INR?	Yes	Yes	Yes
Influences aPTT?	Yes	Yes	Yes
Monitor?	No; aPTT and TT used to detect presence of dabigatran	No; PT and anti-Xa levels used to detect presence of rivaroxaban	No; prolongs INR, PT, and aPTT
Drug Interactions	<p>Avoid rifampin, SJW, and, possibly carbamazepine</p> <p>Caution with amiodarone, clarithromycin, dronedarone, ketoconazole, quinidine, verapamil. No dosage adjustment of dabigatran is recommended if CrCl > 50 mL/min</p> <p>Reduce dose to 75 mg PO BID if CrCl 30-50 mL/min and co-administered with dronedarone or ketoconazole</p>	<p>Avoid carbamazepine, conivaptan, indinavir/ritonavir, itraconazole, ketoconazole, lopinavir/ritonavir, phenytoin, rifampin, ritonavir, SJW</p> <p>Caution with the concomitant administration of combined P-gp inhibitors and/or weak or moderate inhibitors of CYP3A4 (e.g., amiodarone, azithromycin, diltiazem, dronedarone, erythromycin, felodipine, quinidine, ranolazine, verapamil) with rivaroxaban, particularly in patients with impaired renal function</p>	<p>Avoid carbamazepine, phenytoin, rifampin, SJW</p> <p>Avoid clarithromycin, itraconazole, ketoconazole, and ritonavir in patients already taking ELIQUIS at a reduced dose of 2.5 mg twice daily</p> <p>Caution with clarithromycin, itraconazole, ketoconazole, and ritonavir</p>
Switching from Novel Oral Anticoagulant (NOAC) to warfarin	<p>Consider d/c dabigatran and bridging with parenteral anticoagulant</p> <p>[Initiate parenteral anticoagulant 12 hrs (CrCl ≥30 mL/min) or 24 hrs (CrCl <30 mL/min) after the last dose of dabigatran]</p>	<p>Consider d/c rivaroxaban and bridging with parenteral anticoagulant</p> <p>(Initiate parenteral anticoagulant at the time the next dose of rivaroxaban would have been taken)</p>	<p>Consider d/c apixaban and bridging with parenteral anticoagulant</p> <p>(Initiate parenteral anticoagulant at the time the next dose of apixaban would have been taken)</p>
Warfarin to NOAC	INR < 2.0	INR < 3.0	INR < 2.0
Peri-surgery *if high bleed risk surgery, hold dose for max number of days	<p>CrCl ≥ 50 mL/min: last dose 2-3* days prior to surgery CrCl <50 mL/min: last dose 3-5* days prior to surgery</p>	<p>CrCl >30 mL/min last dose 2-3* days prior to surgery CrCl 15-30 mL/min last dose 3-4* days prior to surgery</p>	<p>CrCl > 50 mL/min last dose 2-3* days prior to surgery CrCl 30-50 last dose 3-4* days prior to surgery</p>
Age Considerations	>75 yo shows increased major bleeds	Contraindicated if <18 yo	2.5 mg PO BID if >80 yo and <60kg or SCr >1.5mg/dL
Special Considerations	<p>Dyspepsia is common and starts within 1st 10 days GI bleeding risk higher with dabigatran vs warfarin Dabigatran unlikely to provide cardioprotection (unlike warfarin)</p>	GI bleeding risk higher with rivaroxaban vs warfarin	
Supportive Care	Activated charcoal, dialysis, supportive care	Activated charcoal, supportive care	Activated charcoal, supportive care

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Studies	<p>RE-LY (AFIB)⁸ Superior to warfarin in reducing CVA, with equivalent bleeding rates to warfarin except decreased ICH</p>	<p>ROCKET-AF (AFIB)⁹ Non-inferior in reducing CVA; equivalent bleeding rates to warfarin except decreased ICH</p> <p>EINSTEIN (VTE)¹⁰ Equivalent to warfarin for prevention of VTE recurrence; equivalent or lower bleeding risk</p> <p>RECORD (hip/knee)^{11,12} Superior efficacy for DVT, nonfatal PE, and death; equivalent bleeding rates to warfarin</p>	<p>ARISTOTLE (AFIB)¹³ Mortality benefit, superior efficacy in preventing CVA, and decreased risk for bleeding to warfarin including ICH</p>

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5. *Rivaroxaban VTE Treatment Criteria for Use*. VA Pharmacy Benefits Management Services, March 2013. Web. 6 May 2013.
6. *Rivaroxaban VTE Prophylaxis Criteria for Use*. VA Pharmacy Benefits Management Services, June 2012. Web. 6 May 2013.
7. Pfizer (2013). *Apixaban: Highlights of prescribing information*. New York City, NY.
8. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. *N Engl J Med*. 2009;361:1139-1151.
9. Manesh RP, Mahaffey KW, Garg J, et al. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. *N Engl J Med*. 2011;365:883-891.
10. Einstein Investigators. Oral Rivaroxaban for Symptomatic Venous Thromboembolism. *N Engl J Med*. 2010;363:2499-2510.
11. Eriksson BL, Borris LC, Friedman RJ, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med*. 2008;358:2765-2775.
12. Lassen MR, Ageno W, Borris LC, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty *N Engl J Med*. 2008;358:2776-86.
13. Granger CB, Alexander JH, McMurray JJV, et al. Apixaban versus Warfarin in Patients with Atrial Fibrillation. *N Engl J Med*. 2011;365:981-992.