Direct Oral Anticoagulants (DOACs)

		Dabigatran (Pradaxa)	Rivaroxaban (Xarelto)	Apixaban (Eliquis)	Edoxaban (Savaysa)
Drug Classification		Selective thrombin inhibitor	Selective direct Xa inhibitor	Selective direct Xa inhibitor	Selective direct Xa inhibitor
FDA Approved Indications		- Nonvalvular AF - Treatment of VTE - Reduce risk of recurrent VTE - VTE prophylaxis (hip)	- Nonvalvular AF - Treatment of VTE - Reduce risk of recurrent VTE - VTE prophylaxis (hip & knee)	- Nonvalvular AF - Treatment of VTE - Reduce risk of recurrent VTE - VTE prophylaxis (hip & knee)	- Nonvalvular AF - Treatment of VTE
Half-life		12-17 hrs 14-17 hrs (elderly)	5-9 hrs 9-12 hrs (elderly)	8-15 hrs	10-14 hrs
Time to max effect		2 hrs	2-4 hrs	3 hrs	1-2 hrs
Renal Clearance		80% renal 20% biliary	66% renal 33% biliary	25% renal 75% biliary	50% renal 50% biliary
Dosage		*AF*: • 150 mg BID *VTE treatment & Recurrent VTE*: • 150 mg BID after 5-10 days of parenteral anticoagulant *VTE Prophylaxis:* • 110 mg 1-4 hrs post hip surgery then 220 mg daily x 35 days	*AF*: • 20 mg DAILY with PM meal *VTE treatment*: • 15 mg BID x 21 days, then 20 mg DAILY with PM meal *Recurrent VTE*: • 20 mg daily with PM meal *VTE prophylaxis*: • Hip surgery: 10 mg daily x 35 days • Knee surgery: 10 mg daily x 12 days	*AF*: • 5 mg BID *VTE treatment*: • 10 mg BID x 7 days, then 5 mg BID *Recurrent VTE:* 2.5 mg BID *VTE prophylaxis*: • Hip surgery: 2.5 mg BID x 35 days • Knee surgery: 2.5 mg BID x 12 days	*AF*: • 60 mg DAILY *VTE treatment*: • 60 mg daily after 5-10 days of parenteral anticoagulant
Dosing Adjustments and Considerations		*AF:* CrCl 15-30: 75 mg BID CrCl < 15: avoid use *VTE:* CrCl < 30: avoid use	*AF:* CrCl 15-50: 15 mg daily CrCl < 15: avoid use *VTE Treatment and Prophylaxis*: CrCl < 30: avoid use	*AF:* if 2 of 3 criteria met then decrease to 2.5 mg BID: • Age ≥ 80 • Wt ≤ 60 kg • Creatinine ≥ 1.5 Hemodialysis: 5 mg BID (reduce dose if 2 of 3 criteria above met) VTE Treatment and Prophylaxis: CrCl < 15: avoid use	*AF:* CrCl > 95: avoid use CrCl 15 – 30: 30 mg daily CrCl < 15: avoid use VTE: CrCl 15 – 30: 30 mg daily CrCl < 15: avoid use
Contraindications		- Avoid in pregnancy, breastfeeding or in severe liver disease			
Monitoring		No lab testing available. All DOACs affect the INR. Measuring INRs during co-administration may not be useful for determining an appropriate dose of warfarin.			
Peri-procedure use (see U-Connect	Pre-op	- Standard bleed risk procedure • CrCl ≥ 50: stop 1-2 days prior • CrCl < 50: stop 3-5 days prior	- Standard bleed risk procedure • CrCl > 30: stop 24 hrs prior • CrCl ≤ 30: stop 48 hrs prior	- Standard bleed risk procedure • Scr ≥ 50: stop 24 hrs prior • Scr < 50: stop 48 hrs prior	- Standard bleed risk procedure • CrCl ≥ 50: stop 24 hrs prior • CrCl < 50: stop 48 hrs prior

Direct Oral Anticoagulants (DOACs)

for UW guidelines)		- High bleed risk procedure: • CrCl ≥ 50: stop 2-4 days prior • CrCl < 50: stop ≥ 5 days prior	- High bleed risk procedure: • CrCl > 30: stop 48 hrs prior • CrCl ≤ 30: stop 72 hrs prior	- High bleed risk procedure: • CrCl ≥ 50: stop 48 hrs prior • CrCl < 50: stop 72 hrs prior	- High bleed risk procedure: • CrCl ≥ 50: stop 48 hrs prior • CrCl < 50: stop 72 hrs prior
	Post-op	- For low bleed risk surgery restart within 24 hrs post-op if ok with surgeon - For high bleed risk surgery restart within 72 hrs post-op if ok with surgeon			
Switching from DOAC to warfarin		- If CrCl ≥ 50: start warfarin 3 days prior to stopping dabigatran - If CrCl 31-50: start warfarin 2 days prior to stopping dabigatran - If CrCl 15-30: start warfarin 1 day prior to stopping dabigatran	Initiate warfarin & a parenteral anticoagulant 24 hrs after stopping rivaroxaban	If continuous anticoagulation is necessary, stop apixaban & begin both a parenteral anticoagulant & warfarin when next dose is due; stop parenteral anticoagulant when INR at goal	- If taking 60 mg, reduce to 30 mg and begin warfarin - If taking 30 mg, reduce to 15 mg and begin warfarin - measure INR at least weekly and just prior to the use of edoxaban - when INR ≥ 2.0 stop edoxaban
Switching from DOAC to IV UFH or enoxaparin		- If CrCl >30, start UFH or enoxaparin 12 hrs after last dose - If CrCl <30, consider starting UFH or enoxaparin 24 hrs after last dose	- If CrCl >30, start UFH or enoxaparin 12 hrs after last dose - If CrCl <30, consider starting UFH or enoxaparin 24 hrs after last dose	Start UFH or enoxaparin 12 hrs after the last apixaban dose	D/c edoxaban and start parenteral AC at the time of next dose of edoxaban
Switching from warfarin to DOAC		Allow INR to drop to < 2.0 before initiating	Allow INR to drop to < 3.0 before initiating	Allow INR to drop to < 2.0 before initiating	Start when INR is ≤ 2.5
Switching from parenteral AC to DOAC		• Start DOAC 2 hrs before the time to next subcutaneous anticoagulant dose • Start DOAC at the time of IV heparin discontinuation			• Discontinue LMWH and start edoxaban at the time of next schedule dose LMWH • - Discontinue heparin drip and start edoxaban 4 hrs later
Recommendations for bleeding besides blood products (see UW guidelines on U-Connect)		- Only DOAC with antidote: Idarucizumab - Only DOAC that can be moderately reversed by dialysis	- For all DOACs hemostasis expected within 12-24 hrs after last dose - Oral activated charcoal given within 2 hrs may decrease plasma concentrations		
Missed Dose		- Take missed dose ASAP, but if next dose is < 6 hrs away, skip the missed dose - Do not take 2 doses at the same time	- If taking 15 mg BID: Take ASAP to ensure 30 mg daily - For daily dose: Take missed dose immediately	- Take missed dose ASAP on same day - The dose should not be doubled to make up for a missed dose	
Drug Interactions		- P-gp & strong CYP3A4 inhibitors (amiodarone, cyclosporine, ketoconazole, quinidine, verapamil, azole antifungals, nicardipine, ritonavir), may ↑ serum concentration - P-gp & strong CYP3A4 inducers (carbamazepine, dexamethasone, phenytoin, prazosin, rifampin, nafcillin, rifampin) may decrease the serum concentration			
Use for electrical cardioversion		Demonstrated to be effective anti-coagulant in the setting of cardioversion with guidelines similar to warfarin			
Nonbleeding Side Effects		Dyspepsia (5-10%)	None		
Advantages		- Fixed dose - No bridging - No INR monitoring required - No food restrictions & fewer drug interactions			

Direct Oral Anticoagulants (DOACs)

Disadvantages	- Cost - Lack of antidote & difficult to manage bleeding - Difficult to determine compliance - Missed dose may place pt at increased risk of thromboembolic event - Renal monitoring and dose adjustment required
Lab Frequency follow-up	Yearly: Hgb, renal and liver function 6 monthly: Renal function if CrCl 30-60 ml/min, or if on dabigatran and > 75 years or fragile 3 monthly: If co-morbidity or condition that may impact renal or hepatic function

References:

- European Heart Rhythm Association Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation (2013) 15, 625-651.
- Chest Supplement, Antithrombotic Therapy and Prevention of Thrombosis, 9th edition, ACCP.
- RE-LY trial: NEJM 2009; 361:1139
- ROCKET-AF trial: NEJM 2011: 365:883.
- ARISTOTLE trial: NEJM 2011: 365:981.
- Package inserts from Pradaxa, Xarelto, Eliquis, Savaysa

Developed by Kathy Wackerle, APRN-BC
Reviewed by Dr. Craig January

October 2015