# Target Specific Oral Anticoagulants

<table>
<thead>
<tr>
<th>Drug Classification</th>
<th>Dabigatran (Pradaxa)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Apixaban (Eliquis)</th>
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</table>
| **FDA Approved Indications** | - Nonvalvular AF  
- Treatment of VTE & PE  
- Reduce risk of recurrent VTE & PE | - Nonvalvular AF  
- Treatment of VTE & PE  
- Reduce risk of recurrent VTE or PE  
- VTE prophylaxis (hip & knee) | - Nonvalvular AF  
- Treatment of VTE & PE  
- Reduce risk of recurrent VTE or PE  
- VTE prophylaxis (hip & knee)  
- FDA approved for nonvalvular AF patients on hemodialysis |

| **Relative risk reduction compared to warfarin** | **Trial:**  
AF: VTE/PE: RE-LY (150 and 110 mg)  
RE-COVER | **ROCKET-AF** (20 and 15 mg)  
EINSTEIN | **ARISTOTLE** (5 and 2.5 mg)  
AMPLIFY and AMPLIFY-EXT |
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<tbody>
<tr>
<td>Stroke &amp; embolism</td>
<td>35% (CHADS₂ 2.1), 150 mg superior, 110 mg noninferior</td>
<td>21% (CHADS₂ 3.47), noninferior to warfarin</td>
<td>21% (CHADS₂ 2.1), superior to warfarin</td>
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<tr>
<td>ICH</td>
<td>74% (both doses)</td>
<td>41%</td>
<td>49%</td>
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<tr>
<td>GI bleed</td>
<td>48% increase (150 mg) but post-market suggests similar</td>
<td>38% increase</td>
<td>No increase</td>
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<tr>
<th><strong>Half-life</strong></th>
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<tr>
<td><strong>Time to max effect</strong></td>
<td>2 hrs</td>
<td>2-4 hrs</td>
<td>3 hrs</td>
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<td><strong>Elimination</strong></td>
<td>80% renal 20% biliary</td>
<td>66% renal 33% biliary</td>
<td>25% renal 75% biliary</td>
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| **Dosage** | **AF:**  
- 150 mg BID  
- If CrCl 15-30 use 75 mg bid  
**VTE treatment & Recurrent VTE:**  
CrCl > 30: 150 mg BID after 5-10 days of parenteral AC  
CrCl < 30: dosing recs not provided | **AF:**  
- 20 mg DAILY with pm meal  
- If CrCl 15-50 use 15 mg daily  
**VTE prophylaxis:** 10 mg DAILY for 35 days after hip surgery & 12 days after knee surgery  
**VTE treatment:** 15 mg BID for 21 days, then 20 mg DAILY  
**Recurrent VTE:** 20 mg daily | **AF:**  
- 5 mg BID  
- Reduce from 5 mg to 2.5 mg BID for pts with 2 of 3 “high-risk” criteria: age ≥ 80, wt ≤ 60 kg, creat ≥ 1.5  
- Can be given to pts on HD  
**VTE prophylaxis:** 2.5 mg BID for 35 days after hip surgery & 12 days after knee surgery  
**VTE treatment:** 10 mg BID for 7 days, followed by 5 mg BID  
**Recurrent VTE:** 2.5 mg BID |

| **Dosing considerations and Contraindications** | - Do not use if CrCl < 15 mL/min  
- Avoid in pregnancy, breastfeeding or in severe liver disease |
| **Monitoring** | No lab testing available. All NOACs 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 for UW guidelines)** | **Pre-op**  
- CrCl ≥ 50: d/c 1-2 days prior to standard risk procedure; d/c 3-5 days prior to high bleeding risk surgery  
- CrCl < 50: d/c 3-5 days prior to standard risk procedure; d/c > 5 days prior to high risk surgery | **Stop warfarin:** 1500 mg daily or 20 mg daily as a single dose before procedure  
**72-hour bridging:**  If CrCl ≤ 30, d/c 48 hrs prior to standard risk procedure; d/c 72 hrs before high risk surgery  
**24-hour bridging:** CrCl > 30  
**High risk:** CrCl ≤ 30  
**Low risk:** CrCl > 30  
**Holiday bridging:** 1500 mg daily or 20 mg daily as a single dose before procedure  
**High risk:** CrCl ≤ 30  
**Low risk:** CrCl > 30  
**1-hour bridging:** CrCl > 30  
**Continuous anticoagulation:** 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 |

| **Post-op** | - For low bleed risk surgery restart 12-24 hrs post-op if ok with surgeon (for all 3 NOACs)  
- For high bleed risk surgery restart 48-72 hrs post-op if ok with surgeon (for all 3 NOACs) | - Discontinue 24 hrs prior to elective moderate to high risk surgery for bleeding  
- Discontinue 24 hrs prior to elective low risk surgery for bleeding  
- Bridging usually not needed |

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<th><strong>Switching from NOAC to warfarin</strong></th>
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| **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 |
### Target Specific Oral Anticoagulants

#### Switching from NOAC 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

#### Switching from warfarin to NOAC
- Allow INR to drop to < 2.0 before initiating
- Start NOAC at the time of IV heparin discontinuation

#### Switching from parenteral AC to NOAC
- Start NOAC 2 hrs before the time to next subcutaneous anticoagulant dose
- Start NOAC at the time of IV heparin discontinuation

#### Recommendations for bleeding besides blood products (see UW guidelines on U-Connect)
- For all NOACs hemostasis expected within 12-24 hrs after last dose
- No antidote currently available
- Dabigatran is only NOAC that can be moderately reversed by hemodialysis
- 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 inhibitors may ↑ serum concentration (i.e. amiodarone, cyclosporine, ketoconazole, quinidine, verapamil)
- P-gp inducers may ↓ serum concentration (i.e. carbamazepine, dexamethasone, phenytoin, prazosin, rifampin)
- P-gp & strong CYP3A4 inhibitors may ↑ serum concentration (i.e. amiodarone, cyclosporine, ketoconazole, quinidine, verapamil, azole antifungals, nicardipine, ritonavir)
- P-gp & strong CYP3A4 inducers may ↓ serum concentration (i.e. carbamazepine, dexamethasone, phenytoin, prazosin, rifampin, nafcillin)

#### Use for electrical cardioversion
- Demonstrated to be effective anticoagulant 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

#### 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

#### Pricing
- All 3 NOACs are covered by major insurers in Madison area. GHC required a prior authorization. May consider checking with pt’s insurance company before prescribing to see what their copayment will be.

### References:
- Chest Supplement, Antithrombotic Therapy and Prevention of Thrombosis, 9th edition, ACCP.
- RE-LY trial: NEJM 2009; 361:1139
- Package inserts from Pradaxa, Xarelto, & Eliquis