# Direct Oral Anticoagulants (DOACs)

<table>
<thead>
<tr>
<th>Drug Classification</th>
<th>Dabigatran (Pradaxa)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Apixaban (Eliquis)</th>
<th>Edoxaban (Savaysa)</th>
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</table>
| **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** | - 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  
| - 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  
| - 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  
| - 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  
VTE Treatment and Prophylaxis:  
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)

| 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  
- 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  
- 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%) |
| Advantages | - Fixed dose  
- - No bridging  
- - No INR monitoring required  
- - No food restrictions & fewer drug interactions |
## Direct Oral Anticoagulants (DOACs)

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

### 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, Savaysa