<table>
<tr><td></td><td colspan="3">Dabigatran (Pradaxa)</td></tr>
<tr><td>Mechanism</td><td colspan="3">Direct Thrombin Inhibitor</td></tr>
<tr><td rowspan="2">Indication Specific Dosing and Adjustments Due to Renal Insufficiency</td><td colspan="3">Atrial fibrillation (nonvalvular):

CrCl > 30: 150 mg BID

CrCl 15 – 30: 75 mg BID

CrCl < 15: Do not use</td></tr>
<tr><td colspan="3">DVT/PE treatment: (after 5-10 days of parenteral anticoagulation)

CrCl > 30: 150 mg BID

CrCl < 30: use not recommended (not studied)</td></tr>
<tr><td>Elderly</td><td colspan="3">Patients ≥80 years: Use with extreme caution or consider other treatment options. No dosage adjustment provided in manufacturer’s labeling; however, numerous cases of hemorrhage, including hemorrhagic stroke, have been reported. Due to a lack of available dosing options available in the U.S. avoiding use of dabigatran in this population.</td></tr>
<tr><td>Conversions Involving other Anticoagulants</td><td colspan="3">Conversion from enoxaparin: Initiate dabigatran ≤2 hours prior to the time of the next scheduled dose of enoxaparin

Conversion from heparin drip: Initiate dabigatran at time of heparin drip discontinuation

Conversion to enoxaparin or heparin drip:

CrCl ≥ 30: Wait 12 hours after last dabigatran dose before initiating enoxaparin or heparin drip (no bolus)

CrCl <30: Wait 24 hrs after the last dose of dabigatran before initiating enoxaparin or heparin drip (no bolus)

Conversion from warfarin: Discontinue warfarin and initiate dabigatran when INR <2.0

Conversion to warfarin: Since dabigatran contributes to INR elevation, warfarin’s effect on the INR will be better reflected only after dabigatran has been stopped for ≥2 days. Start time must be adjusted based on CrCl:

CrCl >50: Initiate warfarin 3 days before discontinuation of dabigatran

CrCl 31 to 50: Initiate warfarin 2 days before discontinuation of dabigatran

CrCl 15 to 30: Initiate warfarin 1 day before discontinuation of dabigatran

CrCl <15 mL/minute: Do not use</td></tr>
<tr><td rowspan="3">Stopping Prior to Surgery</td><td></td><td>High Bleeding Risk</td><td>Low Bleeding Risk</td></tr>
<tr><td>CrCl > 50</td><td>Give last dose three days before procedure (ie, skip 4 doses on the two days before the procedure; 48 hrs)</td><td>Give last dose two days before procedure (ie, skip 2 doses on the day before the procedure; 24 hrs)</td></tr>
<tr><td>CrCl < 50</td><td>Give last dose five days before procedure (ie, skip 8 doses on the four days before the procedure; 96 hrs)</td><td>Give last dose three days before procedure (ie, skip 4 doses on the two days before the procedure; 48 hrs)</td></tr>
<tr><td rowspan="2">Restarting After Procedure</td><td colspan="2">High Bleeding Risk</td><td>Low Bleeding Risk</td></tr>
<tr><td colspan="2">Resume 48 – 72 hrs after surgery (ie, postoperative day 2 – 3)
Resume 6 hours after removal of epidural catheter</td><td>Resume 24 hrs after surgery (ie, postoperative day 1)
Resume 6 hours after removal of epidural catheter</td></tr>
<tr><td>Effects on coagulation tests</td><td colspan="3">INR: may be elevated but cannot be used to determine activity as test is calibrated to warfarin only

PT: ↑ - Low sensitivity; unsuitable as primary measure of anticoagulant activity

aPTT: ↑ - Can be used to determine excess anticoagulant activity, but changes during treatment should be interpreted with caution (qualitative rather than quantitative)</td></tr>
<tr><td>Monitoring</td><td colspan="3">Measurement of activated partial thromboplastin time (aPTT) (values >2.5x control may indicate overanticoagulation), ecarin clotting test (ECT) if available, or thrombin time (TT; most sensitive) may be useful to determine presence of dabigatran and level of coagulopathy</td></tr>
<tr><td>Major Bleeding Management</td><td colspan="2">Reversal agent NOT available at this time

Supportive Measures:
• Antifibrinolytic agent (eg tranexamic acid)
• Activated charcoal (if last dose ingested within prior 2 hrs)
• Hemodialysis
• RBC transfusions if needed for anemia and/or platelet transfusions if needed for thrombocytopenia
• Consider activated PCC (FEIBA) or activated Factor VII – due to limited clinical evidence for efficacy and associated thrombosis risk use only if continued bleeding is reasonably likely to be fatal within hours</td><td>Given relatively short elimination half-life time is most important antidode

Estimated normalization of hemostasis:

CrCl > 80: 12–24 hrs

CrCl 50–80 mL/min: 24–36 hrs

CrCl 30–50 mL/min: 36–48 hrs

CrCl < 30 mL/min: ≥48 hrs</td></tr>
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<tr><td></td><td colspan="3">Rivaroxaban (Xarelto)</td></tr>
<tr><td>Mechanism</td><td colspan="3">Direct inhibition of coagulation factor Xa. Prevents thrombin formation</td></tr>
<tr><td rowspan="3">Indication Specific Dosing and Adjustments Due to Renal Insufficiency</td><td colspan="3">Atrial fibrillation (nonvalvular):

CrCl > 50: 20 mg once daily with evening meal

CrCl 15 – 50: 15 mg once daily with evening meal

CrCl < 15: Do not use</td></tr>
<tr><td colspan="3">DVT/PE treatment and reduction of risk of recurrent DVT/PE:

CrCl > 30: Initial: 15 mg BID with food for 21 days followed by 20 mg once daily with food

CrCl > 30: Reduction of recurrence: 20 mg once daily with food (after initial 6 months of treatment)

CrCl < 30: Avoid use</td></tr>
<tr><td colspan="3">Postoperative DVT thromboprophylaxis (Knee/Hip replacement):

CrCl >30: 10 mg once daily beginning after hemostasis has been established, 6 to 10 hours postoperatively

CrCl < 30: Do not use</td></tr>
<tr><td>Elderly</td><td colspan="3">Patients ≥65 years: Use with caution. Elderly patients exhibit higher rivaroxaban concentrations compared to younger patients due primarily to reduced clearance.</td></tr>
<tr><td>Conversions Involving other Anticoagulants</td><td colspan="3">Conversion from enoxaparin: Initiate rivaroxaban ≤2 hours prior to the next regularly scheduled evening dose of enoxaparin

Conversion from heparin drip: Initiate rivaroxaban at time of heparin drip discontinuation

Conversion to enoxaparin or heparin drip: Wait 24 hrs (if once daily dosing) or 12 hrs (if twice daily dosing) after the last dose of rivaroxaban before initiating enoxaparin or heparin drip (no bolus)

Conversion from warfarin: Discontinue warfarin and initiate rivaroxaban as soon as INR falls < 3.0

Conversion to warfarin: If continuous anticoagulation is necessary, discontinue rivaroxaban and begin both a parenteral anticoagulant with warfarin when the next dose of rivaroxaban is due; discontinue parenteral anticoagulant when INR reaches an acceptable range.</td></tr>
<tr><td>Stopping Prior to Surgery</td><td></td><td>High Bleeding Risk
Give last dose three days before procedure (ie, skip doses on the two days before the procedure; 48 hrs)</td><td>Low Bleeding Risk
Give last dose two days before procedure (ie, skip dose on the day before the procedure; 24 hrs)</td></tr>
<tr><td rowspan="2">Restarting After Procedure</td><td colspan="2">High Bleeding Risk</td><td>Low Bleeding Risk</td></tr>
<tr><td colspan="2">Resume 48 – 72 hrs after surgery (ie, postoperative day 2 – 3)
Resume 6 hours after removal of epidural catheter</td><td>Resume 24 hours after surgery (ie, postoperative day 1)
Resume 6 hours after removal of epidural catheter</td></tr>
<tr><td>Effects on coagulation tests</td><td colspan="3">INR: may be elevated but cannot be used to determine activity as test is calibrated to warfarin only

PT: ↑ - Can be used to determine excess anticoagulant activity as linear response may be seen when concentration of drug increases, but changes during treatment should be interpreted with caution (qualitative rather than quantitative)

aPTT: ↑ - Less sensitive than PT; unsuitable as primary measure of anticoagulant activity</td></tr>
<tr><td>Monitoring</td><td colspan="3">Prothrombin time (PT) or antifactor Xa activity may be used to detect presence of rivaroxaban (neither is intended to be used for dosage adjustment). However, variability exists among PT assays and even more so when converted to INR. Therefore, antifactor Xa activity measurement is the preferred test (must be calibrated to rivaroxaban). A therapeutic range has not been defined, and dosage adjustment based on results has not been established.</td></tr>
<tr><td>Major Bleeding Management</td><td colspan="2">Reversal agent NOT available at this time

Supportive Measures:

• Antifibrinolytic agent (eg tranexamic acid)
• Activated charcoal (if last dose ingested within prior 2 hrs)
• RBC transfusions if needed for anemia and/or platelet transfusions if needed for thrombocytopenia
• Consider 4 – Factor unactivated PCC (Kcentra) – due to limited clinical evidence for efficacy and associated thrombosis risk use only if continued bleeding is reasonably likely to be fatal within hours</td><td>Given relatively short elimination half-life time is most important antidode

Estimated normalization of hemostasis:

12 – 24 hrs</td></tr>
</table>

<table>
<tr><th></th><th colspan="3">Apixaban (Eliquis)</th></tr>
<tr><td>Mechanism</td><td colspan="3">Direct inhibition of coagulation factor Xa. Prevents thrombin formation</td></tr>
<tr><td rowspan="3">Indication Specific Dosing and Adjustments Due to Renal Insufficiency</td><td colspan="3">Atrial fibrillation (nonvalvular):

5 mg twice daily

If any 2 of the following: Age ≥ 80 years, body weight ≤ 60 kg, or Scr ≥ 1.5: 2.5 mg twice daily

CrCl < 25 or Scr > 2.5: Avoid use</td></tr>
<tr><td colspan="3">DVT/PE treatment and reduction of risk of recurrent DVT/PE:

Treatment: 10 mg twice daily for 7 days followed by 5 mg twice daily

Reduction of recurrence: 2.5 mg twice daily (after at least 6 months of above treatment dose)

CrCl < 25 or Scr > 2.5: Do not use</td></tr>
<tr><td colspan="3">Postoperative DVT thromboprophylaxis (Knee/Hip replacement):

Hip replacement surgery: 2.5 mg twice daily beginning 12 to 24 hours postoperatively; duration: 35 days

Knee replacement surgery: 2.5 mg twice daily beginning 12 to 24 hours postoperatively; duration: 12 days

CrCl < 25 or Scr > 2.5: Do not use</td></tr>
<tr><td>Elderly</td><td colspan="3">Nonvalvular Afib: If patient ≥ 80 years old and either weighs ≤60 kg or Scr ≥1.5 mg/dL, reduce dose to 2.5 mg twice daily</td></tr>
<tr><td>Conversions Involving other Anticoagulants</td><td colspan="3">Conversion from enoxaparin: Initiate apixaban ≤2 hours prior to the next regularly scheduled evening dose of enoxaparin

Conversion from heparin drip: Initiate apixaban at time of heparin drip discontinuation

Conversion to enoxaparin or heparin drip: Wait 12 hrs after the last dose of apixaban before initiating enoxaparin or heparin drip (no bolus)

Conversion from warfarin: Discontinue warfarin and initiate apixaban as soon as INR falls < 2.0

Conversion to warfarin: If continuous anticoagulation is necessary, discontinue apixaban and begin both a parenteral anticoagulant with warfarin when the next dose of apixaban is due; discontinue parenteral anticoagulant when INR reaches an acceptable range</td></tr>
<tr><td rowspan="2">Stopping Prior to Surgery</td><td></td><td>High Bleeding Risk</td><td>Low Bleeding Risk</td></tr>
<tr><td></td><td>Give last dose three days before procedure (ie, skip 4 doses on the two days before the procedure; 48 hrs)</td><td>Give last dose two days before procedure (ie, skip 2 doses on the day before the procedure; 24 hrs)</td></tr>
<tr><td rowspan="2">Restarting After Procedure</td><td colspan="2">High Bleeding Risk</td><td>Low Bleeding Risk</td></tr>
<tr><td colspan="2">Resume 48 – 72 hrs after surgery (ie post-op day 2 – 3)
Resume 6 hours after removal of epidural catheter</td><td>Resume 24 hrs after surgery (ie, postoperative day 1)
Resume 6 hours after removal of epidural catheter</td></tr>
<tr><td>Effects on coagulation tests</td><td colspan="3">INR: may be elevated but cannot be used to determine activity as test is calibrated to warfarin only

PT: ↑ - Can be used to determine excess anticoagulant activity as linear response may be seen when concentration of drug increases, but changes during treatment should be interpreted with caution (qualitative rather than quantitative)

aPTT: ↑ - Less sensitive than PT; unsuitable as primary measure of anticoagulant activity</td></tr>
<tr><td>Monitoring</td><td colspan="3">Although not recommended to assess effectiveness, the prothrombin time (PT), INR, and aPTT are prolonged with apixaban. Anti-FXa assay may be helpful in guiding clinical decisions as plasma concentrations and anti-FXa activity exhibit linear relationship (assay must be calibrated to apixaban).</td></tr>
<tr><td>Major Bleeding Management</td><td colspan="2">Reversal agent NOT available at this time

Supportive Measures:
• Antifibrinolytic agent (eg tranexamic acid)
• Activated charcoal (if last dose ingested within prior 2 hrs)
• RBC transfusions if needed for anemia and/or platelet transfusions if needed for thrombocytopenia
• Consider 4 – Factor unactivated PCC (Kcentra) – due to limited clinical evidence for efficacy and associated thrombosis risk use only if continued bleeding is reasonably likely to be fatal within hours</td><td>Given relatively short elimination half-life time is most important antidode

Estimated normalization of hemostasis:
12 – 24 hrs</td></tr>
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