TARGET SPECIFIC ORAL ANTICOAGULANTS (TSAOCs)

This document is intended as a guideline only and should not replace sound clinical judgment
Please refer to UNMH formulary in Lexicomp for approved use(s) within hospital

PURPOSE:
- This document is intended as a guide to managing oral anticoagulant therapy in hospitalized patients
- It should be coupled with, and not supersede, clinical judgment.
- Evidence-based tools, such as dosing algorithms, should always be used in conjunction with clinical information pertaining to specific patient characteristics and conditions.

BACKGROUND:
- Target specific oral anticoagulants represent a shift in the therapeutic landscape of antithrombosis.
- They are the first oral anticoagulants available since the discovery of warfarin over 60 years ago.
- Due to their specificity, they do not require routine monitoring. They also have an improved pharmacokinetic profile compared to warfarin.

PHARMACOKINETIC COMPARISON TABLE:

<table>
<thead>
<tr>
<th>TARGET</th>
<th>WARFARIN</th>
<th>RIVAROXABAN</th>
<th>APIXABAN</th>
<th>DABIGATRAN ETEXILATE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vitamin K epoxide reductase reducing the functional levels of vitamin K dependent coagulation factors</td>
<td>Factor Xa</td>
<td>Factor Xa</td>
<td>Thrombin</td>
</tr>
<tr>
<td>PRODRUG</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>BIOAVAILABILITY</td>
<td>&gt;95%</td>
<td>&gt;80%</td>
<td>&gt;50%</td>
<td>~6%</td>
</tr>
<tr>
<td>T (MAX)</td>
<td>72-96h</td>
<td>2.5-4h</td>
<td>3h</td>
<td>2h</td>
</tr>
<tr>
<td>HALF-LIFE</td>
<td>40h</td>
<td>5-9 h healthy; 9-13 h elderly</td>
<td>8-15 h</td>
<td>14-17 h</td>
</tr>
<tr>
<td>MONITORING</td>
<td>INR adjusted</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Not needed</td>
</tr>
<tr>
<td>ADMINISTRATION</td>
<td>Once daily</td>
<td>Once or twice daily</td>
<td>Twice daily</td>
<td>Once or twice daily</td>
</tr>
<tr>
<td>METABOLISM/ELIMINATION</td>
<td>CYP 2C9, 3A4, 1A2</td>
<td>CYP3A4; 66% renal, 33% fecal</td>
<td>CYP3A4; 75% fecal, 25% renal</td>
<td>80% renal, 20% fecal</td>
</tr>
<tr>
<td>DRUG INTERACTIONS</td>
<td>CYP 2C9, 1A2, and 3A4</td>
<td>Potent CYP 3A4 inhibitor and P-gp inhibitors</td>
<td>Potent CYP 3A4 inhibitor and P-gp inhibitors</td>
<td>P-gp inhibitors</td>
</tr>
</tbody>
</table>

T (max) indicates peak plasma levels; h, hours; P-gp, P-glycoprotein
INITIATION OF TSOAC:

- When considering use of these agents, the pros and cons (in comparison to warfarin) must be weighed, along with patient preferences and values.

<table>
<thead>
<tr>
<th>PRO(S)</th>
<th>CON(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No INR monitoring required</td>
<td>No clear advantage over well-controlled warfarin</td>
</tr>
<tr>
<td>Bridging/induction therapy likely not needed</td>
<td>TSOACs with BID dosing may have negative impact on compliance</td>
</tr>
<tr>
<td>Short half-life allows easier peri-operative management</td>
<td>Missed doses place a patient at higher risk for adverse event due to short half-life</td>
</tr>
<tr>
<td>Convenient for rural patients or those with other barriers to clinic visits</td>
<td>No specific antidote or monitoring parameter</td>
</tr>
<tr>
<td>Fewer drug/diet/disease interactions</td>
<td>Higher incidence of GI side effects &amp; discontinuation rate</td>
</tr>
<tr>
<td>Potentially better efficacy &amp; safety for patients with poor INR control on warfarin</td>
<td>Possible increased incidence of adverse events (e.g. MI, GI bleed, etc) depending on TSOAC</td>
</tr>
<tr>
<td>Increased patient satisfaction</td>
<td>Lack of monitoring may foster non-compliance</td>
</tr>
<tr>
<td>Less complex patient/family education</td>
<td>Renal monitoring and dose adjustment required</td>
</tr>
<tr>
<td>Follow up can likely be performed by community providers as well as specialty clinics</td>
<td>Higher out-of-pocket costs and copays</td>
</tr>
</tbody>
</table>

- Please refer to the UNMH formulary in Lexicomp for approved uses within the hospital

- **Patients that meet the following criteria may be considered candidates for TSOAC therapy**
  - History of poor INR control on warfarin despite good compliance
  - Considerable barriers to routine monitoring, such as physical or transportation issues
  - Documented warfarin allergy
  - Documented history of non-hemorrhagic adverse effects with warfarin
  - Documented, confirmed warfarin failure such as an ischemic stroke while consistently therapeutic on warfarin

- **Prior to initiation of a TSOAC, the patient should be evaluated for the following:**
  - Appropriate, approved indication at UNMH
  - Adequate insurance coverage or prescription assistance prior to discharge
  - Adequate renal function
  - Compliance history
  - Lack of medication interactions that would preclude use of TSOAC
  - History of any clinical conditions that might preclude use of TSOAC (e.g. history of MI, history of GI bleed, advanced age, low body weight, etc)
  - Ability to comply with prescribed follow-up plan

OUTPATIENT FOLLOW-UP FOR PATIENTS ON TSOAC

- While TSOACs do not require routine monitoring, it is advisable to develop an alternative follow-up plan with either the patient’s primary care provider or a specialty outpatient clinic to periodically assess the following:
  - Renal and hepatic function
  - Existence of drug interactions
  - Occurrence of adverse events
  - Development of contraindications
  - Questioning about upcoming procedures
  - Ability to obtain and maintain the medication
  - Barriers to adherence
  - Patient satisfaction with therapy
DABIGATRAN (Pradaxa®)1

I. MECHANISM AND INDICATIONS
   A. Mechanism: Oral direct thrombin inhibitor (DTI)
   B. FDA approved indications: Stroke and systemic embolism prevention in non-valvular atrial fibrillation.

II. DOSING
   A. Dosing based on renal function and potential drug-drug interactions
   B. Following dosing based on dabigatran prescribing information

<table>
<thead>
<tr>
<th>RENAL FUNCTION</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &gt; 30 mL/min</td>
<td>150 mg PO BID</td>
</tr>
<tr>
<td>CrCl 30-50 mL/min on concomitant dronedarone or ketoconazole therapy†</td>
<td>75 mg PO BID</td>
</tr>
<tr>
<td>CrCl 15-30 mL/min on concomitant P-gp inhibitor therapy†</td>
<td>Avoid use</td>
</tr>
<tr>
<td>CrCl 15-30 mL/min</td>
<td>75 mg PO BID*</td>
</tr>
<tr>
<td>CrCl &lt; 15 mL/min</td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>

†See drug-drug interaction explanation below
*Use extreme caution

III. CONVERSION BETWEEN DABIGATRAN AND OTHER ANTICOAGULANTS

<table>
<thead>
<tr>
<th>DOING BASED ON CRCL AND/OR TIMING</th>
</tr>
</thead>
</table>

DABIGATRAN TO WARFARIN

CrCl > 50 mL/min: Start warfarin 3 days before discontinuing dabigatran
CrCl 31-50 mL/min: Start warfarin 2 days before discontinuing dabigatran
CrCl 15-30 mL/min: Start warfarin 1 day before discontinuing dabigatran
CrCl < 15 mL/min: Not recommended

WARFARIN TO DABIGATRAN

Discontinue warfarin and wait until INR < 2.0, then...
CrCl > 30 mL/min: Start dabigatran 150 mg PO BID
CrCl 15-30 mL/min: Start dabigatran 75 mg PO BID
CrCl < 15 mL/min: Contraindicated

DABIGATRAN TO PARENTERAL ANTICOAGULANT

CrCl ≥ 30 mL/min: Wait 12 hours after last dose of dabigatran before initiating treatment
CrCl < 30 mL/min: Wait 24 hours after last dose of dabigatran before initiating treatment

PARENTERAL ANTICOAGULANTS TO DABIGATRAN

Start dabigatran 0 – 2 hours before the time that the next dose of the parenteral anticoagulant (e.g. LMWH) was to have been administered
OR
Start dabigatran at the time of discontinuation of a continuously administered parenteral drug (e.g. IV UFH)

IV. DRUG-DRUG INTERACTIONS (DDI) WITH DABIGATRAN
   A. Dabigatran exposure may be affected by concomitant use of P-glycoprotein (P-gp) inducers and inhibitors

<table>
<thead>
<tr>
<th>P-GLYCOProTEIN EFFECT</th>
<th>INTERACTION</th>
<th>SPECIFIC EXAMPLES</th>
<th>RECOMMENDED ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inducer of dabigatran metabolism</td>
<td>Reduces exposure to dabigatran</td>
<td>Rifampin</td>
<td>Avoid concomitant use</td>
</tr>
</tbody>
</table>
| Inhibitor of dabigatran metabolism | Increases exposure to dabigatran | Ketoconazole, dronedarone | Consider decreasing dose to 75 mg PO BID in patients with CrCl 30-50 mL/min*  
Avoid concomitant use of dabigatran and P-gp inhibitors in patients with CrCl 15-30 mL/min |

*The use of other P-gp inhibitors (e.g. verapamil, amiodarone, quinidine, clarithromycin) in patients with CrCl 30-50 mL/min does not require a dose adjustment of dabigatran.
RIVAROXABAN (Xarelto®)

I. MECHANISM AND INDICATIONS
   A. Mechanism: Oral direct Factor Xa inhibitor
   B. FDA-approved indications:
      − Stroke and systemic embolism prevention in non-valvular atrial fibrillation
      − DVT and PE treatment
      − DVT and PE prevention following initial 6 months of treatment for DVT or PE
      − DVT prophylaxis following hip or knee replacement surgery

II. DOSING
   A. Dosing based on indication and renal function
   B. Following dosing based on rivaroxaban prescribing information

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>RENAL FUNCTION</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/systemic embolism prevention in non-valvular atrial fibrillation</td>
<td>CrCl &gt;50 mL/min</td>
<td>20 mg PO once daily with evening meal</td>
</tr>
<tr>
<td></td>
<td>CrCl 15-50 mL/min</td>
<td>15 mg PO once daily with evening meal</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;15 mL/min</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>DVT and PE treatment</td>
<td>CrCl ≥ 30 mL/min</td>
<td>15 mg PO BID with food, for first 21 days, THEN 20 mg PO once daily with food, for remaining treatment</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;30 mL/min</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>DVT and PE prevention following initial 6 months of treatment for DVT or PE</td>
<td>CrCl ≥ 30 mL/min</td>
<td>20 mg PO once daily with food</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;30 mL/min</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>DVT prophylaxis following hip or knee replacement surgery</td>
<td>CrCl ≥ 50 mL/min</td>
<td>Hip replacement: 10 mg PO once daily for 35 days</td>
</tr>
<tr>
<td></td>
<td>CrCl 30-50 mL/min</td>
<td>Knee replacement: 10 mg PO once daily for 12 days</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;30 mL/min</td>
<td>Use extreme caution</td>
</tr>
</tbody>
</table>

III. CONVERSION BETWEEN RIVAROXABAN AND OTHER ANTICOAGULANTS

- **RIVAROXABAN TO WARFARIN**
  - No clinical trial data available
  - Rivaroxaban affects INR, so INR measurements made during co-administration with warfarin may not be useful for determining the appropriate dose of warfarin
  - One approach is to discontinue rivaroxaban and begin both a parenteral anticoagulant and warfarin at the time the next dose of rivaroxaban would have been taken

- **WARFARIN TO RIVAROXABAN**
  - Discontinue warfarin and wait until **INR < 3.0**; then start rivaroxaban

- **RIVAROXABAN TO ANTICOAGULANTS OTHER THAN WARFARIN**
  - Adjust starting time of oral or parenteral rapid-onset anticoagulant based on timing of last rivaroxaban dose
  - Give first dose at the time the next dose of rivaroxaban would have been taken

- **ANTICOAGULANTS OTHER THAN WARFARIN TO RIVAROXABAN**
  - Adjust starting time of rivaroxaban based on timing of parenteral or oral anticoagulant other than warfarin
  - Start rivaroxaban 0 – 2 hours before the time that the next evening dose of the other anticoagulant (e.g. LMWH or non-warfarin oral anticoagulant) was to have been administered, OR
  - Start rivaroxaban at the time of discontinuation of a continuously administered parenteral drug (e.g. IV UFH)
IV. DRUG-DRUG INTERACTIONS (DDI) WITH RIVAROXABAN
A. DDI involving rivaroxaban include substrates of isoenzymes CYP 3A4/5 and 2J2 and transporters P-glycoprotein (P-gp) and ABCG2.

<table>
<thead>
<tr>
<th>SUBSTRATE</th>
<th>EFFECT</th>
<th>EXAMPLES</th>
<th>RECOMMENDED ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dual CYP 3A4 and P-gp inhibitors</td>
<td>Increased rivaroxaban exposure</td>
<td>Ketoconazole, itraconazole,</td>
<td>Avoid concomitant use</td>
</tr>
<tr>
<td></td>
<td>and pharmacodynamic effects</td>
<td>ritonavir, conivaptan</td>
<td></td>
</tr>
<tr>
<td>Dual CYP 3A4 and P-gp inducers</td>
<td>Decreased rivaroxaban exposure</td>
<td>Carbamazepine, phenytoin,</td>
<td>Avoid concomitant use</td>
</tr>
<tr>
<td></td>
<td>and possibly decreased efficacy</td>
<td>rifampin, St. John's Wort</td>
<td></td>
</tr>
</tbody>
</table>

V. HEPATIC IMPAIRMENT
A. Moderate (Child Pugh class B) to severe (Child Pugh class C) hepatic impairment: avoid use
B. Any hepatic disease associated with coagulopathy: avoid use

APIXABAN (Eliquis®³)

I. MECHANISM AND INDICATIONS
A. Mechanism: Oral direct Factor Xa inhibitor
B. FDA approved indication: Stroke and systemic embolism prevention in non-valvular atrial fibrillation.

II. DOSING

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended dosing</td>
<td>5 mg PO BID</td>
</tr>
<tr>
<td>Patients with any 2 of the following:</td>
<td></td>
</tr>
<tr>
<td>▪ Age ≥ 80 years</td>
<td></td>
</tr>
<tr>
<td>▪ Body weight ≤ 60 kg</td>
<td></td>
</tr>
<tr>
<td>▪ Scr ≥ 1.5 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Concomitant dual CYP3A4 and P-gp inhibitor therapy*</td>
<td>2.5 mg PO BID</td>
</tr>
</tbody>
</table>

*See drug-drug interaction explanation below; P-gp: P-glycoprotein

III. CONVERSION BETWEEN APIXABAN AND OTHER ANTICOAGULANTS

<table>
<thead>
<tr>
<th>APIXABAN TO WARFARIN</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Apixaban affects INR, so INR measurements during co-administration with warfarin may not be useful for determining the appropriate dose of warfarin</td>
<td></td>
</tr>
<tr>
<td>▪ Discontinue apixaban and start both a parenteral anticoagulant and warfarin at the time the next dose of apixaban would have been taken, discontinuing the parenteral anticoagulant when INR reaches an acceptable range</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WARFARIN TO APIXABAN</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Discontinue warfarin and wait until INR &lt; 2.0; then start apixaban</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>APIXABAN AND ANTICOAGULANTS OTHER THAN WARFARIN</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Discontinue anticoagulant being taken and begin the other anticoagulant at the next scheduled dose</td>
<td></td>
</tr>
</tbody>
</table>

IV. DRUG-DRUG INTERACTIONS (DDI) WITH APIXABAN
A. DDI involving apixaban include substrates of isoenzyme CYP 3A4 and transporter P-glycoprotein (P-gp).

<table>
<thead>
<tr>
<th>SUBSTRATE</th>
<th>EFFECT</th>
<th>EXAMPLES</th>
<th>RECOMMENDED ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dual CYP 3A4 and P-gp inhibitors</td>
<td>Increased apixaban exposure</td>
<td>Ketoconazole, itraconazole,</td>
<td>▪ Decrease dose to 2.5 mg PO BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ritonavir, clarithromycin</td>
<td>▪ Patients already taking 2.5 mg PO BID: avoid concomitant use</td>
</tr>
<tr>
<td>Dual CYP 3A4 and P-gp inducers</td>
<td>Decreased apixaban exposure</td>
<td>Carbamazepine, phenytoin,</td>
<td>Avoid concomitant use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>rifampin, St. John’s Wort</td>
<td></td>
</tr>
</tbody>
</table>

V. HEPATIC IMPAIRMENT
A. Severe hepatic impairment: avoid use
PERIOPERATIVE MANAGEMENT OF TSOACs\textsuperscript{1-5}

Please refer to "UNMH guideline for perioperative management of antithrombotic therapy" on the pharmacy webpage (https://hospitals.health.unm.edu/intranet/pharmacy/index.shtml) for additional guidance

- Assessment of bleeding risk and adequate post-operative hemostasis should be considered prior to anticoagulation re-initiation
- Should not be used concomitantly with warfarin at either prophylactic or treatment doses, as this has not been studied. If overlap therapy is needed, use UFH or enoxaparin

<table>
<thead>
<tr>
<th>Medication</th>
<th>Cessation</th>
<th>Re-Initiation Post-Op*</th>
</tr>
</thead>
</table>
| DABIGATRAN (Pradaxa®) 150 mg BID | Low bleeding risk procedure: \( ^* \)  
- CrCl \( \geq 50 \text{ mL/min} (t_{1/2} 14-17h) \)  
  Skip 2 doses  
- CrCl 30-50 mL/min (t\(_{1/2}\) 16-18h):  
  Skip 4 doses  
High bleeding risk procedure\( ^* \)  
- CrCl \( \geq 50 \text{ mL/min} (t_{1/2} 14-17h) \)  
  Skip 4 doses  
- CrCl 30-50 mL/min(t\(_{1/2}\) 16-18h)  
  Skip 6-8 doses |  
- More invasive procedures (e.g. major surgery, spinal puncture, placement of a spinal or epidural catheter or port)  
  Consider longer period of cessation  
  APPLIES TO ALL TSOACs  
  ▪ No specific information available  
  ▪ Peak plasma concentrations reached  
  - Dabigatran: 1-2 hours  
  - Rivaroxaban: 2-4 hours  
  - Apixaban: 3-4 hours  
  ▪ Recommend re-initiating only if hemostasis is achieved, and  
  - 24-48 hours after minor procedures  
  - 48-72 hours after major procedures  
  ▪ If TSOAC cannot be used post-procedure, consider initiation of parenteral agent  
  ▪ If parenteral agent used as initial bridging therapy (e.g. UFH, LMWH), TSOAC therapy should be resumed  
  - At least 1 hour after discontinuation of UFH infusion  
  - At least 10 hours after last dose of LMWH  
  ▪ Recommend consultation with anticoagulation service |
| RIVAROXABAN (Xarelto®) 20 mg PO daily | Low bleeding risk procedure: \( ^* \)  
- CrCl \( \geq 30 \text{ mL/min} (t_{1/2} 8-9h) \)  
  Skip 1 dose  
- CrCl 15-29 mL/min (t\(_{1/2}\) 9-10h)  
  Skip 2 doses  
High bleeding risk procedure\( ^* \)  
- CrCl \( \geq 30 \text{ mL/min} (t_{1/2} 8-9h) \)  
  Skip 2 doses  
- CrCl 15-29 mL/min (t\(_{1/2}\) 9-10h)  
  Skip 3 doses |  
- More invasive procedures (e.g. major surgery, spinal puncture, placement of a spinal or epidural catheter or port)  
  Consider longer period of cessation  
  APPLIES TO ALL TSOACs  
  ▪ No specific information available  
  ▪ Peak plasma concentrations reached  
  - Dabigatran: 1-2 hours  
  - Rivaroxaban: 2-4 hours  
  - Apixaban: 3-4 hours  
  ▪ Recommend re-initiating only if hemostasis is achieved, and  
  - 24-48 hours after minor procedures  
  - 48-72 hours after major procedures  
  ▪ If TSOAC cannot be used post-procedure, consider initiation of parenteral agent  
  ▪ If parenteral agent used as initial bridging therapy (e.g. UFH, LMWH), TSOAC therapy should be resumed  
  - At least 1 hour after discontinuation of UFH infusion  
  - At least 10 hours after last dose of LMWH  
  ▪ Recommend consultation with anticoagulation service |
| APIXABAN (Eliquis®) 5 mg PO BID | Low bleeding risk procedure: \( ^* \)  
- CrCl \( \geq 50 \text{ mL/min} (t_{1/2} 7-8h) \)  
  Skip 2 doses  
- CrCl 30-49 mL/min (t\(_{1/2}\) 17-18h)  
  Skip 4 doses  
High bleeding risk procedure\( ^* \)  
- CrCl \( \geq 50 \text{ mL/min} (t_{1/2} 7-8h) \)  
  Skip 4 doses  
- CrCl 30-49 mL/min (t\(_{1/2}\) 17-18h)  
  Skip 6 doses |  
- More invasive procedures (e.g. major surgery, spinal puncture, placement of a spinal or epidural catheter or port)  
  Consider longer period of cessation  
  APPLIES TO ALL TSOACs  
  ▪ No specific information available  
  ▪ Peak plasma concentrations reached  
  - Dabigatran: 1-2 hours  
  - Rivaroxaban: 2-4 hours  
  - Apixaban: 3-4 hours  
  ▪ Recommend re-initiating only if hemostasis is achieved, and  
  - 24-48 hours after minor procedures  
  - 48-72 hours after major procedures  
  ▪ If TSOAC cannot be used post-procedure, consider initiation of parenteral agent  
  ▪ If parenteral agent used as initial bridging therapy (e.g. UFH, LMWH), TSOAC therapy should be resumed  
  - At least 1 hour after discontinuation of UFH infusion  
  - At least 10 hours after last dose of LMWH  
  ▪ Recommend consultation with anticoagulation service |
REVERSAL STRATEGIES FOR TSOACs

Please refer to "Antithrombotic reversal guidelines" on the pharmacy webpage (https://hospitals.health.unm.edu/intranet/pharmacy/index.shtml) for additional guidance.

- There is no reversal agent for dabigatran, rivaroxaban or apixaban
- Management of life-threatening bleed remains empirical
- Measurement of aPTT, TT or ECT may help guide therapy
- Hemodialysis:
  - HD removed 62% of circulating dabigatran within 2 hours and 68% within 4 hours
  - Rivaroxaban is NOT removed by hemodialysis
  - Apixaban is NOT expected to be removed by hemodialysis
- Activated charcoal: Administration in < 1-2 hours of ingestion may be helpful in the event of an acute overdose
- Supportive care:
  - Early volume repletion
  - Early RBC repletion
  - Recombinant factor VII or PCC

LABORATORY MEASUREMENT AND INTERPRETATION FOR TSOACs

- The target specific oral anticoagulants, in general, have predictable pharmacokinetics, pharmacodynamics and metabolism. Therefore, routine laboratory monitoring is NOT recommended
- Routine laboratory monitoring has not been correlated to clinical outcomes
- Coagulation tests should be interpreted with caution
- Clinical scenarios where TSOAC measurement may be desirable or necessary include:
  - Surgery or invasive procedure
  - Hemorrhagic or thrombotic event
  - Suspected drug failure
  - Suspected overdose
  - Assess adherence
  - Presence of major drug-drug interactions
  - Extremes of weight
  - Extremes of age
  - Declining renal function
  - Need for thrombolytics

Coagulation test results are mostly helpful as a QUALITATIVE assessment (e.g. determine if anticoagulant effect is present or absent)

**NOTE: standard anti-Factor Xa levels cannot be used to measure the effects of rivaroxaban or apixaban. An assay specific to each drug must be used, and these are not currently available**

<table>
<thead>
<tr>
<th>LAB TEST</th>
<th>DABIGATRAN</th>
<th>RIVAROXABAN/APIXABAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT/INR</td>
<td>Poor sensitivity - DO NOT USE</td>
<td>Normal INR (+ normal aPTT) suggests minimal anticoagulant activity</td>
</tr>
<tr>
<td>aPTT</td>
<td>Normal aPTT suggests minimal anticoagulant activity*</td>
<td>Normal aPTT (+ normal INR) suggests minimal anticoagulant activity</td>
</tr>
<tr>
<td>TT (thrombin time)</td>
<td>Normal TT excludes presence of significant dabigatran levels**</td>
<td>DO NOT USE</td>
</tr>
<tr>
<td>ECT (ecarin clotting time)</td>
<td>Normal ECT excludes presence of significant dabigatran levels***</td>
<td>DO NOT USE</td>
</tr>
<tr>
<td>Chromogenic assays</td>
<td>Chromogenic anti-IIa assay not available</td>
<td>Normal anti-Xa assay excludes presence of significant rivaroxaban or apixaban levels†</td>
</tr>
<tr>
<td>dPT (dilute PT)</td>
<td>Unknown (promising results) - more sensitive than PT</td>
<td>Unknown (promising results)</td>
</tr>
<tr>
<td>Heptest</td>
<td>DO NOT USE</td>
<td>Normal Heptest suggests minimal anticoagulant activity†</td>
</tr>
<tr>
<td>PICT (prothrombinase induced clotting time)</td>
<td>Unknown (no available evidence)</td>
<td>Normal PICT suggests minimal anticoagulant activity‡</td>
</tr>
</tbody>
</table>

*Mildly elevated aPTT can be associated with clinically important levels of dabigatran
**Can be affected by other anticoagulants and therefore be oversensitive and inaccurate at high concentrations**

***Is not affected by other anticoagulants and sensitive at all concentrations

†Chromogenic anti-Xa assay must be calibrated for rivaroxaban or apixaban to correctly measure levels

‡Preferred over PT or aPTT in measuring FXa inhibitor activity

**CLINICAL MONITORING RECOMMENDATIONS FOR ALL TSOACS**

- Current renal function (serum creatinine, CrCl)
- Recent liver function panel

**References:**