DIRECT ORAL ANTICOAGULANTS: USE IN HIGH RISK PATIENTS

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I, Haley Phillippe, have no actual or potential conflict of interest in relation to this program.
Objectives

- Determine the appropriateness of the new oral anticoagulants in high risk patients
- Recognize appropriate dosing for the new oral anticoagulants in high risk patients
- Review common errors during the prescribing and dispensing of the direct oral anticoagulants
## Approved Indications and Dosing

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke Prevention in Nonvalvular AFIB</strong></td>
<td>150 mg BID</td>
<td>20 mg daily</td>
<td>5 mg BID**</td>
<td>60 mg daily</td>
</tr>
<tr>
<td><strong>VTE Treatment</strong></td>
<td>150 mg BID*</td>
<td>15 mg BID x 21 days, then 20 mg daily</td>
<td>10 mg BID x 7 days, then 5 mg BID</td>
<td>60 mg daily*</td>
</tr>
<tr>
<td><strong>VTE Extended</strong></td>
<td></td>
<td>20 mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VTE prevention post TKR/THR</strong></td>
<td></td>
<td>10 mg daily</td>
<td>2.5 mg BID</td>
<td></td>
</tr>
</tbody>
</table>

*Initiate after 5-10 days of parenteral anticoagulant

**2.5 mg BID if **two** of the following: > 80 yoa, < 60 kg, or SCr > 1.5 mg/dL
Case 1: MR

- MR is a 74-year old male currently taking dabigatran 150 mg twice daily for recurrent DVTs
- PMH: HTN, recurrent DVT
- Pertinent labs/vitals:
  - BMP WNL with exception of SCr 3.8 mg/dL; CBC WNL
  - BP 132/76; HR 88; Ht 6’3”; wt 95 kg
  - CrCL: 26 mL/min
- Social history: Insignificant
- Meds:
  - Lisinopril 40 mg daily, amlodipine 10 mg daily, dabigatran 150 mg twice daily
- Do you agree with this patient’s current therapy?
### Renal Impairment

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Design</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RELY</td>
<td>Dabigatran 110mg or 150mg BID</td>
<td>Noninferiority - NVAF</td>
<td>CrCL&lt;30mL/min</td>
</tr>
<tr>
<td>RE-MEDY</td>
<td>Dabigatran 150mg BID</td>
<td>Noninferiority - DVT or PE</td>
<td>CrCL&lt;30mL/min</td>
</tr>
<tr>
<td>ROCKET-AF</td>
<td>Rivaroxaban 20mg daily or 15mg daily</td>
<td>Noninferiority - NVAF</td>
<td>CrCL&lt;30mL/min</td>
</tr>
<tr>
<td>EINSTEIN Investigators</td>
<td>Rivaroxaban 15mg BID for 3 wks, then 20mg daily</td>
<td>Noninferiority - symptomatic DVT</td>
<td>CrCL&lt;30mL/min</td>
</tr>
<tr>
<td>EINSTEIN-PE Investigators</td>
<td>Rivaroxaban 15mg BID for 3 wks, then 20mg daily</td>
<td>Noninferiority - symptomatic PE</td>
<td>CrCL&lt;30mL/min</td>
</tr>
</tbody>
</table>

### Renal Impairment

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Design</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARISTOTLE</td>
<td>Apixaban 5mg BID or 2.5mg BID</td>
<td>Noninferiority - NVAF</td>
<td>CrCl&lt;25mL/min, SCr&gt;2.5mg/dL</td>
</tr>
<tr>
<td>AVERROES</td>
<td>Apixaban 5mg BID or 2.5mg BID</td>
<td>Superiority - NVAF</td>
<td>CrCl&lt;25mL/min, SCr&gt;2.5mg/dL</td>
</tr>
<tr>
<td>Lassen et al</td>
<td>Apixaban 2.5mg BID</td>
<td>Noninferiority - DVT, PE, Mortality</td>
<td>Significant renal impairment</td>
</tr>
<tr>
<td>Hokusai-VTE Investigators</td>
<td>Edoxaban 60mg daily or 30mg daily</td>
<td>Noninferiority - symptomatic VTE</td>
<td>CrCl&lt;30mL/min</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 Investigators</td>
<td>Edoxaban 60mg daily or 30mg daily</td>
<td>Noninferiority - NVAF</td>
<td>CrCl&lt;30mL/min</td>
</tr>
</tbody>
</table>

Renal Impairment

- **Dabigatran**
  - PK/PD study: AUC levels found to be 1.5, 3.2, and 6.3 fold higher in subjects with mild, moderate and severe renal impairment, respectively.
  - Excretion time: 24 h vs 96 h for patients with severe renal impairment.

- **Rivaroxaban**
  - PK/PD study: In patients with CrCl of 30-49 mL/min, 15 mg dose achieved an AUC similar to a 20 mg dose in patients with normal renal function.

Renal Impairment

- **Apixaban**
  - PK/PD study: In patients with CrCl of 30-50 mL/min a 43% increase in apixaban exposure is expected when compared to patients without renal impairment

- **Edoxaban**
  - PK/PD study: Systemic exposure increases by 57%, 35%, and 11.6% in patients with CrCl of 30, 50, and 80 mL/min, respectively, when compared to patients without renal impairment

## Renal Impairment

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF</td>
<td>150 mg BID</td>
<td>20 mg daily</td>
<td>5 mg BID**</td>
<td>60 mg daily</td>
</tr>
<tr>
<td>CrCl &lt; 50 mL/min</td>
<td>150 mg BID*</td>
<td>15 mg daily</td>
<td>5 mg BID**</td>
<td>30 mg once daily</td>
</tr>
<tr>
<td>CrCl &lt; 30 mL/min</td>
<td>75 mg BID†</td>
<td>15 mg daily</td>
<td>5 mg BID**</td>
<td>30 mg once daily</td>
</tr>
<tr>
<td>CrCL &lt; 15 mL/min</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

*75 mg BID if receiving concomitant dronedarone or oral ketoconazole
† avoid if receiving concomitant P-gp inhibitor
**2.5 mg BID if 2 of the following: age >80 year, body weight <60 kg, SCr >1.5 mg/dL

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Dabigatran (Pradaxa) [Prescribing Information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2015.
### Renal Impairment

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VTE Treatment</strong></td>
<td>150 mg BID*</td>
<td>15 mg BID x 21 days, then 20 mg daily</td>
<td>10 mg BID x 7 days, then 5 mg BID</td>
<td>60 mg daily*</td>
</tr>
<tr>
<td><strong>CrCl &lt; 50 mL/min</strong></td>
<td>Avoid co-administration with P-glycoprotein Inhibitor</td>
<td>Monitor bleeding risk closely</td>
<td>5 mg daily**</td>
<td>30 mg once daily†</td>
</tr>
<tr>
<td><strong>CrCl &lt; 30 mL/min</strong></td>
<td>Avoid</td>
<td>Avoid</td>
<td>5 mg daily**</td>
<td>30 mg once daily†</td>
</tr>
<tr>
<td><strong>CrCl &lt; 15 mL/min</strong></td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

*Initiate after 5-10 days of parenteral anticoagulant

**2.5 mg BID if 2 of the following: age ≥80 year, body weight ≤60 kg, SCr ≥1.5 mg/dL

†Also recommended dose if body weight < 60 kg, or concomitant P-glycoprotein inhibitors

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### Dabigatran Case Reports

<table>
<thead>
<tr>
<th>Age(y)/Sex</th>
<th>Weight (Kg)</th>
<th>CrCl</th>
<th>Dose (mg)</th>
<th>Therapy duration (Months)</th>
<th>Bleeding Event</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>66/F</td>
<td>123</td>
<td>15</td>
<td>150 BID</td>
<td>2</td>
<td>Upper GI bleed</td>
<td>Dabigatran D/C’d Aggressive interventions</td>
</tr>
<tr>
<td>78/F</td>
<td>80</td>
<td>15</td>
<td>150 BID</td>
<td>9</td>
<td>Retroperitoneal, GI, and pleural hemorrhage</td>
<td>Death 2⁰ to hemorrhagic shock</td>
</tr>
<tr>
<td>70/M</td>
<td>75</td>
<td>43</td>
<td>150 BID</td>
<td>2</td>
<td>Hemopericardium</td>
<td>Dabigatran D/C’d Pericardiocentesis</td>
</tr>
<tr>
<td>84/F</td>
<td>40</td>
<td>32</td>
<td>75 BID</td>
<td>4</td>
<td>Rectal/Lower GI bleeding</td>
<td>Death 2⁰ to hemorrhagic shock</td>
</tr>
<tr>
<td>89/F</td>
<td>45</td>
<td>29</td>
<td>110 BID</td>
<td>5</td>
<td>Recurrent epistaxis x 1 wk</td>
<td>Dabigatran D/C’d nasal cauterization</td>
</tr>
</tbody>
</table>

MR is a 74-year old male currently taking dabigatran 150 mg twice daily for recurrent DVTs

PMH: HTN, recurrent DVT

Pertinent labs/vitals:
- BMP WNL with exception of SCr 3.8 mg/dL; CBC WNL
- BP 132/76; HR 88; Ht 6’3”; wt 95 kg
- CrCL: 26 mL/min

Social history: Insignificant

Meds:
- Lisinopril 40 mg daily, amlodipine 10 mg daily, dabigatran 150 mg twice daily

Do you agree with this patient’s current therapy?
Back MR

- MR is a 74-year old male currently taking dabigatran 150 mg twice daily for recurrent DVTs
- PMH: HTN, T2DM, recurrent DVT
- Pertinent labs/vitals:
  - BMP WNL with exception of SCr 3.8 mg/dL; CBC WNL
  - BP 132/76; HR 88; Ht 6’3”; wt 95 kg
  - CrCL: 26 mL/min
- Social history: Insignificant
- Meds:
  - Lisinopril 40 mg daily, amlodipine 10 mg daily, dabigatran 150 mg twice daily
- Do you agree with this patient’s current therapy?
Which agent do you recommend for this patient?

A. Continue dabigatran 150 mg daily
B. Stop dabigatran and initiate rivaroxaban 20 mg daily
C. Stop dabigatran and initiate apixaban 5 mg daily
D. Stop dabigatran and initiate warfarin
Case 2

- GG is a 93-year old female with newly onset non-valvular AFIB
- PMH: HLD, HTN, h/o GI bleed, osteoarthritis
- Pertinent labs/vitals:
  - BMP WNL; CBC WNL
  - BP: 126/72; HR 74; Ht 5’10”; wt 84 kg
  - CrCl: 54 mL/min
- Meds:
  - Atorvastatin 80 mg daily, lisinopril 40 mg daily, diclofenac ER 100 mg once daily, aspirin 81 mg daily
- Social history: Drinks socially
- Does GG have any bleeding risk?
## Factors Influencing Rate of Bleeding

- Antiplatelet therapy or other high risk medications
- History of bleed
- Age > 75
- Cancer
- Renal insufficiency
- Hepatic disease
- Arterial HTN
- Uncontrolled HTN
- Prior stroke
- Alcohol abuse
- Anemia
- Low platelets
- High risk of falls

*Chest. 2012;141(2)(suppl 1):e44S-e88S.*
## Bleeding Risk

<table>
<thead>
<tr>
<th></th>
<th>RE-LY</th>
<th>ROCKET - AF</th>
<th>ARISTOTLE</th>
<th>ENGAGE-AF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Expressed as RRR (%)</strong></td>
<td>Dabigatran 110mg BID</td>
<td>Dabigatran 150mg BID</td>
<td>Rivaroxaban</td>
<td>Apixaban</td>
</tr>
<tr>
<td><strong>Primary Outcome</strong></td>
<td>↓10*</td>
<td>↓35*</td>
<td>↓21*</td>
<td>↓21*</td>
</tr>
<tr>
<td><strong>Hemorrhagic Stroke</strong></td>
<td>↓69*</td>
<td>↓74*</td>
<td>↓41*</td>
<td>↓49*</td>
</tr>
<tr>
<td><strong>Ischemic/Unknown Stroke</strong></td>
<td>↑11</td>
<td>↓24*</td>
<td>↓6</td>
<td>↓8</td>
</tr>
<tr>
<td><strong>Major Bleed</strong></td>
<td>↓20*</td>
<td>↓7</td>
<td>↓4</td>
<td>↓31*</td>
</tr>
<tr>
<td><strong>Intracranial Hemorrhage</strong></td>
<td>↓70*</td>
<td>↓59*</td>
<td>↓33*</td>
<td>↓58*</td>
</tr>
<tr>
<td><strong>GI Bleed</strong></td>
<td>↑8</td>
<td>↑48*</td>
<td>↑46*</td>
<td>↓11</td>
</tr>
<tr>
<td><strong>All death</strong></td>
<td>↓9</td>
<td>↓12</td>
<td>↓15</td>
<td>↓11*</td>
</tr>
</tbody>
</table>

*P < 0.05. | RRR = Relative Risk Reduction

**In modified intention-to-treat analysis, statistical significance was not reported.**

## Patients aged more than 75 years: Major or clinically relevant bleeding

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>NOAC Events</th>
<th>NOAC Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.1 Rivaroxaban</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EINSTEIN PE, 2012</td>
<td>58</td>
<td>440</td>
<td>67</td>
<td>401</td>
<td>13.9%</td>
<td>0.76 [0.52, 1.11]</td>
<td></td>
</tr>
<tr>
<td>EINSTEIN, 2010</td>
<td>19</td>
<td>215</td>
<td>20</td>
<td>223</td>
<td>10.2%</td>
<td>0.98 [0.51, 1.90]</td>
<td></td>
</tr>
<tr>
<td>EINSTEIN-Extension, 2010</td>
<td>7</td>
<td>88</td>
<td>3</td>
<td>98</td>
<td>4.4%</td>
<td>2.74 [0.69, 10.93]</td>
<td></td>
</tr>
<tr>
<td>MAGELLAN, 2013</td>
<td>75</td>
<td>1,530</td>
<td>29</td>
<td>1,548</td>
<td>13.1%</td>
<td>2.70 [1.75, 4.17]</td>
<td></td>
</tr>
<tr>
<td>ROCKET-AF, 2011</td>
<td>82</td>
<td>3,073</td>
<td>124</td>
<td>3,077</td>
<td>15.0%</td>
<td>0.65 [0.49, 0.87]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>5,346</td>
<td>241</td>
<td>5,347</td>
<td>243</td>
<td>5.67%</td>
<td>1.18 [0.64, 2.19]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>241</td>
<td>243</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.39; Chi² = 32.62, df = 4 (P < 0.00001); I² = 88%
Test for overall effect: Z = 0.52 (P = 0.60)

| **1.2 Apixaban**  |             |            |                |               |        |                                |                                |
| ARISTOTLE, 2011   | 151         | 2,542      | 224            | 2,393         | 15.8%  | 0.61 [0.49, 0.76]              |                                |
| AVERROES, 2011    | 26          | 909        | 24             | 983           | 11.5%  | 1.18 [0.67, 2.06]              |                                |
| **Subtotal (95% CI)** | 3,451       | 177        | 3,376          | 248           | 27.2%  | 0.80 [0.43, 1.51]              |                                |
| Total events      | 177         | 248        |                |               |        |                                |                                |

Heterogeneity: Tau² = 0.17; Chi² = 4.54, df = 1 (P = 0.03); I² = 78%
Test for overall effect: Z = 0.68 (P = 0.50)

| **1.3 Dabigatran** |             |            |                |               |        |                                |                                |
| RE-LY, 2009       | 450         | 4,828      | 206            | 2,360         | 16.1%  | 1.07 [0.90, 1.28]              |                                |
| **Subtotal (95% CI)** | 4,828       | 450        | 2,360          | 206           | 16.1%  | 1.07 [0.90, 1.28]              |                                |
| Total events      | 450         | 206        |                |               |        |                                |                                |

Heterogeneity: Not applicable
Test for overall effect: Z = 0.82 (P = 0.41)

| **Total (95% CI)** |             |            |                |               |        |                                |                                |
| Total events      | 13,625      | 11,083     | 100.0%         |               |        | 1.02 [0.73, 1.43]              |                                |

Heterogeneity: Tau² = 0.17; Chi² = 50.25, df = 7 (P < 0.00001); I² = 86%
Test for overall effect: Z = 0.13 (P = 0.89)

LB is a 93-year old female with newly onset non-valvular AFIB

PMH: HLD, HTN, h/o GI bleed, osteoarthritis

Pertinent labs/vitals:
- BMP WNL; CBC WNL
- BP: 126/72; HR 74; Ht 5’10”; wt 84 kg
- CrCl: 54 mL/min

Meds:
- Atorvastatin 80 mg daily, lisinopril 40 mg daily, diclofenac ER 100 mg once daily, aspirin 81 mg daily

Social history: Drinks socially

Does GG have any bleeding risk?
GG is a 93-year old female with newly onset non-valvular AFIB

PMH: HLD, HTN, h/o GI bleed, osteoarthritis

Pertinent labs/vitals:
- BMP WNL; CBC WNL
- BP: 126/72; HR 74; Ht 5’10”; wt 84 kg
- CrCl: 54 mL/min

Meds:
- Atorvastatin 80 mg daily, lisinopril 40 mg daily, diclofenac ER 100 mg once daily, aspirin 81 mg daily

Social history: Drinks socially

Does GG have any bleeding risk?
Which agent do you recommend for the treatment of LB’s AFIB?

A. Warfarin
B. Dabigatran 150 mg daily
C. Apixaban 5 mg twice daily
D. Edoxaban 30 mg daily
Case 3

- MM is a 43 year old female admitted with acute pulmonary embolism
- PMH: HTN, COPD, PE
- Pertinent labs/vitals:
  - BMP WNL; CBC WNL
  - BP: 142/84; HR 74; Ht: 5’4”; Wt: 55 kg
  - CrCl: 60 mL/min
- Meds:
  - HCTZ 25 mg daily, albuterol PRN, tiotropium daily
- Social history: Smokes 2 ppd
- Which anticoagulant is most appropriate for MM?
**Body Weight**

- **RE-LY: Dabigatran**
  - Average weight = 82.5 kg or 181.5 lbs
  - Trough concentrations approx. 20% lower in patients >100 kg
  - Limited data on patients < 50 kg

- **ROCKET-AF: Rivaroxaban**
  - Average weight = 82.1 kg or 180.6 lbs
  - Cmax increased by approx. 24% in subjects weighing ≤ 50 kg
  - Patients ≥ 120 kg unaffected

References:

- Postgrad Med. 2013 Jan;125(1):34-44;
- Drugs. 2014; 74(11): 1209–1231
Body Weight

- **ARISTOTLE: Apixaban**
  - Average weight = 82 kg or 180.4 lbs
  - AUC 20% higher in patient ≤50 kg and 23% lower in patients ≥ 120 kg

- **ENGAGE AF-TIMI 48: Edoxaban**
  - Average weight = 84 kg or 185 lbs
  - Increase Exposure for patient ≤ 60 kg

MM is a 43 year old female admitted with acute pulmonary embolism

PMH: HTN and COPD

Pertinent labs/vitals:
- BMP WNL; CBC WNL
- BP: 142/84; HR 74; Ht: 5’4”; Wt: 55 kg
- CrCl: 60 mL/min

Meds:
- HCTZ 25 mg daily, albuterol PRN, tiotropium daily

Social history: Smokes 2 ppd

Which anticoagulant is most appropriate for MM?
Which agent do you recommend for the treatment of MM’s PE?

A. Warfarin
B. Rivaroxaban 15 mg daily
C. Apixaban 5 mg twice daily
D. Edoxaban 30 mg daily
What do you need to know?

- **Renal Impairment**
  - Monitor SCr levels closely
  - Reassess eligibility for warfarin therapy

- **Bleeding Risk**
  - Dabigatran, rivaroxaban, and edoxaban associated with GI bleeding
  - TSOACs are associated with intracranial hemorrhage
  - Consider drug interactions

- **Body Weight Extremes**
  - May affect drug kinetics and should be taken into account when recommending TSOACs
## Clinical Application

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical Valve or Valvular AFIB</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>CrCl 30-50 mL/min</td>
<td>?</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>CrCl &lt; 30 mL/min</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatic Impairment</td>
<td>✓</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Dual Antiplatelet</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>GI Bleeding</td>
<td>X</td>
<td>X</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Labile INRs</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Body Weight Extremes &lt; 60 kg or &gt; 120 kg</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>✓</td>
</tr>
<tr>
<td>Swallowing Difficulty</td>
<td>X</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>✓</td>
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</table>
Initiation of Therapy

1. Approved indication
2. Appropriate dose
3. Drug interactions
4. Consideration for co-medications to reduce GI bleeding risk
5. Baseline hemoglobin, renal and hepatic function
6. Patient/Family education
7. Schedule follow-Up
# Lab Follow-up

<table>
<thead>
<tr>
<th>Interval</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Labs</td>
<td>Yearly</td>
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<tr>
<td></td>
<td>CBC, renal and liver function</td>
</tr>
<tr>
<td>6 months</td>
<td>Renal function if CrCl 30-50 mL/min or if on dabigatran and &gt; 75 years or fragile</td>
</tr>
<tr>
<td>3 months</td>
<td>CrCl 15-30 mL/min</td>
</tr>
<tr>
<td>PRN</td>
<td>Signs/symptoms of bleed</td>
</tr>
<tr>
<td></td>
<td>Concern for declining renal or hepatic function</td>
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<tr>
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<td>High bleed risk</td>
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</tbody>
</table>

DIRECT ORAL ANTICOAGULANTS: USE IN HIGH RISK PATIENTS

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