Anticoagulation Safety: Reducing Adverse Drug Events

Kunal J. Shah, PharmD
Clinical Coordinator
Pharmacy Department
Morristown Medical Center
Disclosure

- I have nothing to disclose.
Objectives

- Review reasons for errors in relation to prescribing and administering anticoagulants
- Identify opportunities for improvement in the medication use process for safer anticoagulation use
Statistics

- Incidence of Disease Requiring Anticoagulation
  - Atrial fibrillation: 6.1 million Americans
  - Venous thromboembolism: 183 per 100,000 patient-years

- In 2016, over 11 million prescriptions for oral anticoagulants were filled in the US.

- Anticoagulants account for 17.6% of ED visits annually.
## Agents Used for Anticoagulation

### Parenteral Agents

<table>
<thead>
<tr>
<th>Factor Xa Inhibitors</th>
<th>Direct Thrombin Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>Heparin</td>
</tr>
<tr>
<td>Enoxaparin (Lovenox®)</td>
<td>Argatroban</td>
</tr>
<tr>
<td>Fondaparinux (Arixtra®)</td>
<td>Bivalirudin (Angiomax®)</td>
</tr>
<tr>
<td>Dalteparin (Fragmin®)</td>
<td></td>
</tr>
</tbody>
</table>

### Oral Agents

<table>
<thead>
<tr>
<th>Vitamin K Antagonists</th>
<th>Factor Xa Inhibitors</th>
<th>Direct Thrombin Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin (Coumadin®)</td>
<td>Rivaroxaban (Xarelto®)</td>
<td>Dabigatran (Pradaxa®)</td>
</tr>
<tr>
<td></td>
<td>Apixaban (Eliquis®)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Edoxaban (Savaysa®)</td>
<td></td>
</tr>
</tbody>
</table>
Question

“What’s the usual dose for Xarelto®?”
Complexities of Dosing Agents

- Based on weight and renal function
  - Fondaparinux for VTE prophylaxis – contraindicated if body weight < 50 kg or CrCl < 30 mL/min

- Based on indication and renal function

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban for atrial fibrillation</td>
<td>20 mg with dinner</td>
<td>CrCl &gt; 50 mL/min</td>
</tr>
<tr>
<td></td>
<td>15 mg with dinner</td>
<td>CrCl 15-50 mL/min</td>
</tr>
<tr>
<td>Rivaroxaban for VTE treatment</td>
<td>15 mg BID x 21 days followed by 20 mg daily</td>
<td>Not recommended if CrCl &lt; 30 mL/min</td>
</tr>
</tbody>
</table>
Parenteral Anticoagulants

- Potential for medication error in transcription, administration, monitoring and titration of continuous infusion agents

- Heparin
  - Selection of appropriate dosing nomogram
  - Drawing of blood samples for activated partial thromboplastin time (aPTT) or anti-Factor Xa levels
  - Dose adjustment based on interpretation of blood sample levels
Example Titration Nomogram

<table>
<thead>
<tr>
<th>PTT (sec)</th>
<th>BOLUS DOSE</th>
<th>STOP INFUSION</th>
<th>RATE CHANGE</th>
<th>REPEAT PTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 39</td>
<td>Re-bolus with 5000 units IV</td>
<td>No</td>
<td>Increase infusion rate by 200 units/hr (2mL/hr)</td>
<td>6 hours</td>
</tr>
<tr>
<td>39 - 54</td>
<td>Re-bolus with 2500 units IV</td>
<td>No</td>
<td>Increase infusion rate by 100 units/hr (1mL/hr)</td>
<td>6 hours</td>
</tr>
<tr>
<td>55 - 75</td>
<td>None</td>
<td>No</td>
<td>No Change</td>
<td>6 hours until therapeutic times 2 values then every 12 hours</td>
</tr>
<tr>
<td>76 - 100</td>
<td>None</td>
<td>No</td>
<td>Decrease infusion rate by 100 units/hr (1 mL/hr)</td>
<td>6 hours</td>
</tr>
<tr>
<td>101 - 115</td>
<td>None</td>
<td>Hold infusion for 30 minutes</td>
<td>Decrease infusion rate by 100 units/hr (1 mL/hr)</td>
<td>6 hours after restarting infusion</td>
</tr>
<tr>
<td>116 - 139</td>
<td>None</td>
<td>Hold infusion for 1 hour</td>
<td>Decrease infusion rate by 200 units/hr (2 mL/hr)</td>
<td>6 hours after restarting infusion</td>
</tr>
<tr>
<td>Greater than 139</td>
<td>None</td>
<td>Hold infusion and recheck PTT in 2 hours Contact prescriber with PTT results</td>
<td>*If PTT less than 39 re-bolus with 5000 units IV bolus and decrease rate by 200 units/hr (2 mL/hr)</td>
<td>6 hours after restarting infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*If PTT 39-54 re-bolus with 2500 units IV bolus and decrease rate by 200 units/hr (2 mL/hr)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*If PTT therapeutic (55-75) decrease rate by 300 units/hr (3 mL/hr)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*If PTT still greater than 75 contact prescriber</td>
<td></td>
</tr>
</tbody>
</table>

- How would you adjust the rate if the patient’s current PTT is 50 seconds while the previous aPTT was 140 seconds?
Examples of Anticoagulation Medication Errors
Examples of Anticoagulation Errors

- Transcription/Documentation
  - Reading handwriting
- Prescribing
  - Two prescribers entering orders for same patient
- Dispensing
  - Similar looking packaging
  - Mix-ups in medication names
- Administration
  - Titration of continuous infusion medications
  - Double dosing due to poor timing/scheduling
Classic Examples of High Risk Errors
The Joint Commission Sentinel Events

- From 1997-2007, 32 sentinel events reported related to anticoagulants
  - Heparin: 21
  - Warfarin: 6
  - Enoxaparin: 3

- Most events occurred in hospital settings

- 28/34 patients died
The Joint Commission

- National Patient Safety Goal (NPSG) 03.05.01
  - Reduce the likelihood of patient harm associated with the use of anticoagulation therapy

- Elements of Performance
  - Use approved protocols for initiation and maintenance of anticoagulation therapy
  - Before starting a patient on warfarin, assess the patient’s baseline coagulation status and titrate warfarin based on INR.
  - Provide education to the patient and family.
  - Evaluate anticoagulation safe practices.
Strategies for Reducing the Risk of Anticoagulation Errors
ISMP Risk Assessment

- Patient Information
- Drug Information
- Communication of Drug Orders
- Drug Storage
- Medication Device Acquisition
- Quality Processes and Risk Management
- Competency and Staff Education
- Patient Education
ISMP Risk Assessment

- Patient Information
- Drug Information
- Communication of Drug Orders
- Drug Storage
- Medication Device Acquisition
- Quality Processes and Risk Management
- Competency and Staff Education
- Patient Education
**Patient Information**

- Readily available in the patient’s medical record
  - Diagnosis
  - Allergies, height, weight
  - Laboratory values (PTT, INR, platelet count)
  - Concomitant diseases/conditions
  - History of heparin induced thrombocytopenia (HIT)

- Used to make monitor and manage the effects of anticoagulants
  - Goal INR for warfarin patients
  - Guidelines/protocols for unfractionated heparin use
  - Bridging parenteral and oral anticoagulation
  - Assessment of subtherapeutic INRs
  - 4T score if concerned about HIT
Focus on Warfarin

2. Baseline INR obtained
5. INR obtained prior to initiating warfarin therapy
6. INR on admission for patients on warfarin as an outpatient
7. Defined frequency for INR monitoring during hospitalization
9. Blood specimens for INR drawn at standard times each day
11-12. Access to inpatient and outpatient labs as necessary
19. Indication for anticoagulation is documented
20. Monitor INR levels to adjust warfarin dosing
24. Bridging for patients with active thrombosis
25. If discharged with subtherapeutic INR, close monitoring to determine when to discontinue parenteral therapy
Strategies for Implementation of “Patient Information” Recommendations

- Electronic medical records
  - Complete with demographic, laboratory and other information necessary for making appropriate decisions
- Policies, Guidelines and Dosing Protocols
  - Anticoagulation policy
  - Oral anticoagulant dosing support
  - Heparin infusion protocols
- Heparin Induced Thrombocytopenia
  - Alerts regarding platelet drops
  - HIT antibody testing
  - Argatroban infusion protocol
Warfarin in Computerized Physician Order Entry (CPOE) System

- Require all warfarin orders to be entered with indication and goal INR
- Allows all providers and pharmacists to be aware of goal for patient and evaluate daily INRs appropriately

<table>
<thead>
<tr>
<th>Indication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ATRIAL FIBRILLATION</td>
</tr>
<tr>
<td>2. DVT/PE TREATMENT</td>
</tr>
<tr>
<td>3. CARDIAC THROMBUS</td>
</tr>
<tr>
<td>4. HYPERCOAGULABLE STATE</td>
</tr>
<tr>
<td>5. LVAD ANTICOAGULATION</td>
</tr>
<tr>
<td>6. MECHANICAL HEART VALVE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Goal INR:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. INR BETWEEN 2 AND 3</td>
</tr>
<tr>
<td>2. INR BETWEEN 2.5 TO 3.5</td>
</tr>
<tr>
<td>3. INR BETWEEN 2 TO 2.5</td>
</tr>
<tr>
<td>4. INR BETWEEN 2.5 TO 3</td>
</tr>
<tr>
<td>5. INR BETWEEN 1.8 TO 2.2 (LVAD)</td>
</tr>
</tbody>
</table>
Direct Oral Anticoagulants in CPOE

- Currently listed apixaban, dabigatran and rivaroxaban with indications and indication-specific dosing
- Default doses and frequencies
  - 15 mg vs. 20 mg
  - With meals vs. standard administration times
  - Daily vs. BID

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**rivaroxaban [XARELTO]**

Please select an indication:

1. non-valvular atrial fibrillation
2. venous thromboembolism treatment initial 3 weeks
3. venous thromboembolism treatment beyond 3 weeks
4. orthosurgery vte prophylaxis

**rivaroxaban [XARELTO]**

Weight=5 KG on Tue Jun 05 14:05
Information: 20mg Daily if Crcl>50mL/min (Cockroft-Gault formula);
15mg Daily if Crcl 15-50mL/min; Contraindicated if Crcl<15mL/min, on
dialysis, or moderate to severe hepatic impairment (Child-Pugh Class
B or C).
Future State

- Enhanced decision support for prescribers

- rivaroxaban (XARELTO) tablet Atrial Fibrillation
- rivaroxaban (XARELTO) tablet VTE Prophylaxis Post Hip Replacement
- rivaroxaban (XARELTO) tablet VTE Prophylaxis Post Knee Replacement
- rivaroxaban (XARELTO) tablet VTE Treatment Beyond 3 Weeks
- rivaroxaban (XARELTO) tablet VTE Treatment Initial 3 Weeks
Future State

- Key is to ensure that “it’s easy to do the right thing”
ISMP Risk Assessment

- Patient Information
- **Drug Information**
- Communication of Drug Orders
- Drug Storage
- Medication Device Acquisition
- Quality Processes and Risk Management
- Competency and Staff Education
- Patient Education
Drug Information

- Essential patient information used to monitor effects and adjust therapy
  - Disease-specific guidelines for antithrombotic therapy
  - Reviewed by practitioners prior to use
  - Reviewed every 3 years
  - Guidelines for periprocedural management (cessation, resumption) and management when using neuraxial analgesia
  - Weight-based protocol for unfractionated heparin
  - Alerts for practitioners regarding serious drug interactions

- Essential drug information readily available to guide management of adverse reactions
  - Protocols and guidelines for managing supratherapeutic INRs, life-threatening bleeding
  - Management of HIT
Strategies for Implementation of “Drug Information” Recommendations

- Antithrombotic Reversal Guidelines
- Periprocedural Management of Antithrombotic Therapy Guidelines
- Heparin and Heparin Induced Thrombocytopenia (HIT) Order Sets
Antithrombotic Reversal Guidelines

**Oral Direct Thrombin Inhibitor**

Dabigatran (Pradaxa®)

*Half-life*
- CrCl > 80: 14-17 hours
- CrCl 50-79: 16.6 hours
- CrCl 30-49: 18.7 hours
- CrCl < 30: 27.5 hours
Continuous Anticoagulant Infusion Order Set

- Key Points to Cover
  - Indications
  - Dosing
  - Titration
  - Laboratory testing

- Key to ensure that all parties who will use the order set find it user-friendly
  - Prescribers for ordering
  - Nursing for titrating
Heparin Order Set

- Baseline labs
- Duplicate anticoagulants
- Patient weight
- Clear indication for dosing and boluses
- Titration algorithm

### Doctor's Order

<table>
<thead>
<tr>
<th>DOCTOR'S ORDER</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATRIAL FIBRILLATION/ACS HEPARIN TREATMENT ORDERS - ADULT</td>
</tr>
</tbody>
</table>

**- DATE & TIME ALL ORDERS -**

**Drug Allergies:**

1. STAT CBC & PTT prior to initiating heparin
2. Daily CBC x 14 days
3. Orders for the following anticoagulants should be discontinued by ordering prescriber: apixaban, argatroban, bivalirudin, danaparoid, enoxaparin, fondaparinux, heparin (subcutaneous), rivaroxaban.
4. **Actual Body Weight for Bolus and Infusion Dosing (must calculate):** __________ kg

5. **Initial Heparin Bolus** (Choose one of the following orders):
   - Heparin Bolus 80 units/kg IV push (maximum initial bolus of 4,000 units - refer to table)
   - **NO INITIAL BOLUS**
   - Alternate initial bolus dose of ______ units/kg IV push x _______ kg = ______ units (round to nearest 500 units)

6. **Heparin Infusion** (standard concentration 25,000 units in 250 mL)
   - Initial Heparin Infusion Rate (Choose one of the following orders):
     - 12 units/kg/hr (maximum initial infusion rate of 1,000 units/hr - refer to table)
     - **NO INTRAVENOUS** should be given during heparin titration

7. **Subsequent Heparin Bolus**
   - **NO INTRAVENOUS** should be given during heparin titration

8. **PTT 6 hours after heparin infusion is started.**

9. **Heparin dosing to be titrated according to PTT as per Protocol below:****

<table>
<thead>
<tr>
<th>PTT (seconds)</th>
<th>BOLUS DOSE</th>
<th>STOP INFUSION</th>
<th>RATE CHANGE</th>
<th>REPEAT PTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 50</td>
<td>If ordered, re-bolus 6,000 units IV</td>
<td>No</td>
<td>Increase rate by 200 units/hr (2 mL/hr)</td>
<td>6 hours</td>
</tr>
<tr>
<td>50 - 54</td>
<td>If ordered, re-bolus 2,000 units IV</td>
<td>No</td>
<td>Increase rate by 100 units/hr (1 mL/hr)</td>
<td>6 hours</td>
</tr>
<tr>
<td>55 - 100</td>
<td><strong>No</strong></td>
<td><strong>No</strong></td>
<td><strong>No change</strong></td>
<td>6 hours until therapeutic for two values, then every 12 hours</td>
</tr>
<tr>
<td>101 - 115</td>
<td><strong>No</strong></td>
<td>Hold infusion for 30 minutes</td>
<td>Decrease infusion rate by 200 units/hr (2 mL/hr)</td>
<td>6 hours after restarting infusion</td>
</tr>
<tr>
<td>116 - 139</td>
<td><strong>No</strong></td>
<td>Hold infusion for 1 hour</td>
<td>Decrease infusion rate by 200 units/hr (2 mL/hr)</td>
<td>6 hours after restarting infusion</td>
</tr>
<tr>
<td>140 - 180</td>
<td><strong>No</strong></td>
<td>Hold infusion for 1 hour</td>
<td>Decrease infusion rate by 300 units/hr (3 mL/hr)</td>
<td>6 hours after restarting infusion</td>
</tr>
<tr>
<td>Greater than 180</td>
<td><strong>HOLD</strong> heparin infusion. Repeat PTT hourly until less than 101</td>
<td>When PTT less than 101, decrease rate by 400 units/hr (4 mL/hr). Call MD if two consecutive PTTs are greater than 180</td>
<td>6 hours after restarting infusion</td>
<td></td>
</tr>
</tbody>
</table>

If suspected improper timed sample, or potentially contaminated sample, repeat PTT

1 If patient’s PTT is less than 39 seconds for 12 hours or greater, call prescriber.

*P TT range between 51 and 64 suggests a PTT between 3.5 and 4.5 seconds.*
# Argatroban Order Set

## Step 1: Diagnosis

<table>
<thead>
<tr>
<th>Scoring System for the Pretest Probability for the presence of HIT</th>
<th>Individual Point Score</th>
<th>Section Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>A score (from 0 to 2) is determined for each of the below categories, resulting in the potential score from zero to eight</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. **Thrombocytopenia**
   - Platelet count decrease greater than 50% and nadir greater than or equal to 20,000
   - Platelet count decrease 30-50% or nadir between 10,000-19,000
   - Platelet count decrease less than 30% or nadir less than 10,000
   - Platelet count fall at less than 4 days without recent exposure
   - Clear onset between 5 to 10 days or platelet count fall less than or equal to 1 day if prior heparin exposure within the last 30 days
   - Consistent with fall at 5 to 10 days but not clear (e.g. missing platelet counts) or onset after day 10 or fall less than or equal to 1 day with prior heparin exposure within the last 30-100 days

2. **Timing of platelet count fall**
   - Platelet count fall at less than 4 days without recent exposure
   - Clear onset between 5 to 10 days or platelet count fall less than or equal to 1 day if prior heparin exposure within the last 30 days
   - Consistent with fall at 5 to 10 days but not clear (e.g. missing platelet counts) or onset after day 10 or fall less than or equal to 1 day with prior heparin exposure within the last 30-100 days

3. **Thrombosis or other sequelae**
   - Confirmed new thrombosis, skin necrosis, or acute systemic reaction post-IV unfractionated heparin bolus
   - Progressive or recurrent thrombosis, non-necrotizing (erythematous) skin lesions, or suspected thrombosis which has not been proven
   - None

4. **Other causes for thrombocytopenia present**
   - None apparent
   - Possible: ________________
   - Definite: ________________

Total Score (1+2+3+4) = Total Score

- **Total Score**
  - 0-3: Low
  - 4-5: Intermediate
  - 6-8: High
Argatroban Order Set (cont.)

- Step 2: Determine next steps based on 4T score

<table>
<thead>
<tr>
<th>Pretest Probability</th>
<th>Heparin Induced Platelet Antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (Greater than or equal to 0.4 optical density)</td>
<td>Negative (Less than 0.4 optical density)</td>
</tr>
<tr>
<td>High</td>
<td>HIT confirmed</td>
</tr>
<tr>
<td>Stop all heparin and LMWH products</td>
<td></td>
</tr>
<tr>
<td>Start DTI (see orders page 2)</td>
<td>HIT possible</td>
</tr>
<tr>
<td>• Continue DTI</td>
<td>• Send SRA for confirmation</td>
</tr>
<tr>
<td>• Consider other causes of thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>HIT possible</td>
</tr>
<tr>
<td>Stop all heparin and LMWH products</td>
<td></td>
</tr>
<tr>
<td>Start DTI (see orders page 2)</td>
<td>• Use clinical judgement regarding continued use of heparin and LMWH products</td>
</tr>
<tr>
<td>Low</td>
<td>HIT possible</td>
</tr>
<tr>
<td>• Send SRA for confirmation</td>
<td></td>
</tr>
<tr>
<td>• Consider other causes of thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>• Use clinical judgement regarding continued use of heparin and LMWH products</td>
<td></td>
</tr>
<tr>
<td>• Use of DTI specific to patient risk vs. benefit</td>
<td></td>
</tr>
</tbody>
</table>
## Argatroban Order Set (cont.)

### Step 3: Dosing of Argatroban

DISCONTINUE ALL HEPARIN PRODUCTS (including flushes and LMWH products)  
ADD heparin to patient allergy list

Obtain specimen:  
- ☐ Heparin Induced Platelet Antibody (ELISA)  
- ☐ Serotonin Release Assay (SRA) (if indicated, refer to table on Page 1)

Indication for direct thrombin inhibitor use  
- ☐ Anticoagulation for prophylaxis/treatment of thrombosis in patients with suspected/documentedor HIT  
- ☐ Anticoagulation for prophylaxis/treatment of thrombosis in patients refractory or allergic to heparin

Baseline CBC, Basic Metabolic Panel, LFTs, PTT, INR  
Daily CBC, Basic Metabolic Panel, PTT, INR while patient on argatroban or bivalirudin therapy

Patient weight: ______________________ kg (calculations are based on total body weight)

Order ☐ STAT ☐ Begin at (date and time) ________________

- ☐ BIVALIRUDIN 250 mg/250 mL D5W  
  - ☐ Standard dose: _____ mg/kg/hr (normal renal function, recommended dose is 0.15 mg/kg/hr)  
  - ☐ Adjusted dose: Renal impairment (*CrCl less than 60 mL/min)  
    - ☐ CrCl 30-59 mL/min: 0.08 mg/kg/hr  
    - ☐ CrCl less than 30 mL/min: 0.05 mg/kg/hr  
    - ☐ CVVH: 0.05 mg/kg/hr  
    - ☐ Hemodialysis: 0.02 mg/kg/hr

*CrCl = [(140-age) x body weight (kg) / (72 x SCr) x 0.85 for women]

- ☐ ARGATROBAN 125 mg/125 mL D5W  
  - ☐ Standard dose _____ mcg/kg/min (recommended dose is 1 mcg/kg/min, max start dose is 2 mcg/kg/min)  
  - ☐ Adjusted dose: _____ mcg/kg/min (recommended dose is 0.5 mcg/kg/min in patients with moderate hepatic failure (Child Pugh Score of 6 or greater; refer to table on reverse page for calculations), heart failure, multiple system organ failure/critically ill, severe anasarca, the early post cardiac surgery period)
Transitioning to Warfarin

Measure INR Daily

If INR ≤ 4, continue concomitant therapy.

If INR > 4, stop argatroban.

Recheck INR in 4-6 hours.

If INR therapeutic, discontinue argatroban.

If INR subtherapeutic, resume argatroban.
ISMP Risk Assessment

- Patient Information
- Drug Information
  - Communication of Drug Orders
- Drug Storage
- Medication Device Acquisition
- Quality Processes and Risk Management
- Competency and Staff Education
- Patient Education
Communication of Drug Orders and Other Drug Information

- Computer order entry system
  - Interfaced with laboratory system
  - Alerts regarding abnormal laboratory values
  - Duplicate anticoagulation order alerts

- Dosing Standardization
  - Ordering and charting of heparin boluses
  - Rounding of doses
Strategies for Implementation of “Communication of Drug Orders and Other Drug Information”

<table>
<thead>
<tr>
<th>Enoxaparin Dose (mg)</th>
<th>Round To (mg)</th>
<th>Administer (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>75-84</td>
<td>80</td>
<td>0.8</td>
</tr>
<tr>
<td>85-94</td>
<td>90</td>
<td>0.9</td>
</tr>
<tr>
<td>95-104</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>105</td>
<td>105</td>
<td>0.7</td>
</tr>
<tr>
<td>106-111</td>
<td>111</td>
<td>0.74</td>
</tr>
<tr>
<td>112-114</td>
<td>114</td>
<td>0.76</td>
</tr>
<tr>
<td>114-124</td>
<td>120</td>
<td>0.8</td>
</tr>
<tr>
<td>125-129</td>
<td>129</td>
<td>0.86</td>
</tr>
<tr>
<td>130-135</td>
<td>135</td>
<td>0.9</td>
</tr>
<tr>
<td>136-141</td>
<td>141</td>
<td>0.94</td>
</tr>
</tbody>
</table>
ISMP Risk Assessment

- Patient Information
- Drug Information
- Communication of Drug Orders
- **Drug Storage**
- Medication Device Acquisition
- Quality Processes and Risk Management
- Competency and Staff Education
- Patient Education
Drug Storage, Stock, Standardization and Distribution

- Standard concentrations for unfractionated heparin
- Premixed solutions used whenever possible
  - Intravenous heparin
  - Glycoprotein IIb/IIIa inhibitors
- Thrombolytic therapy prepared by the pharmacy or trained practitioners
- Standard administration times for antithrombotics
- Ready access to reversal agents or antidotes
Strategies for Implementation of “Drug Storage, Stock, Standardization and Distribution”
ISMP Risk Assessment

- Patient Information
- Drug Information
- Communication of Drug Orders
- Drug Storage
- Medication Device Acquisition
- Quality Processes and Risk Management
- Competency and Staff Education
- Patient Education
Medication Device Acquisition, Use and Monitoring

- Laboratory reagents used to test aPTT
  - Re-establishment of therapeutic range required when reagents are changed
  - Updates to protocols must occur simultaneously

- Use of smart infusion pumps
  - Ensure accuracy of pump libraries
  - Annual updates and testing
  - Minimal deviation allowed to minimize risk of errors
  - Involvement of multidisciplinary team
Impact of a Pharmacist on Anticoagulation Safety
Clinical Pharmacist Anticoagulation Services

- Pharmacy-driven warfarin dosing
- Pharmacist monitoring of argatroban
  - Appropriate prescribing
  - Appropriate dose titration
- Automatic renal dose adjustment policies
Inpatient Warfarin Management

- Study conducted by the Clinical Pharmacist Anticoagulation Service (CPAS) at Kaiser Permanente
- Evaluated the impact of 24/7 warfarin dosing by pharmacists in an inpatient setting
- Included over 6,000 patients in final analysis
- Results
  - Pharmacist-dosing led to significantly increased percent of time in therapeutic range and less time outside of therapeutic range
  - Reduced risk of hemorrhagic and thromboembolic complications

Inpatient Argatroban Management

- Study conducted by pharmacists at the Medical University of South Carolina
- Evaluated the impact of pharmacist-driven dosing and titration of argatroban infusions
- Final analysis included 50 patients
- Results
  - Therapeutic PTT values were achieved significantly more quickly in the pharmacist arm
  - Lower rate of medication errors
  - No difference in adverse events

Conclusion

- Anticoagulants are high risk medication with a narrow therapeutic window that require appropriate dosing and monitoring.

- Requires the involvement of all healthcare professionals to ensure appropriate use.

- Strategies to minimize ADRs include multidisciplinary involvement in patient care, identification of weakness in the medication use process and optimization of electronic methods.
Anticoagulation Safety: Reducing Adverse Drug Events

Kunal J. Shah, PharmD
Clinical Coordinator
Pharmacy Department
Morristown Medical Center