Anticoagulation: A Review of Medication Safety

St. Vincent’s Medical Center
2010
Objectives

• Define The Joint Commission’s National Patient Safety Goal (NPSG) 3
• List the Elements of Performance for NPSG 3
• Describe the mechanism of action, side effects, drug interactions, and monitoring parameters, for Warfarin, Heparin, Low Molecular Weight Heparin (LMWH), and Direct Thrombin Inhibitors
• Review the ACCP dosing and reversal guidelines for Warfarin
• Discuss patient education and documentation requirements for SVMC
NPSG 03.05.01

• Reduce the likelihood of patient harm associated with the use of anticoagulation therapy
• Anticoagulation therapy is the second most common drug class associated with adverse drug events (ADEs) requiring treatment in the Emergency Department due to:
  – Complex dosing
  – Requisite follow-up monitoring
  – Inconsistent patient compliance
• Standardized practices
  – Include patient involvement
  – Reduce the risk of ADEs associated with the use of heparin, LMWH, and warfarin
NPSG 3: Elements of Performance

1. Implement a defined anticoagulant management program to individualize the care provided to each patient
2. Use only oral unit dose products and pre-mixed infusions to reduce compounding and labeling errors
3. Dispense warfarin for each patient in accordance with established monitoring procedures
4. Use approved protocols for initiation and maintenance of anticoagulation therapy appropriate to the medication used, condition being treated, and potential for drug interactions
5. For patients started on warfarin, a baseline INR is available, and for all patients receiving warfarin therapy, a current INR is available and used to monitor and adjust therapy
NPSG 3: Elements of Performance

6. Dietary services is notified of all patients receiving warfarin and responds according to its established food/drug interaction program
7. When heparin is administered intravenously and continuously, use programmable infusion pumps
8. Use a policy that addresses baseline and ongoing lab tests that are required for heparin and LMWH
9. Provide education regarding anticoagulation therapy to prescribers, staff, patients, and families
10. Patient/family education includes importance of follow-up monitoring, compliance issues, dietary restrictions, and potential for adverse drug reactions and interactions
11. Evaluate anticoagulation safety practices
Warfarin (Coumadin®, Jantoven®): Mechanism of Action

- Limits activation of Vitamin K dependent clotting factors
  - Factors II, VII, IX, X
  - Antithrombotic effect primarily due to reduction of Factor II (prothrombin)
- Inhibit synthesis of Vitamin K dependent anticoagulant Proteins C & S
  - Potential procoagulant effect (i.e., increase risk of clot)

http://www.frca.co.uk/article.aspx?articleid=100096
Warfarin: Pharmacokinetics

• Rapidly and completely absorbed
• Half-life of clotting factors
  – VII: 6 hrs
  – IX: 24 hrs
  – X: 40 hrs
  – II: 60 hrs
  – Acronym: SNOT
    • Seven, Nine, 10, Two
• Anticoagulant effect may be seen via increased INR due to inhibition of Factor VII within 24 hours after drug administration, but peak effect delayed for 72-96 hours due to Factor II inhibition
  – Full anticoagulation does not occur for 2-3 days after first therapeutic INR
• Metabolized by hepatic enzymes
  – Requires dose reduction in hepatic dysfunction
  – Hepatic enzyme involvement results in significant drug interaction
### Warfarin: Indication/Optimal Therapeutic Range

<table>
<thead>
<tr>
<th>Indication</th>
<th>INR</th>
<th>Therapy Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atrial Fibrillation/Atrial Flutter</strong></td>
<td>2 - 3</td>
<td>High risk of stroke: Indefinite</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Persistent: Indefinite</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elective cardioversion: 3 week before and 4 weeks after conversion</td>
</tr>
<tr>
<td><strong>DVT/PE</strong></td>
<td>2 - 3</td>
<td>1st episode w/ reversible risk factors: 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1st episode, idiopathic: 6-12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recurrent: Indefinite</td>
</tr>
<tr>
<td><strong>Total Knee Arthroplasty</strong></td>
<td>2 - 3</td>
<td>At least 10 days</td>
</tr>
<tr>
<td><strong>Total Hip Replacement/Hip Fracture Surgery</strong></td>
<td>2 - 3</td>
<td>28-35 days</td>
</tr>
<tr>
<td><strong>Valvular Disease</strong></td>
<td>2 - 3</td>
<td>Long term</td>
</tr>
<tr>
<td><strong>Myocardial Infarction/Coronary Heart Disease</strong></td>
<td>2 - 3</td>
<td>Long term</td>
</tr>
<tr>
<td><strong>Valve Replacement</strong></td>
<td>Tissue Values: 2 - 3</td>
<td>Tissue: 3 months</td>
</tr>
<tr>
<td></td>
<td>Bileaflet mechanical value in aortic position: 2 - 3</td>
<td>Mechanical: Long term</td>
</tr>
<tr>
<td></td>
<td>Mechanical valve: 2.5 - 3.5</td>
<td></td>
</tr>
<tr>
<td><strong>Antiphospholipid syndrome</strong></td>
<td>2 - 3</td>
<td>Indefinite</td>
</tr>
</tbody>
</table>
Warfarin: Contraindications/Precautions

• Black Box Warning
  – Can cause fatal bleeding
    • Hemorrhage in any tissue or organ

• Contraindications
  – Pregnancy
  – Hemorrhagic/bleeding tendencies
  – Blood dyscrasia
  – Surgery of CNS, eye, or trauma with large open surfaces
Warfarin: Side Effects

• Minor bleeding (9.6% of patients)
  – Blood in urine or stool
  – Excessive menstrual bleeding
  – Melena
  – Petechiae
  – Excessive bruising
  – Persistent oozing from superficial injuries

• Fatal bleeding (0.6% of patients)
  – Risk factors: INR >4.0, age >65, highly variable INRs, history of GI bleed, HTN, cerebrovascular disease, serious heart disease, anemia, malignancy, trauma, renal insufficiency, concomitant medications, and long duration of therapy

• Skin Necrosis
  – Purple toe syndrome
Warfarin: Drug Interactions

• Inhibition of platelets ➔ increase risk of bleeding
  – Aspirin (in addition to prescribed amount)
  – NSAIDS (ibuprofen, naproxen)
    • Acetaminophen best option for OTC pain control
  – High dose penicillin
  – Herbals
    • St. John’s Wart, Gingko

• Increase INR ➔ risk of bleeding
  – Antibiotics
    • Fluoroquinolones, Flagyl, Bactrim
  – Antifungals
    • Fluconazole
  – Amiodarone

• Decrease INR ➔ increase risk of clotting
  – Rifampin
  – Phenobarbital, Carbamazepine
  – Cholestyramine, Sucralfate
Warfarin: Other Interactions

• Changes in lifestyle habits can effect INR
  – Physical activity
    • Increased physical activity may result in increase warfarin metabolism and decrease in INR
  – Smoking
    • Liver makes more enzymes to eliminate the toxic substances ingested from smoking and, in the process, eliminates more warfarin
    • Decreasing smoking can increase INR
  – Alcohol
    • Large amounts and/or concomitant liver disease can increase INR
  – Diet
    • Large amounts of Vit K foods decrease INR
Warfarin: Dietary Considerations

- Vitamin K foods inhibit the action of warfarin
  - Leafy green vegetables (spinach, broccoli, greens)
  - Mayonnaise
  - Green tea
  - Liver
- Should not be eliminated from diet due to health benefits
- Consistency week to week in amount of Vitamin K key to maintaining therapeutic INRs
- SVMC Dietary Services
  - Automatically informed of patients receiving warfarin
  - Menu at SVMC does not contain foods with significant amounts of Vitamin K
Warfarin: Monitoring

• Laboratory tests at baseline and daily
  – PT, INR, HGB, HCT
• The prescribing physician shall be notified
  – If there is a significant change in the patient's condition or labs
  – If the INR >3.5
• Baseline INR should be below or within the goal INR range prior to initiation or continuation of warfarin therapy
• If the baseline INR is above the desired goal, the pharmacist shall contact the prescriber
Warfarin: Dosing

- Dose variable and dependent on a number of patient specific and environmental factors
- Initial dose: 5-10mg
  - Limited data supporting loading dose
- Lower initial doses (2.5-5mg)
  - Elderly
  - Hepatic dysfunction
  - Heart failure
  - Possible drug interactions
- Goal for INR to increase no more than 0.5 / day
  - Increases > 0.5 per day, may result in supra-therapeutic levels
# Warfarin: SVMC Initial Dosing Guideline & Pharmacy Protocol

<table>
<thead>
<tr>
<th>Day</th>
<th>INR</th>
<th>Dosing – Moderate Warfarin Sensitivity (patients &lt;70)</th>
<th>Dosing – High Warfarin Sensitivity (patients &gt;=70, baseline INR &gt;1.5, significant hepatic disease, albumin &lt;2, known genetic polymorphism of CYP450 2C9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;1.5</td>
<td>5mg</td>
<td>3mg</td>
</tr>
<tr>
<td>2</td>
<td>&lt;1.5</td>
<td>5mg</td>
<td>3mg</td>
</tr>
<tr>
<td></td>
<td>1.5 – 1.9</td>
<td>2.5mg</td>
<td>2mg</td>
</tr>
<tr>
<td></td>
<td>2.0 – 2.5</td>
<td>1mg - 2.5mg</td>
<td>1mg or skip a dose</td>
</tr>
<tr>
<td></td>
<td>&gt;2.5</td>
<td>Skip a dose</td>
<td>Skip a dose</td>
</tr>
<tr>
<td>3</td>
<td>&lt;1.5</td>
<td>5mg - 10mg</td>
<td>3mg</td>
</tr>
<tr>
<td></td>
<td>1.5 – 1.9</td>
<td>2.5mg to 5mg</td>
<td>2mg - 3mg</td>
</tr>
<tr>
<td></td>
<td>2.0 – 3.0</td>
<td>2.5mg or skip a dose</td>
<td>1mg or skip a dose</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0</td>
<td>Skip a dose</td>
<td>Skip a dose</td>
</tr>
<tr>
<td>4</td>
<td>&lt;1.5</td>
<td>10mg</td>
<td>4mg - 5mg</td>
</tr>
<tr>
<td></td>
<td>1.5 – 1.9</td>
<td>5mg - 7.5mg</td>
<td>3 - 4mg</td>
</tr>
<tr>
<td></td>
<td>2.0 – 3.0</td>
<td>5mg</td>
<td>0 - 3mg</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0</td>
<td>Skip a dose</td>
<td>Skip a dose</td>
</tr>
<tr>
<td>5</td>
<td>&lt;1.5</td>
<td>10mg</td>
<td>4mg - 5mg</td>
</tr>
<tr>
<td></td>
<td>1.5 – 1.9</td>
<td>7.5mg - 10mg</td>
<td>4mg</td>
</tr>
<tr>
<td></td>
<td>2.0 – 3.0</td>
<td>5mg or skip a dose</td>
<td>0 - 3mg</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0</td>
<td>Skip a dose</td>
<td>Skip a dose</td>
</tr>
<tr>
<td>&gt;=6</td>
<td>Make adjustment based on total weekly dose (increase or decrease by 5-15% depending on current and target INR)</td>
<td>Make adjustment based on total weekly dose (increase or decrease by 5-15% depending on current and target INR)</td>
<td></td>
</tr>
</tbody>
</table>
Warfarin: Administration

• Given daily at same time each day
• Standard administration time at SVMC is 1300
  – Allows for lab results and adjustments to dose in a timely manner
  – All doses will be administered at this time unless the prescriber specifies "now" or "stat"
• If a dose is missed, take if same day as the missed dose
  – Never double up dose, unless prescribed
Warfarin: Reversal

• Several options
  – Hold warfarin
  – Vitamin K
    • PO
    • IV
      – Must be diluted in 50ml of D5W
      – Only stable for 30 minutes after dilution
      – Potential for anaphylaxis reaction
  • SQ is no longer recommended
    – Erratic and unpredictable absorption
  • High doses of Vit K can result in warfarin resistance for up to 1 week after reversal
    – Use the lowest amount of Vit K possible for the situation
  – Fresh Frozen Plasma (FFP)

• Method of reversal depends on
  – Elevation in INR
  – Severity of bleeding
  – How fast reversal needed
## Warfarin: Reversal

ACCP Guidelines for Management of Excessive Anticoagulation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR above therapeutic goal but ≤ 5; no significant bleeding</td>
<td>Decrease or omit dose, monitor more frequently, and resume at lower dose when INR is therapeutic</td>
</tr>
</tbody>
</table>
| INR ≥ 5 but ≤ 9; no significant bleeding | • Omit 1-2 doses, monitor more frequently, and resume at lower dose when INR is therapeutic  
• Omit dose and give Vit K (≤ 5 mg PO), particularly if at increased risk of bleeding  
• If more rapid reversal is required because patient requires urgent surgery, Vit K (2-4 mg PO) can be given with the expectation that a reduction of the INR will occur in 24 hrs. If the INR is still high, additional vitamin K (1-2 mg PO) can be given |
| INR ≥ 9; no significant bleeding | Hold warfarin and give higher dose of Vit K (5-10 mg PO) with the expectation that the INR will be reduced substantially in 24-48 hr. Monitor more frequently and use additional Vit K if necessary. |
| Serious bleeding at any elevation of INR | Hold warfarin and give higher dose of Vit K (10 mg by slow IV infusion), supplemented with FFP or prothrombin complex concentrate, depending on the urgency of the situation; recombinant factor VIIa may be considered as alternative to prothrombin complex concentrate; Vit K can be repeated every 12 hrs. |
| Life-threatening bleeding | Hold warfarin and give prothrombin complex concentrate supplemented with Vit K (10 mg by slow IV infusion); recombinant factor VIIa may be considered as alternative to prothrombin complex concentrate; repeat if necessary, depending on INR. |
### Warfarin: SVMC Guideline for Managing Elevated INR Values

<table>
<thead>
<tr>
<th>INR Value</th>
<th>Bleeding Status</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Any elevation | Life-threatening         | 1. Hold warfarin  
                             | 2. Vitamin K 10mg IV                                               |
| Any elevation | Serious bleeding         | 1. Hold warfarin  
                             | 2. Vitamin K 10mg IV                                               |
| INR >9        | No significant bleeding  | 1. Hold warfarin  
                             | 2. Give Vitamin K 5mg PO  
                             | 3. Resume lower dose when INR normalized                             |
| INR >5, <9    | No significant bleeding  | 1. Hold 1-2 doses and resume lower dose when INR normalized **OR**  
                             | 2. If high risk for bleeding, hold 1-2 doses and wait for INR to normalize and give Vitamin K  
                             | 5mg PO x1 dose, then resume lower dose once INR is normalized       |
| INR <5        | No significant bleeding  | 1. Omit one dose and lower warfarin dosage                                                   |
Warfarin: Patient Education

- Nursing will provide education to all patients on
  - Previous therapy prior to admission
  - Short term therapy (i.e., orthopedic surgery where duration of treatment less than 2 months)

- Pharmacy will provide education for all patients newly started on long-term treatment
  - RN to ask pharmacy to provide education
Heparin: Mechanism of Action

- Binds to antithrombin III, causing a conformational change resulting in the inactivation of clotting factors
  - Factor IIa (thrombin), Xa, IXa, XIa, and XIIa
- Low doses predominately affect Xa (prophylaxis)
- Full-doses affect Factor IIa (thrombin) for established clot

http://www.frca.co.uk/article.aspx?articleid=100096
Heparin: Indications

• Indications
  – Prophylaxis
    • VTE, PE
  – Treatment
    • Atrial Fibrillation, VTE, PE, ACS
Heparin: Pharmacokinetics

• **Half-life:** 0.5-2 hrs

• **Mean time to steady state:** 6 hrs
  – Increases with larger doses
  – Decreases with PE, massive thrombus, or new clot due to increased clearance

• **Metabolized by reticuloendothelial system**
  – No dosage adjustments for renal or hepatic dysfunction
Heparin: Contraindications/Precautions

• Contraindications
  – Severe thrombocytopenia
  – Uncontrollable active bleeding

• Precautions/Warnings
  – Hemorrhage
  – Bleeding
  – Thrombocytopenia
Heparin: Side Effects

- Major & Minor bleeding
- Immune mediated thrombocytopenia (HIT)
- Allergic reactions
- Osteoporosis
  - If administered longer than 1 month
- Alopecia
Heparin Induced Thrombocytopenia (HIT)

• Criteria to suspect
  – Received heparin or LMWH within 5 days
  – PLT < 150,000 or 50% decrease from baseline
  – 30% decrease in PLT from baseline with concomitant thrombotic event or new thrombus
  – Places patient at risk for clotting

• Treatment
  – Hold ALL heparin, including flushes
  – Direct Thrombin Inhibitors
Heparin-Associated Bleeding

• Risk factors for increased incidence
  – Higher heparin doses
  – Concomitant thrombolytic or abciximab (ReoPro®) treatment
  – Comorbid conditions
    • Recent surgery
    • Trauma
    • Invasive procedures
    • Concomitant hemostatic defects
  – Elderly
Heparin: Dosing

• Prophylaxis
  – 5,000 units SQ TID or BID
    • TID has been shown to be more effective

• Treatment
  – Dosing protocols based on indication and actual body weight
    • Standard Heparin Protocol
      – ACS, DVT, PE, Afib
        » Goal PTT: 60-85
        » Boluses
        » Starting Dose: 16 units/kg
    • Neurology Heparin Protocol
      – Stroke
        » Goal PTT: 60-85
        » No boluses
        » Starting Dose: 14 units/kg
Heparin: Dosing Protocols

• Stops propagation of clot growth
• Decreases incidence of “recurrent” DVT
  – Doses adjusted within the first 24 hours to achieve an aPTT > 1.5 x control
  – Heparin levels of ≥ 0.2 IU are achieved
• Key to treatment with heparin drip is reaching therapeutic range as soon as possible
  – Time patient sub-therapeutic aPTT, increases risk of recurrent VTE
  – Only a weak association exists between supra-therapeutic aPTT responses and bleeding
Heparin: Monitoring

• Baseline Labs
  – PT, PTT, PLT, HBG, HCT
  – PTT Q6hrs until within therapeutic range

• Daily Labs
  – PTT once stable

• Every Other Day Labs
  – HBG, HCT, PLT

• The prescriber shall be called when:
  – Platelets less than 150,000
  – Decrease in Platelets to less than 70% of baseline
  – Decrease in Platelets to less than 50% of baseline
Heparin: Reversal

• Protamine sulfate IV
  – Indicated for major bleeding
  – Binds heparin forming stable complex that doesn’t have any anticoagulant effects
Low Molecular Weight Heparin (LMWH) (Lovenox®)

- Binds to antithrombin III causing a conformation change thus resulting in the inactivation of Factor Xa

- Enoxaparin (Lovenox®)
  - Derived from porcine heparin
  - 1/3 the molecular weight of heparin and thus bind preferentially to Factor Xa rather than Factor IIa (thrombin)
  - One of three LMWH products on market

http://www.frca.co.uk/article.aspx?articleid=100096
Fondaparinux (Arixtra®)

- Selectively inhibits Factor Xa
- Similar to LMWHs
Enoxaparin/Fondaparinux: Pharmacokinetics

• Half-life
  – Enoxaparin: 4.5-7 hrs
  – Fondaparinux: 17-21 hrs

• Renally eliminated
  – Requires dosage adjustment in renal dysfunction
Enoxaparin/Fondaparinux: Indications

- **Enoxaparin**
  - Prophylaxis
    - DVT
    - PE
    - Ischemic complications of unstable angina
    - Non-Q wave myocardial infarction
  - Treatment
    - DVT
    - PE
    - Acute ST-segment elevation myocardial infarction

- **Fondaparinux**
  - At SVMC, alternative to enoxaparin for orthopedic surgery
Enoxaparin/Fondaparinux: Contraindications/Precautions

- **Black Box Warning**
  - Use in patients undergoing spinal/epidural anesthesia or spinal puncture are at increased risk for spinal or epidural hematomas, which may cause long-term or permanent paralysis
  - **Risk Factors**
    - Use of indwelling epidural catheters
    - Concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
    - A history of traumatic or repeated epidural or spinal punctures
    - A history of spinal deformity or spinal surgery

- **Contraindications**
  - Active major bleeding
  - Thrombocytopenia with positive anti-platelet antibody test in the presence of enoxaparin
  - Hypersensitivity to enoxaparin, heparin, pork products, benzyl alcohol

- **Precautions/Warnings**
  - Hemorrhage
  - Bleeding
  - Thrombocytopenia
Enoxaparin/Fondaparinux: Side Effects

• Bleeding
• Thrombocytopenia
• Injection site irritation
# Enoxaparin: Dosing

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Surgery</td>
<td>2 hrs after surgery: 40mg SQ daily x 7-10 days</td>
</tr>
<tr>
<td>Hip Replacement</td>
<td>12-24 hrs after surgery: 30mg SQ Q12hrs or 40mg SQ daily x 7-10 days (then 40mg SQ daily x 3 weeks)</td>
</tr>
<tr>
<td>Knee Replacement</td>
<td>12-24 hrs after surgery: 30mg SQ Q12hrs</td>
</tr>
<tr>
<td>Unstable Angina, Non-Q-Wave MI</td>
<td>1mg/kg SQ Q12hr plus ASA for up to 8 days</td>
</tr>
<tr>
<td>DVT/PE</td>
<td>1mg/kg SQ Q12hrs or 1.5mg/kg SQ daily x 5-7 days or until INR is 2-3</td>
</tr>
</tbody>
</table>

All treatment doses are rounded to the nearest syringe size based on the patient’s weight.
## Fondaparinux: Dosing

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip Fracture Surgery</td>
<td>6-8 hrs after surgery: 2.5mg SQ daily for up to 24 days</td>
</tr>
<tr>
<td>Hip Replacement Surgery</td>
<td>6-8 hrs after surgery: 2.5mg SQ daily x 5-9 days</td>
</tr>
<tr>
<td>Knee Replacement Surgery</td>
<td>6-8 hrs after surgery: 2.5mg SQ daily x 5-9 days</td>
</tr>
</tbody>
</table>
Enoxaparin/Fondaparinux: Monitoring

- Laboratory tests
  - SCr, HGB, HCT, PLT
    - PTT/PT not needed due to more predictable anticoagulation effect
- Notify the prescribing physician
  - If there is a significant change in the patient's condition
Enoxaparin/Fondaparinux: Reversal

• Enoxaparin
  – Protamine sulfate IV

• Fondaparinux
  – Recombinant Factor VIIa (NovoSeven®)
Direct Thrombin Inhibitors (DTIs): Mechanism of Action

- Dabigatran (Pradaxa®)
- Argatroban
- Lepirudin (Refludan®)
- Indirectly inhibit Factor IIa (thrombin)
  - Inhibit both free and bound thrombin
  - Does not cause HIT

http://www.frca.co.uk/article.aspx?articleid=100096
Dabigatran (Pradaxa®): Indication

- Approved November 2010
- Nonvalvular atrial fibrillation to prevent stroke and systemic embolism
- Alternative treatment to warfarin
- Non-formulary at SVMC
Dabigatran (Pradaxa®): Pharmacokinetics

- Requires renal adjustment
- Capsule should not be opened or crushed
Dabigatran (Pradaxa®): Side Effects

- Nausea
- Vomiting
- Bleeding
Dabigatran (Pradaxa®): Dosing & Monitoring

- 150mg PO BID
- No monitoring required
  - Patients are fully anticoagulated and at risk for bleeding even though no PTT or INR tests are needed
- Should be stopped 1-5 days prior to surgery depending on renal function
- No antidote for reversal
Argatroban and Lepirudin (Refludan®): Indication

• At SVMC, approved for anticoagulation in patients with known or suspected HIT
Argatroban and Lepirudin (Refludan®): Pharmacokinetics

- Argatroban
  - Hepatically eliminated
  - Used in patients with renal dysfunction

- Lepirudin
  - Renally eliminated
  - Used in patients with hepatic dysfunction
Argatroban and Lepirudin (Refludan®): Side Effects

• Bleeding
• Hypersensitivity and allergic reactions
Argatroban and Lepirudin (Refludan®): Dosing & Monitoring

• Dosing based on protocol

• Monitoring
  – Lepirudin: ACT
  – Argabroban: aPTT

• No antidote for reversal
Ordering Anticoagulation at SVMC

• Use SVMC orders sets when initiating anticoagulation to ensure appropriate dosing and lab monitoring
  – SVMC Therapeutic Anticoagulation Order Set
    • Warfarin
    • Enoxaparin (Lovenox®)
    • Fondaparinux (Arixtra®)
  – Standard Heparin Drip Protocol
    • Heparin for DVT, PE, Afib, MI
  – Neurology Low Dose Heparin Drip Protocol
    • Heparin for Stroke
  – Aragatroban Infusion Anticoagulation for Suspected or Known Heparin-Induced Thrombocytopenia
  – Lepirudin Infusion Orders: Heparin-Induced Thrombocytopenia
References


4. Enoxaparin Sodium Prescribing Information.


6. Heparin Sodium Prescribing Information.


9. Warfarin Sodium Prescribing Information.