About This Presentation

Strategic Vectors:
- Clinical Outcomes
- Patient Safety
- Physician Engagement

Team:
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- Dr. Stephen A. Vitkun
- Dr. Lisa Senzel
- Doreen Elitharp, NP
- Jeannene Strianse, Pharm D
- Dr. Mathew Tharakan
- Marie Varela, Pharm D (Team Leader)

Version 1  November 14th, 2017
About This Team

Reporting Structure

- This Team
- Medication Safety SUBcommittee
- Medication Safety Committee
- NPSG Committee
- Patient Safety Committee
- Governing Body
Objectives

At the conclusion of the program, participants will be able to:

1. Summarize the 2018 NPSG (Joint Commission National Patient Safety Goals) regarding anticoagulation education
2. Explain the importance of baseline and follow up monitoring
3. Discuss anticoagulation-related drug-food interactions
4. Give examples of anticoagulant-related drug-drug interactions
5. Explain the potential for adverse drug reactions and interactions
6. Discuss reasons to use the anticoagulation PowerPlans, protocols and order sentences available in Cerner
2018 NPSGs

Provide education regarding anticoagulation to

- Prescribers
- Staff
- Patient
- Families

Regarding:

- Importance of follow up monitoring
- Compliance
- Drug-food interactions
- Potential for adverse drug reactions and interactions
Anticoagulation for Inpatients

May be ordered for

- VTE prophylaxis
- Prophylaxis of stroke with atrial fibrillation
- Continuation of home therapy
- Acute treatment of thrombotic disease
Anticoagulation Monitoring

- Monitoring of anticoagulation at baseline and during therapy optimizes therapeutic effects, improves outcomes and minimizes the risk of untoward effects

- Standard baseline monitoring
  - CBC with platelets
  - PT, INR
  - aPTT

- Monitor ongoing therapy as appropriate

- PowerPlans include orders for baseline and ongoing drug therapy monitoring.
Role of the Prescriber

- Select the appropriate pharmacologic agent
- Consider the indication upon drug selection
- Consider patient comorbidities
- Choose the appropriate dosage and frequency or rate
- Use PowerPlans whenever available
- Manage drug interactions
- Monitor drug therapy
- Discuss with the patient
Role of the Nurse

- Review the medication order for appropriateness
- Indication
- Dose, frequency, route of administration
- Patient specific factors
- Drug interactions
- Provide education to patient and/or patient caregiver
- Administer as directed
- Monitor for therapeutic effects
- Monitor for ADRs
- Discuss with the patient
Role of the Pharmacist

• Review the medication order for appropriateness based on:
  – Indication
  – Dose, frequency, route of administration
  – Patient specific factors
• Monitor for drug interactions
• Insure that dosage adjustments are made based on appropriate monitoring parameters
• Provide drug information
DVT Prophylaxis

• The Cerner VTE advisor incorporates a risk assessment and recommendations for prophylaxis

• Assessment and appropriate preventative measures required for every patient admitted

• Must document prophylaxis plan on day of or day after admission or transfer to ICU
DVT Prophylaxis

• Prevention strategies for VTE prophylaxis include:
  – Mobility
  – Compression stockings
  – Inferior vena cava (IVC) filters
  – Pharmacologic
    • Sub-Q heparin
    • Sub-Q low molecular weight heparin
    • Sub-Q fondaparinux (acute HIT or history of HIT)
    • Oral anticoagulants

• Important for prescriber to reassess risk at transitions of care, added therapies, changes in patient condition
Enoxaparin (LOVENOX®)

- Low molecular weight heparin
- Treatment doses differ from prophylactic doses
- Usual Adult Dose (prophylaxis)
  - 40 mg SQ daily
  - 30 mg SQ every 12 hours
  - 30 mg SQ daily for CrCl < 30 mL/min
- Usual Adult Dose (treatment)
  - 1 mg/kg every 12 hours
  - 1.5 mg/kg daily
- Weight-based dosing uses actual body weight
- See Lexi-Comp for specific dosage recommendations
Enoxaparin (LOVENOX®)

- Contraindicated in HIT
- Caution:
  - epidural or spinal anesthesia or spinal puncture
  - Renal impairment (dosage adjustment for CrCl less than 30 ml/min)
  - Morbidly obese may require dosage adjustments (see Lexi-Comp)
  - Off-label use in pediatrics (see Lexi-Comp for age-based and weight-based dosing recommendations)
- May require anti-Xa monitoring in some patients
Fondaparinux (ARIIXTRA®)

- Polysaccharide anticoagulant
- Reserved for VTE prophylaxis in patients w/ history of HIT
- Dose
  - 2.5 mg SQ daily (patients 50 kg or greater)
  - Renal impairment (CrCl 30-50 mL/min) reduce dose 50%
- Contraindications:
  - patients with CrCl < 30 mL/min
  - patients weighing less than 50 kg
- Caution: epidural or spinal anesthesia or spinal puncture
Using Weight-Based Dosing

- For weight-based anticoagulation, the patient’s actual weight in kg is used.
- Morbidly obese individuals may be dosed too high if total actual body weight is used.
- Heparin PowerPlans cap off bolus dosing and initial infusion rate to avoid overdosing morbidly obese individuals.
- The argatroban protocol uses decreased dosing for morbidly obese individuals.
- For morbidly obese individuals, when no specific dosing is available and weight-based dosing is required, may initial using a modified weight:

  i.e. Lean or ideal body weight plus half of weight in excess of lean or ideal body weight for morbidly obese individuals.
Oral Anticoagulants

– Warfarin
  • (vitamin K antagonist)
  • PowerPlan includes algorithm to guide dosing and monitoring

– DOACs (direct oral anticoagulants)
  • Direct thrombin Inhibitors
  • Anti Xa Inhibitors
  • (Order sentences currently under construction)
Warfarin (COUMADIN®)

• Not usually ordered as prophylaxis unless patient has history of VTE

• Indications
  – in A-fib patients to prevent stroke
  – Treatment of DVT, PE
  – Prophylaxis in ortho post op patients

• Order through the Warfarin PowerPlan

• First dose may be ordered through the VTE Advisor
Warfarin (COUMADIN®) continued

- Monitor with INR
- It requires several days of therapy to reach a therapeutic INR
- Bridge (overlap) therapy with a parenteral anticoagulant is often necessary
- Drug-food interaction
  - warfarin antagonizes vitamin K
  - Requires consistent amount of vitamin K (green leafy vegetables, etc.) in diet to achieve and maintain therapeutic range
- Caution: multiple drug interactions (see Lexi-Comp)
- Reversal PowerPlan available in Cerner
Warfarin Reversal Special Notes

- Don’t routinely use blood products to reverse warfarin
- Patients requiring reversal of warfarin can often be reversed with vitamin K alone
- Prothrombin complex concentrates or plasma should only be used for patients with serious bleeding or requiring emergency surgery.

http://www.choosingwisely.org/clinician-lists/american-society-hematology-non-emergent-reversal-of-vitamin-k-antagonists/
Dabigatran (PRADAXA®)

- Direct thrombin inhibitor anticoagulant
- Uses:
  - VTE treatment (after 5-10 days of parenteral anticoagulant therapy)
  - VTE prophylaxis
  - VTE after hip replacement surgery
- Contraindicated in severe renal impairment
- See Lexi-Comp for all dosage recommendations
- Black box warning for risk of hematoma with epidural or spinal catheter puncture
- Conversion: Initiate dabigatran ≤2 hours prior to the time of the next scheduled dose of the parenteral anticoagulant (e.g., enoxaparin) or at the time of discontinuation of IV anticoagulant
- Reversal agent: Praxbind® (idarucizumab)
Edoxaban (SAVAYSA®)

• Factor Xa inhibitor anticoagulant
• Uses:
  – VTE treatment
  – prevention of stroke and embolism in non-valvular a-fib
• Reduce dosage with renal impairment and specific P-gp inhibitors
• Dosage reduction necessary in all patients with CrCl 15 to 50 mL/minute.
• See Lexi-Comp for complete dosage recommendations

• Black box warnings:
  – Risk of hematoma with epidural or spinal catheter puncture
  – Premature discontinuation of edoxaban increases the risk of ischemic events
  – Do not use if CrCl is greater than 95 mL/minute (reduced efficacy)
Rivaroxaban (XARELTO®)

- Factor Xa inhibitor anticoagulant
- Used for
  - VTE treatment
  - prevention of VTE recurrence
  - prevention of stroke and embolism in non-valvular a-fib
  - post-op (hip and knee) DVT prophylaxis
- See Lexi-Comp for complete dosage recommendations
- Avoid use in patients with CrCl less than 30 mL/min
- Black box warnings:
  - Risk of hematoma with epidural or spinal catheter puncture
  - Premature discontinuation of rivaroxaban increases the risk of ischemic events
Apixaban (ELIQUI®)

- Factor Xa inhibitor anticoagulant
- Uses
  - VTE treatment
  - prevention of VTE recurrence
  - prevention of stroke and embolism in non-valvular a-fib
  - post-op (hip and knee) DVT prophylaxis
- Reduce dose for any two of any of the following: Age $\geq 80$ years, body weight $\leq 60$ kg, or serum creatinine $\geq 1.5$ mg/dL
- Avoid use for CrCl less than 30 mL/min
- See Lexi-Comp for complete dosage recommendations
- Black box warnings:
  - Risk of hematoma with epidural or spinal catheter puncture
  - Premature discontinuation of apixaban increases the risk of ischemic events
Important Point

Recommendations vary for each oral anticoagulant regarding:

– Use in renal or liver impairment
– How long to hold prior to surgery
– When to start when switching between anticoagulants
– Check references (i.e. Lexi-Comp) prior to prescribing
Adult IV Heparin PowerPlan Protocols

• 4 nurse-driven protocols available:
  – DVT/PE
  – Neuro-Cardio
  – Low Dose for High Risk and Stroke Patients No-Bolus
  – DVT/PE protocol for post-surgical patients

• Prescribers orders, reviews daily, reorders and discontinues as appropriate.

• If heparin requires renewal, ensure that prn heparin bolus doses are reordered (unless “Low Dose” or “Post Surgical DVT” protocols are used.)
Adult IV Heparin PowerPlan Protocols

• DVT/PE
  – Full treatment protocol
  – Recommendations as per ACCP*
  – Protocol includes heparin boluses
• Neuro-Cardio
  – Recommendations as per ACCP, ACC**
  – Protocol includes heparin boluses
• Low Dose for High Risk and Stroke Patients
  – Never achieves full anticoagulation
  – May switch to Neuro-Cardio or DVT/PE protocol once stabilized
• No-Bolus DVT/PE protocol for post-surgical patients
  – Any bolus doses must be ordered individually

*ACCP= American College of Chest Physicians,
**ACC = American College of Cardiologists
### Heparin Protocol on the eMAR


#### Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Start Date</th>
<th>Start Time</th>
<th>End Date</th>
<th>End Time</th>
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**Continuous Infusions**

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<td>Heparin additive 25,000 Units (1,000 Units/hr)</td>
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<td>250 ml, Continuous IV NW, First dose is Routine, 03/13/17 20:44:00, 10 ml/hr, 25 ml, Order Weight 127 kg, Total Initial Weight 127 kg</td>
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<td>Isosorbide mononitrate (Emul)</td>
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<td>30 mg, TAB ER, Oral, X1, First dose is Routine, 03/16/17 12:30:00, Hold for SBP ≤100</td>
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**Therapeutic Class View**

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<th>Class</th>
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</table>
eMAR: Heparin Adjustment Nomogram

Order Comment
03/13/2017 20:47
Starting rate is based on 12 units/kg/hr (1000 units/hr max initial rate)

aPTT (seconds): Instructions

< 43: Re-bolus using full dose, Increase rate by 100 units/hr and draw aPTT in 6 hrs
43-59: Give ½ of the initial bolus (max, 2500 units), Increase rate by 50 units/hr, aPTT in 6 hrs
60-85: No bolus, No change in rate, draw aPTT Next Day AM
86-100: No bolus, Decrease rate by 50 units/hr, and draw aPTT in 6 hrs
101-130: No bolus, Decrease rate by 100 units/hr, and draw aPTT in 6 hrs
131-150: Hold infusion for 1 hr & call MD, Decrease rate by 150 units/hr, and draw aPTT in 6 hrs

161-190: Hold infusion 1 hr & call MD, Decrease rate by 200 units/hr, and draw aPTT in 6 hrs
> 190: Hold infusion 1 ½ hour & call MD, Decrease rate by 200 units/hr, and draw aPTT in 6 hrs

03/13/2017 20:45
Starting rate is based on 12 units/kg/hr (1000 units/hr max initial rate)

aPTT (seconds): Instructions

< 43: Re-bolus using full dose, Increase rate by 100 units/hr and draw aPTT in 6 hrs
43-59: Give ½ of the initial bolus (max, 2500 units), Increase rate by 50 units/hr, aPTT in 6 hrs
60-85: No bolus, No change in rate, draw aPTT Next Day AM
86-100: No bolus, Decrease rate by 50 units/hr, and draw aPTT in 6 hrs
101-130: No bolus, Decrease rate by 100 units/hr, and draw aPTT in 6 hrs
131-150: Hold infusion for 1 hr & call MD, Decrease rate by 150 units/hr, and draw aPTT in 6 hrs

161-190: Hold infusion 1 hr & call MD, Decrease rate by 200 units/hr, and draw aPTT in 6 hrs
> 190: Hold infusion 1 ½ hour & call MD, Decrease rate by 200 units/hr, and draw aPTT in 6 hrs
Nurse Responsibilities

- Verify that proper protocol was chosen (arterial vs. venous, stroke)
- Inform and educate the patient
- Obtain a baseline aPTT and CBC as ordered
- Verify calculations of bolus (if applicable) and maintenance rate
- Document bolus administration
- Set pump for infusion using guardrails
- Document begin bag, hourly administration and rate changes
- Obtain an independent double check and signature
- Draw aPTTs when appropriate
- Adjust rate as per nomogram
- Draw routine CBC and platelets as ordered
- Notify prescriber if ADRs occur
- Notify prescriber if patient
HIT

- Heparin Induced Thrombocytopenia
- Results from an allergy to heparin
- Antibodies are formed and attack heparin which has a receptor site on platelets
- First sign is decrease in platelets to 50% of baseline
- Usually occurs after 1 or 2 weeks of heparin therapy (but can occur on day 1 if a re-exposure)
- Can result in thrombosis
- Potential loss of limbs
- Potentially fatal
Management of HIT

For patients with a high suspicion of HIT:

– Discontinue all heparin therapy (including flushes)
– For patients at risk of thrombosis, prescriber must begin therapy with a direct thrombin inhibitor
  • Argatroban
  • Bivalirudin (ANGIOMAX®) off-label for HIT
– Prescriber to order heparin antibody test
– Assessment of heparin allergy (physician/LIP)
– Dopplers
– Documentation of heparin allergy in records
– Discuss with patient
Management of HIT: Special Note

• Don’t test or treat for suspected heparin-induced thrombocytopenia (HIT) in patients with a low pre-test probability of HIT.

• In patients with suspected HIT, use the “4T’s” score to calculate the pre-test probability of HIT.

• This scoring system uses the timing and degree of thrombocytopenia, the presence or absence of thrombosis, and the existence of other causes of thrombocytopenia to assess the pre-test probability of HIT.

• **HIT can be excluded by a low pre-test probability score** (4T’s score of 0-3) without the need for laboratory investigation.

• Do not discontinue heparin or start a non-heparin anticoagulant in these low-risk patients because presumptive treatment often involves an increased risk of bleeding, and because alternative anticoagulants are costly.

Argatroban

• **Class**
  – Direct thrombin inhibitor
  – Anticoagulant

• **Indications**
  – Anticoagulation therapy with history of HIT
  – Treatment of HIT

• **Standard Concentration (1:1)**
  – 250 mg in 250 mL D5W
  – 50 mg in 50 mL (premix in unspecified diluent)
Argatroban

• Dosing (initial rate) for treatment (not PCI)
  – Standard: 2 mcg/kg/min
  – Greater than 140 kg 1 mcg/kg/min
  – Critically ill /hepatic 0.5 mcg/kg/min

• ADRs
  – Bleeding
  – Hypotension
  – Dyspnea
  – N/V

• Monitoring
  – aPTT
  – Target 45-90 seconds
  – Stroke patient target: 45-65 seconds
The Argatroban PowerPlan

- Choice of 3 different dosing strategies based on patient factors (patient weight, organ function)
- Similar to heparin protocol
- No boluses necessary with Argatroban used for treatment
- **This PowerPlan is NOT for PCI dosing of argatroban**
Bivalirudin

• **Class**
  – Direct thrombin inhibitor
  – Anticoagulant

• **Indications**
  – Anticoagulation for PCI
  – Off label use:
    • Anticoagulation therapy with history of HIT
    • Treatment of HIT
    • PowerPlan available

• **Standard Concentration (1:1)**
  – 250 mg in 250 mL D5W
Bivalirudin

• Dosing (initial rate) for treatment (not PCI)
  – Initial dosing 0.15 mg/kg/hour with normal renal function (PowerPlan)
  – Initial rate is reduced with renal impairment

• Most Common ADRs
  – Bleeding
  – Hypotension
  – Pain, headache
  – Nausea

• Monitoring
  – aPTT
  – PowerPlan targets aPTT of 60-80 seconds
Conversion from Argatroban to Warfarin (Bridge Therapy)

- Warfarin initiation requires
  - Platelet recovery
  - Stabilization of aPTT in the target range on argatroban
  - Continuation of argatroban until warfarin is therapeutic
- **Argatroban falsely elevates the INR**
- Monitoring requires checking INR while argatroban is infusing until total INR is above 4 when on warfarin
- Hematology consult during bridge therapy to warfarin is recommended
General Anticoagulation Points to Consider

- Was the patient on anticoagulant medication prior to hospitalization?

- Has the correct anticoagulant been chosen for the patient based on surgical status, bleeding risk, allergy history, other patient factors, other medications?

- Has conditions changed for the patient that could affect the choice of anticoagulant?

- Has the patient been educated regarding their anticoagulant medications?

- If the patient has not reached aPTT goals on IV anticoagulation in 24 hours, reassess the patient
Anticoagulation in Pediatric Patients

- Pediatric Hematology is available for guidance and consultation

- The heparin protocol used in pediatrics is not a nurse-driven protocol, however the adult IV heparin protocols may be used in the PICU in patients who are over 16 years old and greater than or equal to 40 kg.

- When enoxaparin is used, it is routinely monitored by anti-Xa activity.

- Warfarin can be ordered electronically, off the Warfarin PowerPlan, by using the pediatric warfarin dose sentence

- See Lexi-Comp for complete prescribing information
Additional Anticoagulation Points to Consider

• Are there plans for insertion or removal of an epidural catheter; anticoagulation will need to be held.

• Communication with the team, the patient, and patient care taker is important!

• Communication orders, however, are not an acceptable way to order, dose, or adjust anticoagulation.

• Daily review of actual active orders, and lab results.

• For VTE prophylaxis: is the prophylaxis appropriate for the patient’s current level of risk.
Patient and Patient Caregiver Information

• Providing education to patient and caregiver is an essential aspect of successful anticoagulation therapy
• Discharge prescriptions for anticoagulant medications must be carefully reviewed
• All patients who are discharged on anticoagulant medications must be given a face-to-face medication discharge counseling
• Plans for follow up and monitoring must be discussed with the patient
• Document patient education in the patient’s electronic record
For further information regarding anticoagulation

- Dosing
- Monitoring
- ADRs
- Drug-drug interactions
- Drug-Food interactions
- Drug-Lab interactions

please refer to Lexi-Comp 2018
Additional Resources

Many excellent, free educational resources are available on
http://acforum.org/
References

• ACP Recommendations for VTE Prophylaxis in Hospitalized Patients www.aafp.org › Journals › afp › Vol. 85/No. 12(June 15, 2012)


• Argatroban Prescribing Information (GlaxoSmithKline 2009)


References (continued)

- Correction: Weight-Based Argatroban Dosing Nomogram for Treatment of Heparin-Induced Thrombocytopenia. *Ann Pharmacother* February 2009 43:394


- *Lexi-Comp online* 2018

