

**University of Connecticut Health Center- John Dempsey Hospital
Multidisciplinary Policy and Procedure Manual**

**SUBJECT: ANTICOAGULATION PROTOCOL FOR HEPARIN, LOW MOLECULAR WEIGHT
HEPARIN, WARFARIN, DIRECT THROMBIN INHIBITORS**

POLICY #:

DEPARTMENT: PHARMACY

ORIGINATED: 9/08

REVISED:

I. OBJECTIVE

To provide safe and effective anticoagulation therapy through a collaborative approach at John Dempsey Hospital.

II. POLICY

Upon receiving the MD's/LIP's order for IV Heparin, the Pharmacy & Nursing Departments will collaborate to initiate Heparin drip and/or oral warfarin therapy according to our approved anticoagulation protocols.

III. PROCEDURE

A. Heparin Therapy

1. General Indications

- | | | |
|----|--|-----------------------------------|
| a. | Deep vein thrombosis (DVT) | - Use Wt. Based Venous Thrombosis |
| b. | Pulmonary embolism (PE) | - " " |
| c. | Venous thrombosis | - " " |
| d. | Atrial fibrillation with embolism | - Use Acute Cardiac Protocol |
| e. | Prophylaxis of stroke in post MI patient | - Use Acute Ischemic Stroke |
| f. | Unstable angina | - Use Acute Cardiac Protocol |
| g. | Peripheral arterial embolism | |

2. Contraindications

- Hypersensitivity to Heparin products
- Active bleeding
- Heparin Induced Thrombocytopenia- HIT
- Coagulopathy

3. Initial Information

- Patient age, weight (actual), height and gender
- Medical and drug history pertaining to anticoagulation of the patient
 - MD/LIP Responsibility
- Indication for heparin therapy - MD/LIP Responsibility
- Laboratory Baseline Values - MD/LIP Responsibility
 - PT, PTT, CBC with platelet count
 - Stool for blood, urinalysis
 - Platelet count, Hemoglobin & Hematocrit at baseline and q 2-3 days
- Other considerations
 - No IM injections while on Heparin
 - Aspirin, NSAID may be discontinued.

4. Target range for aPTT= 60-90 secs for Venous Thrombosis & Acute Coronary Syndrome, 41-65 secs for Acute Ischemic Stroke

5. Dosing Based on Actual Body Weight (ABW), including obese patients

- A. Dosing:
- Preparation
 - Standard Heparin Infusion with 25,000 units/ 500 mls D5W
= 50 units/ ml
 - The dose will be rounded to the nearest 50 units
 - Conc. of heparin used for bolus: 5,000 units/ 1 ml vial

Heparin (Cont.)

2. Confirmed Venous Thrombosis (PE / DVT)
 - a. Loading dose: 80 units/kg, max. of 10,000 units, follow with
 - b. Infusion dose: 18 units/kg/hour, max. of 1,800 units/hr
3. Acute Cardiac Syndrome
 - a. Loading dose: 70 units/kg, max. of 5,000 units, follow with
 - b. Infusion dose: 12 units/kg/hour, max. rate of 1,500 units/hour
4. Acute Ischemic Stroke
 - a. No loading bolus dose
 - b. Infusion dose: 10 units/kg/hr, max. of 1,500 units/kg/hour

B. Major bleeding risks:

1. Major Surgery within 14 days
2. Recent intracranial bleeding
3. Peptic ulcer disease
4. Platelet count less than 100,000
5. Femoral catheterization
6. Biopsy of an internal organ

6. MD/LIP Responsibility

- a. Patient diagnosis, history and determination of therapy.
- b. Order Heparin , complete printed Heparin Order
- c. Ordering and monitoring of baseline and ongoing laboratory tests.
- d. Monitor patient for therapeutic outcome and adverse events, including ADR reporting via Patient Safety Net
- e. Monitor patient for signs of Heparin Induced Thrombocytopenia: resistance to anticoagulation, signs of thrombosis (arterial/venous/PE), significant drop (30-50% Unexplained decrease) in Plt Ct, skin necrosis with sc heparin, systemic reactions to IV heparin
- f. Perform ongoing assessment for signs and symptoms of bleeding (guaiac positive stools, hematuria, epistaxis, petechiae or ecchymosis, oozing from needle punctures or around invasive devices, other sources of bleeding)
- g. Perform ongoing assessment for signs and symptoms of Pulmonary Embolism : stabbing chest pain that is worse on deep inspiration or coughing, tachypnea, dyspnea, cough, hemoptysis, syncope, pallor/cyanosis, tachycardia, hypotension, desaturation on pulse oximetry or fever.

7. Pharmacist Responsibility

- a. Validate Heparin order by review of chart/discussion with MD/LIP for indication
- b. Verify that the Labs in section A.3. d. are ordered
- c. Verify that the Heparin Nomogram is being followed & result recorded, intervene if aPTT are not in range

8. Nursing Responsibilities:

- a. Must assess for completion of baseline labs (CBC w Plt. Ct., PT/aPTT,urinalysis)
- b. Obtain and document baseline V/S's patient weight and height by inquiry or measurement
- c. Initiate Heparin Dosing Nomogram by inclusion in patients chart
- d. Laboratory monitoring/dosing adjustments
 - Repeat aPTT 6 hours after the start of the heparin infusion, and 6 hours after each dose adjustment until in goal range, then aPTT daily
 - Adjust bolus and infusion accordingly to Disease Specific Heparin Nomogram
 - Follow ordered Heparin Nomogram with dose adjustments when aPTT is out of Range
 - After TWO CONSECUTIVE therapeutic aPTT, order daily aPTT
 - The nurse must document date, time, value of aPTT and dosage changes in the patient's chart per Hospital Policies - Monitor ordered lab values (e.g., CBC, coagulation studies); report abnormal values to MD/LIP.

Heparin (Cont.)

- e. Blood samples for coagulation studies may be drawn from indwelling arterial lines if a sufficient volume of blood is drawn and discarded first (6 times the dead space volume of the tubing). Use a different line for drawing coag. studies than the line infusing with IV Heparin.
- f. Monitor patient for signs of Heparin Induced Thrombocytopenia:
Unexplained resistance to anticoagulation, signs of thrombosis (arterial/venous/PE), significant drop (30-50% decrease) in Plt Ct, skin necrosis with sc heparin, systemic reactions to IV heparin
- g. The nurse must double check the bolus and infusion rate with another nurse before making any change
- h. The nurse can contact the unit pharmacist for any questions regarding Heparin therapy
- i. Heparin infusions are to be run on Alaris infusion pumps using the Guardrails
- j. Heparin infusions require verification by a second RN/LPN. Refer to procedure for Medication: Double Checks.
- k. Nursing Assessments:
 - a. Assess adequacy of circulation (patients with venous thrombo-embolism):
 - b. Assess color, sensation and movement [flexion and extension] (CSM) of all extremities at least every 12 hours or as ordered.
 - c. For checks in affected extremities in addition to CSM, palpate for temperature and peripheral pulses and note color, blanching/capillary refill, swelling and pain.
 - d. Ensure that anti-embolytic stockings or compression devices have been applied when ordered.
- l. Perform ongoing assessment for signs and symptoms of bleeding (guaiac positive stools, hematuria, epistaxis, petechiae or ecchymosis, oozing from needle punctures or around invasive devices, other sources of bleeding)
- m. Implement measures to protect from falls as per protocol for Falls: Risk Identification and Prevention Managem
- n. Perform ongoing assessment for signs/symptoms of pulmonary embolism, e.g., sharp stabbing chest pain that is worse on deep inspiration or coughing, tachypnea, dyspnea, cough, hemoptysis, syncope, pallor/cyanosis, tachycardia, hypotension, desaturation on pulse oximetry or fever.

9. PATIENT TEACHING:

- 1. Nursing to review with patient to report to RN or LIP the following symptoms : signs of bleeding or bruising, shortness of breath, dizziness or chest pain.
- 2. Review activity limitations as appropriate, e.g., avoid using sharp objects, shaving with a razor with a blade or using a hard toothbrush.

10. DESIRED PATIENT OUTCOMES

- 1. Patient will verbalize understanding of the rationale for anticoagulant therapy, side effects and precautions.
- 2. Patient will not experience hemorrhagic or thrombotic complications related to anticoagulant therapy.
- 3. Patient will have risk for fall assessed and precautions implemented

11. Physician/LIP Notification

- a. The physician/LIP must be notified if patient experiences any bleeding so that he/she can determine further therapeutic options.
- c. The physician/LIP must be notified in the event of significant adverse reaction due to Heparin therapy (e.g. thrombocytopenia).
- d. The physician/LIP is also responsible for determining length of therapy

12. Over anticoagulation

- a. Hold if mildly elevated aPTT per protocol
- b. Notify MD as per protocol
- c. Protamine sulfate is the reversal agent for Heparin - see IV Med Guidelines.

Adult Low Molecular Weight Heparin- Enoxaparin Guidelines

DVT Prophylaxis:

High Risk: 30 mg SC BID

Low Risk: 40 mg SC Daily

Renal dosing: CrCl < 30 mls/min - use 30 mg SC q 24 hours

Not recommended in acute renal failure, ESRD or dialysis

DVT Treatment: 1 mg/kg SC q 12 hr – if pt is > 150 kg should use IV heparin or
Monitor anti-Xa activity

OR 1.5 mg/kg SC daily - for outpatient use

Renal dosing: CrCl < 30 mls/min - use 1 mg/kg SC q 24 hrs

Not recommended in acute renal failure, ESRD or dialysis

Unstable Angina/NSTEMI: initial 30 mg IV Push (optional) followed by: 1mg/kg SC q 12hr

Percutaneous Coronary Intervention (PCI):

A. Prior Enoxaparin administration:

> 2 doses of 1 mg/kg SC or 30 mg IV Bolus + 1 mg/kg SC dose

- if the last SC dose of Enoxaparin was given > 8 hours ago, administer an additional 0.3mg/kg IV Push

- if the last 1 mg/kg dose SC dose of Enoxaparin was given < 8 hours ago, do not administer additional doses

- 1 dose of SC with no IV bolus, give additional 0.3 mg/kg IV bolus at the time of PCI

B. No prior Enoxaparin administration

- with or without concurrent Glycoprotein IIb/IIIa inhibitors

- 0.5- 0.75 mg/kg IV Push

STEMI:

- < 75 years of age: 30 mg IV bolus followed by 1 mg/kg SC q 12 hours

- > 75 years of age: 0.75 mg/kg SC q 12 hours (max. 75 mg for each first two SC doses)

Monitoring: Anti Xa level is recommended in the following scenarios:

a. Obesity > 150 kg

b. Pregnancy

c. Newborns

d. Renal failure w high risk for bleeding

Reversal of Enoxaparin:

- Protamine sulfate will partially reverse 50-60% of enoxaparin 's anti- Xa activity .

- 1 mg Protamine IV for every 1 mg of enoxaparin. A second infusion of 0.5 mg protamine for every 1 mg enoxaparin may be administered 2-4 hours after the first protamine infusion.

Converting from IV Heparin Infusion to Enoxaparin SC:

- Stop Heparin infusion

- Wait 0-60 minutes. If PTT is > 100 secs, consider waiting 90 minutes.

- Administer enoxaparin dose

Converting from Enoxaparin to IV Heparin Infusion:

IV heparin infusion with bolus may be started 8-12 hours after the last enoxaparin dose

Epidural catheters with Anticoagulants(LMWH, Heparin, Warfarin) Use:

Avoid LMWHs or use with caution in patients undergoing spinal/epidural anesthesia or spinal punctures. **If enoxaparin use is warranted for reduction of thromboembolism, an epidural catheter should neither be placed nor removed while the patient is receiving enoxaparin in an effort to decrease the risk of hematoma formation.** That is, if an epidural catheter is planned for post-op analgesia in a patient currently receiving enoxaparin, enoxaparin should be discontinued at least 12 hours before catheter placement and at least 24 hours if high dose enoxaparin is used and NOT restarted until at least 4 (four) hours after the epidural catheter is removed. An alternative is to initiate enoxaparin 12-24 hours after epidural catheter placement and continue therapy. Discontinue the enoxaparin 12-24 hours before removal of the epidural catheter. If the patient needs to be restarted on enoxaparin, wait a minimum of 4 (four) hours after catheter is removed.

Additionally, the guidelines for the use of warfarin and heparin are as follows:

IV Heparin-

1. hold heparin 6 hours prior to neuraxial anesthesia placement and have a normalized PTT
2. delay restarting heparin for 2 hours after neuraxial block or catheter placement.
3. remove neuraxial catheter 4 hours after stopping heparin

Warfarin-

1. hold warfarin 5 days prior to initiation of neuraxial block **and obtain an INR less than or equal to 1.3**
2. stop warfarin and remove catheter when INR is **less than or equal to 1.5 and notify anesthesia of any neurological change (suggestive of epidural hematoma**
3. restart warfarin 2 hours after catheter removal.

Enoxaparin (Lovenox[®]) Rounding for Full Dose Therapy:

Enoxaparin Rounding to Nearest Syringe

The P&T Committee has determined dosages of Lovenox may be “rounded-off” to maximize the reliability, cost-effectiveness and consistency of dosing. Dosages should be ordered in 10mg increments. **If an order is placed for a dose that is not a 10mg increment, the pharmacist may make the rounding change per P&T protocol.** An individual physician's signature is not necessary for the order to be carried out.

. Orders should be adjusted to the interval appropriate for the renal function of the patient according to the renal dosing policy. (ie: CrCl < 30 ml/min, Q12H changed to Q 24H).

Enoxaparin Rounding Table

Enoxaparin dose Written (mg)	Rounded Enoxaparin Dose (mg)	Syringe Dispensed
25 – 34	30	30 mg X 1
35 – 44	40	40 mg X 1
45 – 54	50*	60 mg X 1
55 – 64	60	60 mg X 1
65 – 74	70*	80 mg X 1
75 – 84	80	80 mg X 1
85 – 94	90*	100 mg X 1
95 – 104	100	100 mg X 1
105 – 114	110*	120 mg X 1
115 – 124	120	120 mg X 1
125 – 134	130*	150 mg X 1
135 – 144	140*	150 mg X 1
145 – 154	150*	150 mg X 1

*Doses not commercially available. RN will discard the mg amount to reach the ordered dose. It is not necessary to discard the nitrogen bubble in the syringe when administering the entire dose in the syringe. It may be safely injected subcutaneously. If altering the dose in the syringe, the bubble may be cautiously expelled before measuring the dose to be administered.

Warfarin Therapy

1. General Information:

- a. Warfarin therapy may be indicated in patients with a long term need for anticoagulation.
- b. Warfarin may start on day 1 or 2 of heparin therapy.
- c. The International Normalized Ratio (INR) is used to monitor and dose warfarin therapy
- d. Heparin should be given for a minimum of five days and for two consecutive days of a therapeutic INR when converting heparin to warfarin for initial therapy of venous thrombosis.

2. Patient information needed:

- a. Indication for warfarin therapy and target INR
- b. Age
- c. Medication profile including previous warfarin therapy
- d. Nutritional status
- e. Concurrent disease states

3. Dosing:

- a. Initial doses should be ordered after a review of the patient's diagnosis and concomitant disease states, history, medications, age and nutritional status
- b. In younger, healthier patients, doses should begin at 5 mg for the first 1 or 2 days, then subsequent dosing is based on the INR response.
- c. In elderly (age >60), debilitated or malnourished patients, those with CHF or liver dysfunction, those at high risk for bleeding, or those on medications known to increase sensitivity to warfarin a starting dose of less than 5mg is recommended.
- d. For patients who have been on warfarin prior to admission, their outpatient dose should be ascertained and continued unless modification is necessary (elevated INR, active bleeding, impending surgery/procedure, changes in interacting medications or disease states, NPO status, etc.)
- e. Doses should be ordered daily after a review of the most recent INR and are to be given at 6pm for most patients.

4. Initial Monitoring:

- a. Baseline INR, platelet count, hemoglobin and hematocrit, assessment of signs or symptoms of bleeding.
- b. Daily INR's are required with dose adjustments made based on the results.
- c. Therapeutic INR's are usually not achieved for 4-5 days and early increases in INR do not reflect the true anticoagulated state.
- d. The effect of an alteration in dose on the INR will not stabilize for approximately 1 week.
- e. Addition or subtraction of an interacting medication, or a change in its dose, will cause a change in INR necessitating careful monitoring over the next week (longer in some cases).
- f. Loading doses or overly aggressive initial dosing should be avoided as it results in over anticoagulation.
- g. In stable inpatients with no medication or disease state changes with in the past week, consideration may be given to checking the INR 2-3 times a week.

5. Target INR:

- a. The target INR is determined by the prescribing MD/LIP based on disease state and other patient factors. American College of Chest Physician (ACCP) recommended therapeutic range for warfarin:

Indication	Target INR
Prophylaxis of venous thrombosis Treatment of DVT Treatment of PE Prevention of systemic embolism Tissue heart valves AMI Valvular heart disease Atrial Fibrillation	2 - 3
Recurrent systemic embolism Bileaflet valve Lupus Inhibitor with recurrent thrombotic events	2 - 3
Mechanical Valve in mitral position	2,5 - 3,5

Warfarin (Cont.)

6. Long Term Monitoring (appropriate for patients transitioning to outpatient care):
 - a. Once INR is therapeutic for at least 2 days, monitor INR 2 to 3 times per week for 2 weeks.
 - b. Once INR is stable for 2 weeks, monitor INR again in two weeks. Then if stable may monitor monthly in otherwise stable patients (no change in interacting medications, diet, disease states, etc.)
 - c. Patient self monitoring is integral to successful and safe anticoagulation. Patient/caregivers are to be educated regarding warfarin anticoagulation, bleeding risk/signs and basic drug, diet and disease state interactions (see Patient Education section).
 - d. A clear and specific plan for outpatient monitoring of INR must be set up with and understood by patient/caregivers.

7. ACCP recommendations on Management of Non Therapeutic INR:

INR Value	Symptoms	Recommendation
Above therapeutic but below 5	No significant bleeding	Lower the dose OR omit a dose and resume at a lower dose when INR is therapeutic
INR between 5 and 9	No significant bleeding	Omit next one or two doses, monitor INR more frequently, and resume therapy when INR is therapeutic ALTERNATIVELY: Omit the dose and administer Vitamin K 1 to 2.5mg ORALLY, particularly if patient is at increased risk for bleeding. If more rapid reversal is required because of urgent surgery, give Vitamin K 2 to 4 mg ORALLY with the expectation that reduction will occur in 24 hours. If the INR is still high, administer an additional dose of Vitamin K 1 to 2mg ORALLY
Greater than 9	No significant bleeding	Hold warfarin. Administer vitamin K 2.5 to 5mg orally with the expectation that substantial reduction in the INR will occur in 24-48 hours. Monitor INR more frequently and administer additional vitamin K if necessary. Resume therapy at a lower dose when INR is in the therapeutic range.
Serious bleeding or major warfarin overdose and elevated INR		Hold warfarin. Administer vitamin K 10mg by slow IV infusion, supplemented with fresh frozen plasma or prothrombin complex concentrate depending on the urgency of the situation. Administration of vitamin K can be repeated every 12 hours for persistent high INR's
Patients with life-Threatening Bleeding (intracranial hemorrhage & elevated INR's)		Hold warfarin. Administer fresh frozen plasma, prothrombin complex concentrate supplemented with vitamin K 10mg by slow IV infusion and repeat every 12 hours for persistent high INR's, Recombinant factor VIIa may be alternative to prothrombin complex

8. MD/LIP Responsibility

- a. Patient diagnosis, history and determination of therapy.
- b. Ordering and monitoring of baseline and ongoing laboratory tests.
- c. Monitoring of patient for therapeutic outcome and adverse events, including ADR reporting via Patient Safety Net.
- d. Order for warfarin dose or "no warfarin today".
- e. Determination of appropriate outpatient followup.
- f. Orders for any reversal of therapeutic or supratherapeutic INRs as appropriate to patient situation.
- g. Determination of necessity of holding warfarin therapy as appropriate for situation or planned procedures.
- h. Determination of need for bridging therapy with LMWH or Heparin if necessary for patient situation.

Warfarin (cont.)

9. Pharmacist Responsibility

- a. Validate Warfarin order by review of medications/dosing/ potential for drug interactions/appropriateness.
- b. Monitoring and documentation of INRs, warfarin dose, history, drug interactions, therapy plan on Communication Sheet/monitoring form.
- c. Discuss concerns regarding dose, laboratory results or signs of bleeding with prescriber.
- d. Document interventions and/or adverse events.
- e. Dispense each warfarin dose from Pyxis using appropriate order. Avoid sending dose from Central Pharmacy.
- f. Assistance in determining appropriate dose when appropriate.
- g. Patient education when appropriate.
- h. May enter verbal order from MD/LIP if no warfarin order exists.
- i. Education of staff members, provision of drug information pertaining to anticoagulation to staff members.
- j. Review and validate any orders for pharmacologic reversal of supratherapeutic INRs.
- k. Review and validate any orders for bridging with LMWH or Heparin including appropriateness of dose
- l. Document education of patient/caregivers in chart.

11. Nursing Responsibility

- a. Nursing is primarily responsible for warfarin administration and monitoring of side effects. Any symptoms of adverse effects and abnormal lab values pertaining to warfarin therapy must be reported to the MD/LIP for appropriate therapy change. May document ADR in PSN.
- b. Immediate reporting to MD/LIP and pharmacist of any bleeding complication
- c. Education of patient and caregivers using hospital approved patient education materials. May call upon pharmacist or dietitian to supplement education when appropriate to patient.
- d. Documentation of medication administration in MAR and assessments in chart.
- e. Ensure that follow up laboratory monitoring and MD appointment plans are in place and conveyed to patient/caregivers prior to discharge.
- f. Document education of patient/caregivers in chart.

12. Dietitian Responsibility

- a. Provide appropriate meals to patient's medical condition with consistent vitamin K content.
- b. Educate patients and caregivers when appropriate.
- c. Notify pharmacist if Vitamin K containing supplements (Ensure, Boost, Carnation Instant Breakfast, etc.) are provided to patient.
- d. Document education of patient/caregivers in chart.

13. Laboratory Responsibility

- a. Perform and report laboratory testing as ordered by MD/LIP.
- b. Immediate and direct reporting of elevated INRs to MD/LIP and /or unit.

Direct Thrombin Inhibitors

HIT Risk Assessment

Category		0 points	1 points	2 points
I	Thrombocytopenia (Platelet fall from baseline)	< 30%	30%-50%	> 50%
II	Timing of platelet fall (Onset)	<ul style="list-style-type: none"> • < day 4 • No recent heparin 	<ul style="list-style-type: none"> • day 10, or • Timing unclear • < day 1 with recent heparin (ago) 	<ul style="list-style-type: none"> • Day 5-10 • < day 1 with recent heparin (30 days ago)
III	Thrombosis Other Sequelae	None	<ul style="list-style-type: none"> • Progressive thrombosis • Erythematous skin lesions • Suspected (<i>Unproven</i>) thrombosis 	<ul style="list-style-type: none"> • <i>Proven</i> new thrombosis • Skin necrosis • Acute systemic reaction after UFH bolus
IV	Other potential causes of Thrombocytopenia	Definite	Possible	Not evident
Total Score HIT Probability	0-3 Low Risk (<5% Chance)	4-5 Intermediate Risk		6-8 High Risk (>80% Chance)

TREATMENT:

1. If HIT is suspected, Discontinue all sources of Heparin (IV, sc, Heparin coated catheters & flushes) & LMWH's.
2. Treatment is reserved for patients with a HIT score in the 6-8 range (high risk). HIT scores in the 4-5 range (intermediate risk) can be treated based on physician discretion while scores lower than 4 (low risk) may not require treatment.
3. Draw baseline CBC, aPTT, PT/INR, serum creatinine, and liver function test
4. Start a direct-thrombin inhibitor (lepirudin or argatroban) and continue at a therapeutic infusion rate until the platelets have substantially recovered to at least 100,000 cells/mm³ and preferably 150,000 cells/mm³.
 - a. LEPIRUDIN is the drug of choice if the patient's renal function is normal or near normal
 - b. ARGATROBAN is the drug of choice if the patient has significant renal insufficiency
 - c. If the patient has renal and hepatic insufficiency, use ARGATROBAN at doses recommended for hepatic insufficiency
5. Document Heparin Allergy as Heparin Immune Thrombocytopenia in patients permanent record.

Argatroban®

Indication: Treatment of Heparin Induced thrombocytopenia - Use Bivalirudin w HIT + Acute Coronary Syndrome.

Dosing: Infusion Concentration

250 mg/ 250 mls NS= 1mg/1 ml= 1000 mcg/ml

No initial bolus dose required.

Criteria for Use:

Patient at intermediate to high risk for HIT :

Unexplained Platelet Count decline \geq 30- 50% within 5-10 days of heparin or LMWH use, or < 1 day with heparin/LMWH exposure in last 3 months, suspected or proven new thrombosis, erythema or necrosis of skin with sc Heparin or enoxaparin, acute systemic reaction after Heparin bolus.

A. Initial dose: 2 mcg/kg/min for HIT, titrate to maintain aPTT 1.5-3 x pt's baseline or 1.5-3 x mean of lab control range (27 sec).=Goal aPTT 40-70 secs

Draw an aPTT 2 hours after initiation of infusion x 2 and 2 hours after each dose change x 2 then follow the titrating chart below: (use the patient's baseline aPTT value in all of the subsequent titration calculations)

Adjust rate based on aPTT:

Lab result	Infusion Rate Change	Next aPTT
aPTT < 30 sec	increase rate by 1 mcg/kg/min	aPTT in 2 hr
aPTT 30-40 sec	increase rate by 0.5mcg/kg/min	aPTT in 2 hr
aPTT 40-70 sec	same rate	aPTT repeat in 2-4 hrs, if in range aPTT in am
aPTT 71-90 sec	decrease rate by 0.5 mcg/kg/min	aPTT in 2 hrs
aPTT > 90 sec	decrease rate by 1 mcg/kg/min	aPTT in 2 hrs

Max dose is 10 mcg/kg/min. No initial dose adjustment needed with renal impairment and in absence of hepatic dysfunction.

Hepatic elimination. Not renally cleared.

B. Pt's with Mod Hepatic dose or Bilirubin > 1.5, CHF, Multi System Organ Failure, severe anasarca: Reduce initial dose to 0.5 mg/kg/hr, then titrate as above.

Lab result	Infusion Rate Change	Next aPTT
aPTT < 30 sec	increase rate by 0.2 mcg/kg/min	aPTT in 2 hr
aPTT 30-40 sec	increase rate by 0.1mcg/kg/min	aPTT in 2 hr
aPTT 40-70 sec	same rate	aPTT repeat in 2-4 hrs, if in range aPTT in am
aPTT 71-90 sec	decrease rate by 0.1 mcg/kg/min	aPTT in 2 hrs
aPTT > 90 sec	decrease rate by 0.2 mcg/kg/min	aPTT in 2 hrs

Argatroban[®] (Cont.)

Warfarin Overlap with Argatroban

Note: argatroban will significantly elevate PT/INR values. Follow warfarin dosing guideline below when determining adjustment of warfarin dosing.

1. Initiate warfarin only when the platelet count has substantially recovered to $\geq 100,000$ cells/mm³ or greater.
2. Obtain a baseline PT/INR prior to starting the warfarin. Do not give a loading dose of warfarin
3. Initiate warfarin dose at a low, maintenance dose (maximum of 5 mg unless patients was stable on prior doses > 5mg.
4. Adjust warfarin dose for approximate goal of INR 4-5 during the first 5 days of concomitant argatroban and warfarin therapy.
5. After 5 days of concomitant argatroban and warfarin therapy, decrease argatroban rate to 2 mcg/kg/min (if > 2 mcg/kg/min) and check INR:
 - A. If INR ≥ 4 , Discontinue argatroban and recheck INR in 6 hrs.
 - a. If INR is 2-3 , restart argatroban at 2 mcg/kg/min (or original rate if <2 mcg/kg/min) and keep patient on same warfarin dose. Repeat process daily until INR off argatroban remains 2-3 for 2 consecutive days. Then discontinue argatroban.
 - b. If INR >3, restart argatroban and reduce warfarin dose. Repeat process daily until INR is within range for 2 consecutive days. Then discontinue argatroban.
 - c. If INR <2, increase argatroban to original therapeutic rate and increase warfarin dose and repeat above process the next day
 - B. If INR < 4, Return argatroban infusion to original therapeutic rate and increase warfarin dose. Check INR daily for 2 days.
 - a. If after 2 days INR has not increased, increase warfarin dose and repeat process.
 - b. If INR has increased_but still < 4, repeat process at same warfarin dose until INR ≥ 4 , then follow as in a above
 - c. If new INR ≥ 4 , follow as in a above

MD/LIP Responsibility:

Order labs: Baseline: PT, PTT, CBC with platelet count, Stool for blood, urinalysis
Platelet count, Hematocrit q 2-3 days

Nursing Responsibility:

Requires RN/LPN verification double check on MAR.

Infusion via Guardrails on Alaris Volumetric Infusion Pump

Monitor aPTT, bleeding symptoms,

Pharmacist responsibilities:

Warfarin dose validation

Can cause false elevations of INR - refer to references for transition to warfarin.

Adjust dose for approximate goal of INR 4-5 during the first 5 days of concomitant argatroban and warfarin therapy.

Lepirudin- Refludan[®]

Indication: Direct thrombin inhibitor (DTI) for Heparin Induced Thrombocytopenia (HIT)
Use Bivalirudin w HIT + ACS

A. CrCl > 60 mls/min

IVPush : If no renal dysfunction & if perceived life-or limb threatening thrombosis: 0.2 - 0.4 mg/kg (max 44 mg, taken from IV bag & given over 15-20 secs, then maintenance

Continuous Infusion: Standard Infusion Concentration: 100 mg/ 250 mls NS =0.4 mg/ml

0.1 mg/kg/hr (initial rate DNE 16.5 mg/hr) to target aPTT range 1.5 - 2 x pt'd baseline or mean of lab normal range (26 sec). = goal aPTT 40-60 secs

B. CrCl ≤ 60 mls/min- Consider using Argatroban or use Lepirudin in reduced doses

Consider either omit bolus dose or if perceived life-threatening thrombosis lower

IVPush : 0.1 mg/kg (max 10 mg) taken from IV bag & given over 15-20 secs, then maintenance CI:

Cr % reduction in dose mg/kg/hr

1-1.4 50% 0.05

1.4 - 4 30% 0.01

> 4 15% 0.005

With start of Infusion , Draw aPTT q 4 hrs x 2 and after each dose change , then daily when aPTT is within therapeutic range.

JDH aPTT lab control 26 sec (June-08)

Adjust rate based on aPTT:

Lab result	Infusion Rate Change	Next aPTT
aPTT < 40 sec	increase rate by 20 %	aPTT in 4 hr
aPTT 40-60 sec	same rate	aPTT in 4 hr , if in goal range
aPTT >60 sec	Hold x 2 hrs, decrease rate by 50%	aPTT in 4 hr

Warfarin Overlap with Lepirudin

1. Initiate warfarin only when the platelet count has substantially recovered to 100,000 cells/mm³ or greater.
2. Gradually reduce lepirudin dose to reach an aPTT ratio > 1.5 X patient baseline or aPTT= 40-50 secs.
3. Obtain a baseline PT/INR prior to starting the warfarin to determine if a false elevation exists. Do not give a loading dose of warfarin
4. Adjust warfarin doses to goal INR while on lepirudin.
5. Initiate warfarin dose at a low, maintenance dose (maximum of 5 mg unless patients was stable on prior doses > 5mg.
6. Continue lepirudin for 5 days after initiating warfarin to avoid a prothrombotic effect and until INR stabilizes within the therapeutic range for 2 consecutive days.

Heparin References:

1. Raschke RA, et al. The weight-based heparin dosing nomogram compared to a "standard care" nomogram. Ann Intern Med 1993;119:874-81.
2. Yee WP and Norton LL. Optimal weight base for a weight-based heparin dosing protocol. Am J of H S Pharmacists 1998;55(2): 159-162.
3. Hirsch J and Bauer K. Parenteral Anticoagulants. The Eighth ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2008; 141S-159S.

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1. Eighth ACCP Consensus Conference on Antithrombotic Therapy. CHEST Sept 2008
2. ISCI Health Care Guideline: Antithrombotic Therapy Supplement. Sixth Edition. August 2007.
3. ISMP Medication Safety Self Assessment for Antithrombotic Therapy in Hospitals. 2005.
4. 2008 National Patient Safety Goals, Hospital.