UNIVERSITY HOSPTIAL AT DOWNSTATE/DOWNSTATE HEALTH SCIENCES UNIVERSITY

GUIDELINES

No. PTSAF-19

Subject: Adult Therapeutic Heparin and Enoxaparin Guideline (Anticoagulation)

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The JC Standards:
MM.01.01.03: The organization safely manages high-alert and hazardous medications.
NPSG.03.05.01: Reduce the likelihood of patient harm associated with the use of anticoagulant therapy.

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I. PURPOSE

This document provides guidance to clinicians regarding safe and effective utilization of unfractionated heparin and low molecular weight heparin in adult patients at the University Hospital at Downstate. Anticoagulant agents, such as heparin and enoxaparin, are identified as high-risk medications by the Institute for Safe Medication Practices and the University Hospital at Downstate. They possess the potential for serious patient harm if used in error.

II. POLICY

Treatment with heparin and enoxaparin will follow the standardized prescribing, administration, and monitoring guidelines as outlined in this document. Patient-specific deviations shall be discussed on a case-by-case basis and treatment will be individualized as needed by responsible providers with appropriate education and monitoring.

III. DEFINITION(s)

Anticoagulation: Pharmacologic therapy that will alter a patient's coagulation cascade, which will ultimately impair a patient's ability to form fibrin clots. A therapeutically anticoagulated patient will also be at a higher risk of experiencing a hemorrhage.

Reversal of Anticoagulation: The process of administering a pharmacologic reversal agent or blood product to effectively restore an anticoagulated patient's coagulation cascade

IV. PROCEDURES/GUIDELINES FOR THERAPEUTIC UNFRACTIONATED HEPARIN

THERAPEUTIC IV HEPARIN PRESCRIBING

1. The University Hospital at Downstate recognizes the following approved protocols in adult patients (see Appendix A and B):
   a. Heparin Protocol for Adult Medical/Surgical Patients
   b. Transitioning to and from Enoxaparin (LMWH) or Unfractionated Heparin (UFH)

2. Providers will utilize an order set in the electronic medical record to prescribe heparin for adult patients, which includes:
   a. Order for the heparin continuous infusion (with or without an initial loading dose). The order should clearly state the aPTT goal. The order will be defaulted to no more than 24 hours and prescribers must renew the order on a daily basis for continued treatment.
   b. Orders for nurses to notify providers during specific situations or occurrences
   c. Orders for coagulation laboratory tests. Further work-up of abnormal anticoagulation results should be considered prior to initiation of anticoagulation, whenever possible. Consult the Hematology Service if needed.

3. Prior to prescribing and order verification, providers and pharmacists will verify that there is no current aPTT >90 seconds, as well as any contraindications

4. To determine how to transition to and from unfractionated heparin, see Appendix B

THERAPEUTIC IV HEPARIN ADMINISTRATION AND MONITORING

1. Prior to the initiation of an IV heparin infusion, and with each bag change or rate adjustment, there shall be an independent double-check of the drug name, product strength and concentration, dose and rate calculation, pump setting, and patient identity using at least two identifiers

2. Prior to administration, nurses will verify that there is no current aPTT >90 seconds

3. At 6 hours after initiation or rate adjustment of the IV heparin infusion, a STAT aPTT shall be collected in a blue-top, sodium citrate tube and sent immediately
   a. In intensive care units (except the pediatric intensive care unit and the emergency department), nurses shall adjust heparin rates according to aPTT results as per the nomogram (Appendix A). Nurses shall contact providers if there are any questions or uncertainties.
   b. In non-intensive care unit settings, nurses shall notify the providers of the time of the aPTT blood draw to facilitate timely follow-up of results. Providers are responsible for entering a new order if a rate adjustment if needed.

4. Ongoing monitoring of IV heparin therapy includes:
   a. Daily CBC, or more often at prescriber's discretion
   b. aPTT should be checked 6 hours after any heparin rate adjustment until two consecutive aPTT values are within the therapeutic range. Thereafter, aPTT should be checked at least once daily, or more often at prescriber's discretion.

V. PROCEDURES/GUIDELINES FOR THERAPEUTIC ENOXAPARIN

THERAPEUTIC ENOXAPARIN PRESCRIBING

1. Providers will enter enoxaparin orders with a discrete dose (in mg) and frequency
   a. Ensure a CBC and serum creatinine for baseline evaluation are available prior to, or upon, initiation of enoxaparin
   b. For *therapeutic* anticoagulation, use actual body weight in most cases. Special populations may warrant additional considerations based on clinical judgment.
   c. All mg/kg doses should be rounded to the nearest 10 mg

Table 1. Therapeutic Enoxaparin Usual Dosing and Considerations

Indication	Standard Dose	Special Populations and Considerations
Therapeutic Anticoagulation	1 mg/kg q12h *or* 1.5 mg/kg q24h [Actual body weight used in most cases]	CrCl <30 mL/min: • Dosage adjustment warranted (1 mg/kg q24h) • Recommend checking anti-Xa to confirm dosing strategy* End-stage renal disease or acute renal failure: • Consider an alternative anticoagulant if possible Elderly patients with borderline renal function: • Consider utilizing a lower weight-based dose (example: 0.75 mg/kg q12h) to avoid excessive anticoagulation • Recommend checking anti-Xa to confirm dosing strategy* Obese patients: • Consider utilizing a lower weight-based dose (example: 0.75 mg/kg q12h) *or* use adjusted body weight for dosing to avoid excessive anticoagulation • Dose capping based on weight is not recommended. • Recommend checking anti-Xa to confirm dosing strategy* Low weight patients • Weight-based dosing in patients less than 50 kg not encouraged • Recommend checking anti-Xa to confirm dosing strategy*

*Anti-Xa may be elevated with recent use of direct factor Xa inhibitors (apixaban, rivaroxaban). Ensure appropriate timing when transitioning to and from anticoagulant agents.

Table 2. Therapeutic Enoxaparin Dose Rounding Guidelines

Dose Written (mg)	Rounded Dose (mg)	Syringes Dispensed
25 - 34	30 (0.3 mL)	30 mg x 1
35 – 49	40 (0.4 mL)	40 mg x 1
50 – 69	60 (0.6 mL)	60 mg x 1
70 – 89	80 (0.8 mL)	80 mg x 1
90 – 109	100 (1 mL)	100 mg x 1
110 – 134	120 (0.8 mL)	120 mg x 1
135 - 164	150 (1 mL)	150 mg x 1
Dose capping based on weight is not recommended. Doses <25 mg and >164 mg will be prepared as patient-specific syringe by pharmacy, rounded to the nearest 10 mg.		

2. To determine how to transition to and from enoxaparin, see Appendix B.

3. Enoxaparin use with neuraxial anesthesia is not recommended due to the risk of developing a spinal hematoma. Consider an alternative anticoagulant if possible.
   a. If patient is on *therapeutic* enoxaparin, hold dose of enoxaparin for at least 24 hours prior to inserting a spinal/epidural needle/catheter. If patient is on *prophylactic* enoxaparin, hold dose of enoxaparin for at least 12 hours prior to

inserting a spinal/epidural needle/catheter. Do not start/restart enoxaparin for at least 2 hours after removal of the catheter/needle.

b. In spinal surgery patients, do not start *prophylactic* enoxaparin until the indwelling epidural catheter has been removed for at least 24 hours

THERAPEUTIC ENOXAPARIN MONITORING

1. Anti-Xa peak monitoring is not routinely recommended for all patients receiving enoxaparin, but may be considered in patients with the following characteristics:
   a. Severe renal impairment or fluctuating renal function
   b. Elderly patients with borderline renal function and/or higher risk of bleeding
   c. Obesity (BMI >40 kg/m^2) or low-weight (<45 kg)
   d. Patients with coagulation disorders at higher thrombotic risk
   e. Pregnant patients on long-term therapy
   f. Pediatric patients on long-term therapy

2. Goal anti-Xa peak for *therapeutic* enoxaparin
   a. 0.5 to 1 unit/mL for twice-daily dosing
   b. 1 to 2 unit/mL for once-daily dosing

3. Anti-Xa peak should be drawn 4 hours after the 3rd or 4th enoxaparin dose is administered. Dose adjustments may be made based on the anti-Xa results.

Table 2. Anti-Xa Monitoring and Dose Adjustment Recommendations for Therapeutic Enoxaparin

Anti-Xa (unit/mL)	Dose Adjustment*	Time to Repeat Anti-Xa*
<0.35	Increase dose by 25%	4 hours after next dose
0.35 – 0.49	Increase dose by 10%	4 hours after next dose
0.5 – 1	No change	At prescriber's discretion
1.1 – 1.5	Hold next dose for 3 hours, and decrease dose by 20%	4 hours after next dose
1.6 – 2	Hold next dose for 6 hours, and decrease dose by 30%	4 hours after next dose
>2	Hold dose until anti-Xa level ≤0.5 unit/mL (check anti-Xa q12h), then decrease dose by 40%	4 hours after next dose

*Recommendations should not preclude clinical judgment. Contact Pharmacy for any uncertainties.

VI. PROCEDURES/GUIDELINES FOR REVERSAL OF HEPARIN OR ENOXAPARIN

1. In the setting of a major or life-threatening bleed, discontinue anticoagulation immediately. Protamine sulfate is available for the reversal of heparin or enoxaparin.
   a. Fully neutralizes anticoagulant activity of heparin
   b. Partially neutralizes anti-Xa activity of enoxaparin (up to 75% neutralized)

2. All clinicians should review coagulation results and contraindications prior to ordering, verifying, and administering protamine sulfate. The dosing of protamine sulfate is dependent on the anticoagulant received and the timeframe.

Table 3. Protamine Sulfate Dosing

Agent	Protamine Reversal Dose (Maximum 50 mg/dose)*	Laboratory Monitoring†
IV Heparin	• 1 mg of protamine per 100 units of IV heparin received within the previous 2 – 3 hours • May administer a repeat dose if ongoing bleeding or aPTT remains prolonged	Obtain baseline aPTT and repeat aPTT 15 minutes after each protamine dose

SC Heparin	• 1 mg of protamine per 100 units of SC heparin • May administer 50% of dose as bolus over 10 minutes, followed by an infusion of remaining 50% over 8 – 16 hours	Obtain baseline aPTT and repeat aPTT 15 minutes after each protamine dose
Enoxaparin	• If ≤8 hours ago: 1 mg of protamine per 1 mg of enoxaparin • If >8 hours ago: 0.5 mg of protamine per 1 mg of enoxaparin • May administer a repeat dose if ongoing bleeding or anti-Xa remains elevated	Obtain baseline anti-Xa and repeat anti-Xa 15 minutes after each protamine dose

*Maximum single dose of protamine should not exceed 50 mg. Excessive protamine doses may paradoxically worsen the bleed since protamine itself possesses weak anticoagulant activity.

†Phenomenon of "heparin rebound" may occur up to 18 hours after protamine administration. If there is a concern for re-bleeding, can check aPTT to guide further therapy.

3. Protamine sulfate doses should be administered IV over a minimum of 10 minutes. Monitor for infusion-related adverse events:
   a. Hypotension, bradycardia, anaphylactoid reactions, and anaphylaxis
   b. Rapid administration, fish allergy, or previous exposure to protamine or NPH insulin may increase the risk of developing a reaction

VII. ATTACHMENTS

- Attachment A: Heparin Protocol Med/Surg
- Attachment B: Transition of Anticoagulants

VIII. REFERENCES

1. Lexi-Drugs. Lexicomp Online [database online]. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com.
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3. Amsterdam EA, Wenger NK, Brindis RG, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons; American Association for Clinical Chemistry. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64(24):e139-e228.

Date Reviewed	Revision Required (Circle One)		Responsible Staff Name and Title
12/2019	Yes	No	Pharmacy & Therapeutics Committee
3/2022	Yes	(No)	Medication Safety Committee, Pharmacy & Therapeutics Committee
6/2024	(Yes)	No	Medication Safety Committee, Pharmacy & Therapeutics Committee
1/2025	(Yes)	No	Manisa Tanprayoon, PharmD Sun Hyee Park, PharmD

Appendix A. Adult Heparin Protocols at the University Hospital at Downstate

Heparin for Adult Medical/Surgical Patients – Target aPTT 60-80 seconds
(NOT for Stroke or Cardiac Surgery Patients)

Table 1. Initiation of IV Heparin Infusion

LOW Dose Protocol: acute coronary syndrome, atrial fibrillation, concomitant thrombolytic therapy, or therapeutic anticoagulation desired but patient is at a high risk of bleeding due to acute condition, previous history of bleeding

Initial Bolus Dose (Optional)	Initial Infusion Dose
60 units/kg - Round to closest 100 units - Maximum bolus dose of 5,000 units - Bolus dose administered over 3 minutes	12 units/kg/hr - Round to closest 50 units/hr. - Maximum initial rate of 1,000 units/hr - Order defaults to a duration of 24 hours

HIGH Dose Protocol: DVT, PE, mechanical valve replacement

Initial Bolus Dose (Optional)	Initial Infusion Dose
80 units/kg - Round to closest 100 units - Maximum bolus dose of 10,000 units - Bolus dose administered over 3 minutes	18 units/kg/hr - Round to closest 50 units/hr. - Maximum initial rate of 2,000 units/hr - Order defaults to a duration of 24 hours

Table 2. Maintenance Dose Adjustments Based on aPTT Results

aPTT (sec)	Bolus	Maintenance Infusion Dosage Change	Next aPTT After Change
<45	40 units/kg* ***Refer table 3 below for bolus dose adjustment***	Increase rate by 3 units/kg/hr	6 hours
45-60	NONE	Increase rate by 2 units/kg/hr	6 hours
60-80 (Goal)	NONE	NO CHANGE	6 hours until therapeutic x 2 consecutive values, then q24h
81-90	NONE	Decrease rate by 3 units/kg/hr	6 hours
> 90	NONE	**STOP** infusion for 2 hours, Then, decrease rate by 3 units/kg/hr	2 hours after infusion resumed

Table 3. Bolus Dose Adjustment (40 units/kg)

Patient Weight (kg)	<60 kg	60-85 kg	85-110 kg	>110 kg
Dose	2,000 units	3,000 units	4,000 units	5,000 units Maximum

Appendix B. Transitioning to and from Enoxaparin (LMWH) or Unfractionated Heparin (UFH)

From	To	Action
Apixaban (Eliquis®)	LMWH/UFH	• Start enoxaparin or heparin infusion when next apixaban dose would have been due
Dabigatran (Pradaxa®)	LMWH/UFH	• CrCl ≥30 mL/min: start 12 hours after last dose of dabigatran • CrCl <30 mL/min: start 24 hours after last dose of dabigatran
Rivaroxaban (Xarelto®)	LMWH/UFH	• Start enoxaparin or heparin infusion when next rivaroxaban dose would have been due
Warfarin	LMWH/UFH	• Start enoxaparin or heparin infusion when INR <2
LMWH (enoxaparin)	Warfarin	• Start warfarin when clinically indicated • If choosing to bridge warfarin with enoxaparin, may overlap therapy until goal INR achieved
	DOAC*	• Start DOAC when the next enoxaparin dose would have been due - For high-risk thrombotic patients, can consider starting 2 hours before when the next enoxaparin dose would have been due - For high-risk bleeding patients, can consider starting 2 hours after when the next enoxaparin dose would have been due
	UFH	• Start heparin infusion 1 hour before when the next enoxaparin dose would have been due - For high-risk thrombotic patients, can consider starting 2 hours before when the next enoxaparin dose would have been due - For high-risk bleeding patients, can consider starting exactly when the next enoxaparin dose would have been due
UFH Infusion	Warfarin	• Start warfarin when clinically indicated • If choosing to bridge warfarin with heparin infusion, may overlap therapy until goal INR achieved
	DOAC*	• Start DOAC at the same time the heparin infusion is stopped
	LMWH	• Start enoxaparin at the same time the heparin infusion is stopped - For high-risk thrombotic patients, can consider starting 1 hour before stopping the heparin infusion - For high-risk bleeding patients, can consider starting 1 hour after stopping the heparin infusion

*If already received ≥48 hours of therapeutic LMWH or UFH for treatment of DVT/PE, consider discussing with Hematology and/or Pharmacy regarding optimal duration of the *initial load* for apixaban and rivaroxaban. Take into consideration clot burden, thrombotic risk, and bleeding risk of the patient.