ENOXAPARIN (Lovenox®)

NOT recommended for dialysis patients.

Indications	Standard Regimen*	Dose For Creatinine Clearance < 30 mL/min [NOT for Dialysis Patients]	Lab Monitoring:
Inpatient treatment of acute DVT (with or without PE)	1 mg/kg SC every 12 hours (or 1.5 mg/kg SC once daily)	1 mg/kg SC once daily	CBC and serum creatinine within 24 hours of start, then CBC daily Consider anti-factor Xa levels for severe renal impairment, obesity (> 150 kg) or low weight (< 45 kg), pregnant patients Anti-factor Xa targets: 0.6 to 1 unit/mL for q12h dosing ***OR*** 1 to 2 units/mL for once daily dosing
Outpatient treatment of acute DVT (without PE)	1 mg/kg SC every 12 hours	1 mg/kg SC once daily	
Unstable angina and non-Q-wave MI	1 mg/kg SC every 12 hours	1 mg/kg SC once daily	
Acute STEMI in patients < 75 years old	30-mg single IV bolus plus 1 mg/kg SC x 1 dose, followed by 1 mg/kg SC every 12 hours	30-mg single IV bolus plus 1 mg/kg SC x 1 dose, followed by 1 mg/kg SC once daily	
Acute STEMI in patients ≥ 75 years old	0.75 mg/kg SC every 12 hours (no bolus)	1 mg/kg SC once daily (no bolus)	

DVT = deep vein thrombosis, PE = pulmonary embolism, MI = myocardial infarction
*Q 12 hour dosing is preferred in patients with morbid obesity, malignancy, or a large clot burden.

Reversal of Heparin/Enoxaparin with Protamine

Heparin Excess: Calculate dose of protamine based on table below. Give 25-50 mg protamine IV over 10 mins, then remaining dose via continuous infusion over 8-16 hrs. Maximum rate 5 mg/min.

Time Since Heparin Given	Dose of Protamine per 100 units of Heparin in Patient
Immediate	1 – 1.5 mg
30-60 minutes	0.5 – 0.75 mg
> 2 hours	0.25 - 0.375 mg

Enoxaparin Excess: 1 mg protamine for each1 mg of enoxaparin given within the last 4 hours. If aPTT prolonged 2-4 hours after first dose, consider additional 0.5 mg protamine for each mg enoxaparin.

WARFARIN (Coumadin®, Jantoven®)

Lab Monitoring:*
CBC and PT/INR within 24 hours prior to first dose, then CBC daily
INR daily (start day 2-3) until 2 values in target ≥ 24 hrs apart,
then twice weekly x 1 wk, then at least once q2 wks x 1 month

Sample Initiation Nomogram for Target INR 2-3

Day	INR	Dosage
1		5 mg
2	< 1.5	5 mg
	1.5 – 1.9	2.5 mg
	2.0 – 2.5	1 - 2.5 mg
	> 2.5	0
3	< 1.5	5 – 10 mg
	1.5 – 1.9	2.5 – 5 mg
	2.0 – 2.5	0 – 2.5 mg
	2.5 – 3.0	0 – 2.5 mg
	> 3.0	0
4	< 1.5	10 mg
	1.5 – 1.9	5 – 7.5 mg
	2.0 – 3.0	0 – 5 mg
	> 3.0	0
5	< 1.5	10 mg
	1.5 – 1.9	7.5 – 10 mg
	2.0 – 3.0	0 – 5 mg
	> 3.0	0
6	< 1.5	7.5 – 12.5 mg
	1.5 – 1.9	5 – 10 mg
	2.0 – 3.0	0 – 7.5 mg
	> 3.0	0

Adapted from: Arch Intern Med. 1999; 159: 46-48; and Ann Intern Med. 1997; 127: 332-333.

Maintenance Dose: Average daily dose over last week of therapy, once two consecutive INRs in target range.

Common Drug Interactions with Warfarin
(Monitor INR more frequently)
Consult drug references for mechanisms of interactions.

May Increase INR or Bleeding Risk	
Alcohol (in liver disease)	Loop diuretics
Acetaminophen	Macrolide antibiotics
Amiodarone	Metronidazole
Anabolic steroids	NSAIDs
Aspirin	Omeprazole
Azole antifungals	Penicillins (e.g., Amoxicillin)
Cefazolin	Phenytoin
Cefmetazole	Propranolol
Cefoperazone Cefotetan	Sertraline
Cimetidine	Tetracycline
Ciprofloxacin	Ticlopidine
Clopidogrel	Sulfamethoxazole-trimethoprim
Isoniazid	
Levofloxacin	

May Decrease INR
Barbiturates
Carbamazepine
Cholestyramine
Dicloxacillin (unlike other penicillins)
Griseofulvin
Influenza vaccine
Mercaptopurine
Multivitamins with vitamin K
Nafcillin (unlike other penicillins)
Rifampin
Ritonavir
Sucralfate
Vitamin K in foods or enteral feeds

*** Note: INR results from point-of-care testing may vary from centralized lab testing. Centralized laboratory testing is the gold standard and should be used for hospitalized patients.**

WARFARIN — Recommendations for Management of Supratherapeutic INRs.

Consider consultation with specialists for complex patients (e.g., mechanical heart values).

INR	Bleeding Present	Recommended Action
> Therapeutic range to < 5.0	No significant bleeding	Lower warfarin dose, **or**
		Omit one dose and resume warfarin at a lower dose when INR is in therapeutic range, **or**
		No dose reduction needed if INR is minimally prolonged
≥ 5.0 to 9.0	No significant bleeding	Omit the next 1 to 2 doses of warfarin, monitor INR more frequently, and resume treatment at a lower dose when INR is in therapeutic range, **or**
		Omit one dose and administer 2.5 mg oral vitamin K*
≥ 9.0	No significant bleeding	Hold warfarin and administer 2.5 — 5 mg oral vitamin K. (INR should decrease in 12 — 24 hours.) Monitor INR more frequently and administer more vitamin K as needed. Resume warfarin at a lower dose when INR is in therapeutic range
Any elevation of INR	Serious or life-threatening bleeding	Hold warfarin and administer 10 mg vitamin K by slow IV infusion; supplement with prothrombin complex concentrate, fresh frozen plasma, or recombinant human factor VIIa, depending on clinical urgency. Consider consultation with Blood Bank. Monitor and repeat as needed.

* This option is preferred in patients at increased risk for bleeding (e.g., history of bleeding, stroke, renal insufficiency, anemia, hypertension). Adapted from: Chest 2008; (6 Suppl):160s.

Reversal of Warfarin with Vitamin K (Phytonadione)

- Oral route preferred (available as 5-mg tablets).
- No intramuscular injections—Risk of hematomas.
- IV infusion 10 mg in 50 mL NS or D5W over 10—30 minutes.
- IV push associated with greater risk of anaphylaxis.
- Vitamin K treatment may prolong time to return to target INR when warfarin restarted.

Transitions: Heparin to Enoxaparin: Give 1st dose enoxaparin in 2-4 hours after discontinuation of heparin infusion.
Enoxaparin to Heparin: Start heparin infusion in 6-12 hours after last dose of enoxaparin.
Heparin/Enoxaparin to Warfarin: Give 1st dose warfarin 12-24 hrs after start heparin/enoxaparin.
Overlap therapy 4-5 days until INR within target x 2 days > 24 hours apart.

aPTT (sec)	REPEAT BOLUS (if ordered)	Maintenance Infusion Dosage Change	NEXT aPTT After Change
< 60	60 units/kg	↓ by 2 units/kg/hr	6 hours
60-80 (Goal)	NONE	NO CHANGE	6 hours until therapeutic x 2 values, then every 24 hrs
81-90	NONE	↓ by 3 units/kg/hr	6 hours
> 90	NONE	STOP x 1 hour, then ↓ by 3 units/kg/hr	6 hours

Maintenance Dose Adjustments Based on aPTT

Maximum initial bolus 5000 units.	Maximum initial dose 1000 units/hr

Initial Bolus (Optional)	Initial Infusion
60 units/kg, Rounded to nearest 100 units x 1 dose over 3 minutes	16 units/kg/hr, Rounded to nearest 50 units x 24 hours

Initiation of Heparin IV Infusion - Consider Hematology Consult to Override Protocol

Lab Monitoring: CBC, PT/aPTT within 24 hours prior to start of IV heparin, then CBC daily
aPTT at 6 hrs after heparin start/adjustment until 2 consecutive aPTTs within target, then daily

HEPARIN Protocol for Medical Indications

(NOT for STROKE or Cardiothoracic Surgery Patients)

(Available as Heparin 25,000 units in 250 mL D5W Bag)

aPTT target 60 – 80 seconds

Anticoagulation Therapy Guidelines for Medical Indications

Guidelines/recommendations provided for reference. Treatment plans should be individualized as per patient needs.
(Updated June 2010)