## 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<br>Consider anti-factor Xa levels for severe renal impairment, obesity (> 150 kg) or low weight (< 45 kg), pregnant patients<br>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.)<br>Monitor INR more frequently and administer more vitamin K as needed.<br>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)**