

ENOXAPARIN

Class: Low Molecular Weight Heparin

Indications: Acute coronary syndromes: Unstable angina (UA), non-ST-elevation (NSTEMI), and ST-elevation myocardial infarction (STEMI)

DVT prophylaxis: Following hip or knee replacement surgery, abdominal surgery, or in medical patients with severely-restricted mobility during acute illness who are at risk for thromboembolic complications

DVT treatment (acute): Inpatient treatment (patients with or without pulmonary embolism) and outpatient treatment (patients without pulmonary embolism)

Unlabeled : Prophylaxis and treatment of thromboembolism in children; anticoagulant bridge therapy during temporary interruption of vitamin K antagonist therapy in patients at high risk for thromboembolism; DVT prophylaxis following moderate-risk general surgery, major gynecologic surgery and following higher-risk general surgery for cancer; management of venous thromboembolism (VTE) during pregnancy; anticoagulant used during percutaneous coronary intervention (PCI).

Dosage: Note: One mg of enoxaparin is equal to 100 units of anti-Xa activity (World Health Organization First International Low Molecular Weight Heparin Reference Standard). Weight -based doses (eg, 1 mg/kg) are commonly rounded to the nearest 10 mg. Most available prefilled syringes are graduated in 10 mg increments.

-DVT prophylaxis: SubQ:

Obesity: Note: In morbidly-obese patients (BMI ≥ 40 kg/m²), increasing the prophylactic dose by 30% may be appropriate for some indications . For bariatric surgery, dose increases may be $>30\%$ based on clinical trial data.

-Abdominal surgery: 40 mg once daily, with initial dose given 2 hours prior to surgery; continue until risk of DVT has diminished (usually 7-10 days).

-Hip replacement surgery:

-Twice-daily dosing: 30 mg every 12 hours, with initial dose within 12-24 hours after surgery, and every 12 hours for at least 10 days or until risk of DVT has diminished or the patient is adequately anticoagulated on warfarin. The American College of Chest Physicians recommends initiation ≥ 12 hours preoperatively **or** ≥ 12 hours postoperatively; extended duration of up to 35 days suggested.

-Once-daily dosing: 40 mg once daily, with initial dose within 9-15 hours before surgery, and daily for at least 10 days (or up to 35 days postoperatively) or until risk of DVT has diminished or the patient is adequately anticoagulated on warfarin. The American College of Chest Physicians recommends initiation ≥ 12 hours preoperatively **or** ≥ 12 hours postoperatively; extended duration of up to 35 days suggested.

-Knee replacement surgery: 30 mg every 12 hours, with initial dose within 12-24 hours after surgery, and every 12 hours for at least 10 days or until risk of DVT has diminished or the patient is adequately anticoagulated on warfarin. The American College of Chest Physicians recommends initiation ≥ 12 hours preoperatively **or** ≥ 12 hours postoperatively; extended duration of up to 35 days suggested .

-Medical patients with severely-restricted mobility during acute illness: 40 mg once daily; continue until risk of DVT has diminished (usually 6-11 days).

-Bariatric surgery (unlabeled use): Roux-en-Y gastric bypass: Appropriate dosing strategies have not been clearly defined :

BMI ≤ 50 kg/m²: 40 mg every 12 hours, BMI > 50 kg/m²: 60 mg every 12 hours.

Note: Bariatric surgery guidelines suggest initiation 30-120 minutes before surgery and postoperatively until patient is fully mobile (Mechanick, 2009). Alternatively, limiting administration to the postoperative period may reduce perioperative bleeding.

-Prevention of recurrent venous thromboembolism in pregnancy (unlabeled use): 40 mg once daily. Therapy should continue for 6 weeks postpartum in high-risk women (Bates, 2012).

-DVT treatment (acute): SubQ: **Note:** Start warfarin on the first or second treatment day and continue enoxaparin until INR is ≥ 2 for at least 24 hours (usually 5-7 days) .

-Inpatient treatment (with or without pulmonary embolism): 1 mg/kg/dose every 12 hours or 1.5 mg/kg once daily.

-Outpatient treatment (without pulmonary embolism): 1 mg/kg/dose every 12 hours.

-Obesity: Use actual body weight to calculate dose; dose capping not recommended; use of twice daily dosing preferred.

-Pregnant women: 1 mg/kg/dose every 12 hours. Discontinue ≥ 24 hours prior to the induction of labor or cesarean section. Enoxaparin therapy may be substituted with heparin near term. Continue anticoagulation therapy for ≥ 6 weeks postpartum (minimum duration of therapy: 3 months).

LMWH or heparin therapy is preferred over warfarin during pregnancy .

-Percutaneous coronary intervention (PCI), adjunctive therapy (unlabeled dosing): I.V.: In patients treated with multiple doses of enoxaparin undergoing PCI, if PCI occurs within 8 hours after the last SubQ enoxaparin dose, no additional dosing is needed. If PCI occurs 8-12 hours after the last SubQ enoxaparin dose or the patient received only 1 therapeutic SubQ dose (eg, 1 mg/kg), a single I.V. dose of 0.3 mg/kg should be administered. If PCI occurs > 12 hours after the last SubQ dose, it is prudent to use an established anticoagulation regimen (eg, full-dose unfractionated heparin or bivalirudin) .

-If patient has not received prior anticoagulant therapy: 0.5-0.75 mg/kg bolus dose

-ST-elevation MI (STEMI):

-*Patients <75 years of age*: Initial: 30 mg I.V. single bolus plus 1 mg/kg (maximum 100 mg for the first 2 doses only) SubQ every 12 hours. The first SubQ dose should be administered with the I.V. bolus. Maintenance: After first 2 doses, administer 1 mg/kg SubQ every 12 hours.

-*Patients ≥75 years of age*: Initial: SubQ: 0.75 mg/kg every 12 hours (**Note**: No I.V. bolus is administered in this population); a maximum dose of 75 mg is recommended for the first 2 doses. Maintenance: After first 2 doses, administer 0.75 mg/kg SubQ every 12 hours

-Additional notes on STEMI treatment: Therapy was continued for 8 days or until hospital discharge; optimal duration not defined. Unless contraindicated, all patients received aspirin (75-325 mg daily) in clinical trials. In patients with STEMI receiving thrombolytics, initiate enoxaparin dosing between 15 minutes before and 30 minutes after fibrinolytic therapy.

-Unstable angina or non-ST-elevation MI (NSTEMI): 1 mg/kg every 12 hours in conjunction with oral aspirin therapy (100-325 mg once daily); continue until clinical stabilization (a minimum of at least 2 days)

-*Obesity*: Use actual body weight to calculate dose; dose capping not recommended .

- *Conversion from I.V. unfractionated heparin (UFH) infusion to SubQ enoxaparin (Nutescu, 2007)*: Calculate specific dose for enoxaparin based on indication, discontinue UFH and begin enoxaparin within 1 hour.

-*Conversion from SubQ enoxaparin to I.V. UFH infusion (Nutescu, 2007)*: Discontinue enoxaparin, calculate specific dose for I.V. UFH infusion based on indication, omit heparin bolus/loading dose:

-Converting from SubQ enoxaparin dosed every 12 hours: Start I.V. UFH infusion 10-11 hours after last dose of enoxaparin

-Converting from SubQ enoxaparin dosed every 24 hours: Start I.V. UFH infusion 22-23 hours after last dose of enoxaparin.

Geriatric

SubQ: Refer to adult dosing. Increased incidence of bleeding with doses of 1.5 mg/kg/day or 1 mg/kg every 12 hours; injection-associated bleeding and serious adverse reactions are also increased in the elderly. Careful attention should be paid to elderly patients, particularly those <45 kg. **Note**: Dosage alteration/adjustment may be required.

Renal Impairment :

- $Cl_{cr} \geq 30$ mL/minute: No specific adjustment recommended (per manufacturer); monitor closely for bleeding.

- $Cl_{cr} < 30$ mL/minute:

-DVT prophylaxis in abdominal surgery, hip replacement, knee replacement, or in medical patients during acute illness: SubQ: 30 mg once daily

-DVT treatment (inpatient or outpatient treatment in conjunction with warfarin): SubQ: 1 mg/kg once daily

-STEMI:

-<75 years: Initial: I.V.: 30 mg as a single dose with the first dose of the SubQ maintenance regimen administered at the same time as the I.V. bolus; Maintenance: SubQ: 1 mg/kg once daily

-≥75 years of age: Omit I.V. bolus; Maintenance: SubQ: 1 mg/kg once daily

-Unstable angina, NSTEMI: SubQ: 1 mg/kg once daily

Dialysis: Enoxaparin has not been FDA approved for use in dialysis patients. Its elimination is primarily via the renal route. Serious bleeding complications have been reported with use in patients who are dialysis dependent or have severe renal failure. LMWH administration at fixed doses without monitoring has greater unpredictable anticoagulant effects in patients with chronic kidney disease. If used, dosages should be reduced and anti-Xa levels frequently monitored, as accumulation may occur with repeated doses. Many clinicians would not use enoxaparin in this population especially without timely anti-Xa levels.

-Hemodialysis: Supplemental dose is not necessary.

-Peritoneal dialysis: Significant drug removal is unlikely based on physiochemical characteristics.

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling (has not been studied); use with caution.

Available dosage form in the hospital: 20MG SYRINGE, 40MG SYRINGE, 60MG SYRINGE, 80MG SYRINGE

Common side effect: 1% to 10%: Central nervous system: Confusion (2%), pain

Gastrointestinal: Nausea (3%), diarrhea (2%)

Hematologic & oncologic: Major hemorrhage (<1% to 4%; includes cases of intracranial, retroperitoneal, or intraocular hemorrhage; incidence varies with indication/population), thrombocytopenia (moderate 1%; severe 0.1%), anemia (<2%), bruise

Hepatic: Increased serum ALT (6%), increased serum AST (6%)

Local: Hematoma at injection site (9%), irritation at injection site, bruising at injection site, erythema at injection site, pain at injection site, Renal: Hematuria

Pregnancy Risk Factor: B