

Enoxaparin: Overview for Providers



The Centers for Medicare & Medicaid Services (CMS), Medicaid Integrity Group (MIG) has identified issues associated with the prescribing of enoxaparin. The U.S. Food and Drug Administration (FDA) approves product labeling for prescription drugs. The MIG has identified that some providers may have prescribed enoxaparin outside of FDA-approved product labeling for indication, age, dosage, or duration of therapy. Therefore, CMS's goal is to improve quality of care and enhance patient safety by educating providers on the proper use of enoxaparin.

The purpose of this fact sheet is to promote compliance with the FDA-approved product labeling for enoxaparin. After reading this fact sheet, providers should be able to accurately:

- Identify the FDA-approved indications for the use of enoxaparin and the dosage and treatment duration for each indication;
- Identify the available treatment guidelines and dosing options for the use of enoxaparin; and
- Summarize the adverse reactions and risks of enoxaparin.

Enoxaparin

Enoxaparin is a low molecular weight heparin (LMWH) used primarily to prevent and treat blood clots, such as deep vein thrombosis (DVT) and pulmonary embolism (PE). Enoxaparin has antithrombotic properties and decreases fibrin clot formation by specifically inhibiting the coagulation factors Xa and IIa.¹

The LMWHs are depolymerized heparin derivatives that have replaced unfractionated heparin (UFH) for many indications. Because LMWHs are given subcutaneously, a patient with a thrombotic disorder can be managed in an outpatient setting. The use of a LMWH results in a more predictable anticoagulant response without the need for the routine monitoring associated with the use of UFHs.²



FDA-Approved Indications for Enoxaparin

Enoxaparin has demonstrated efficacy and safety for DVT prophylaxis and treatment, as well as for the management of thrombosis in patients with acute coronary syndrome. According to the enoxaparin prescribing information, “When administered concurrently with aspirin, enoxaparin has been shown to reduce the rate of the combined endpoint of recurrent myocardial infarction (MI) or death in patients with acute ST-segment elevation MI (STEMI) who are receiving thrombolysis and being managed medically or with percutaneous coronary intervention (PCI).”³ The FDA-approved indications for enoxaparin are:

- Prophylaxis of DVT in abdominal surgery, hip replacement surgery, knee replacement surgery, or in patients with medical conditions which severely restrict their mobility during acute illness;
- Inpatient treatment of acute DVT with or without PE;
- Outpatient treatment of acute DVT without PE;
- Prophylaxis of ischemic complications of unstable angina and non-Q-wave elevation MI (NSTEMI); and
- Treatment of acute STEMI managed medically or with PCI.⁴

ACRONYMS

AHRQ	Agency for Healthcare Research and Quality
CDER	Center for Drug Evaluation and Research
CMS	Centers for Medicare & Medicaid Services
DVT	deep vein thrombosis
FDA	U.S. Food and Drug Administration
IM	intramuscular
LMWH	low molecular weight heparin
MI	myocardial infarction
MIG	Medicaid Integrity Group
NSTEMI	non-Q-wave elevation myocardial infarction
OTC	over the counter
PE	pulmonary embolism
PCI	percutaneous coronary intervention
STEMI	ST-segment elevation myocardial infarction
UFH	unfractionated heparin

Enoxaparin Dosages

The appropriate dose of enoxaparin is based on the indication for use and the patient’s weight. The FDA-approved indications, standard dosages, and treatment durations for enoxaparin are provided in Table 1 in the document “Enoxaparin: U.S. Food and Drug Administration-Approved Indications, Dosages, and Treatment Durations.”⁵

Patients with renal impairment may have an increased exposure to enoxaparin sodium. Although no dose adjustment is recommended in patients with moderate renal impairment (creatinine clearance 30 to 50 ml per minute) and mild renal impairment (creatinine clearance 50 to 80 ml per minute), all patients with renal impairment should be monitored carefully for signs and symptoms of bleeding.⁶

An adjustment should be made to the standard dosing regimen for patients with severe renal failure (creatinine clearance less than 30 ml per minute).⁷ The recommended prophylaxis and treatment regimens for patients with severe renal impairment are described in Table 2 in the document “Enoxaparin: U.S. Food and Drug Administration-Approved Indications, Dosages, and Treatment Durations.”

Treatment Guidelines for the Use of Enoxaparin

Information on some of the guidelines for the use of enoxaparin can be found in the National Guideline Clearinghouse at <http://www.guideline.gov> on the Agency for Healthcare Research and Quality (AHRQ) website.

LMWH therapy for thromboprophylaxis is supported by guidelines developed by several professional organizations. Links to some of the guidelines that direct the use of enoxaparin are provided in Table 1 below.

Table 1: Treatment Guidelines for the Use of Enoxaparin

Sponsoring Organization	Title of Guideline	Link to Guideline
American Academy of Orthopaedic Surgeons	Preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty.	http://www.guideline.gov/content.aspx?id=35173
American College of Cardiology/ American Heart Association	Guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction.	http://www.guideline.gov/content.aspx?id=11333
American College of Cardiology/ American Heart Association	(1) ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1999 guidelines for the Management of Acute Myocardial Infarction). (2) 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.	http://www.guideline.gov/content.aspx?id=12192
American College of Chest Physicians	Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines.	http://www.guideline.gov/content.aspx?id=35264
American College of Chest Physicians	Prevention of VTE in nonsurgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines.	http://www.guideline.gov/content.aspx?id=35263
American College of Chest Physicians	Prevention of VTE in orthopedic surgery patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines.	http://www.guideline.gov/content.aspx?id=35265

Contraindications for Enoxaparin

Enoxaparin has antithrombotic properties that increase the risk of bleeding. This medication should not be used by a patient with an allergy to any component of the drug or who is at an increased risk of bleeding.

The contraindications for enoxaparin include:

- Active major bleeding;
- Thrombocytopenia with a positive in vitro test for antiplatelet antibodies in the presence of enoxaparin sodium;
- Hypersensitivity to enoxaparin sodium;
- Hypersensitivity to heparin or pork products; and
- Hypersensitivity to benzyl alcohol (for multidose formulation only, which should not be used in pregnancy).⁸

Adverse Reactions and Risks of Enoxaparin

The most common adverse reactions reported with the use of enoxaparin are bleeding, anemia, thrombocytopenia, elevation of serum aminotransferase levels, diarrhea, and nausea. Bleeding can occur at any site during enoxaparin therapy and may be indicated by an unexplained fall in hematocrit or blood pressure. Mild local irritation, pain, hematoma, ecchymosis, and erythema may occur at the injection site.⁹

Enoxaparin should be used with extreme caution with:

- Medical conditions with increased risk of hemorrhage;
- Percutaneous coronary revascularization procedure;
- Concomitant medical conditions (such as gastrointestinal ulceration, renal dysfunction, hemorrhage, diabetic retinopathy, or uncontrolled arterial hypertension);
- Coadministration of other agents that increase the risk of hemorrhage (such as platelet inhibitors, nonsteroidal anti-inflammatory drugs, and salicylates);
- History of heparin-induced thrombocytopenia; and
- Thrombocytopenia.¹⁰

Reports of spinal hematoma occurring spontaneously and in association with regional anesthesia have generated concern about the safety of spinal or epidural anesthesia in patients receiving enoxaparin.¹¹

The boxed warning for enoxaparin states:¹²

WARNING : SPINAL/EPIDURAL HEMATOMAS

Epidural or spinal hematomas may occur in patients who are anticoagulated with low molecular weight heparins (LMWH) or heparinoids and are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- Concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
- A history of traumatic or repeated epidural or spinal punctures
- Use of indwelling epidural catheters
- A history of spinal deformity or spinal surgery.

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary. Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis [see Warnings and Precautions (5.1) and Drug Interactions (7)].



Prescribing and Dosing Considerations for Enoxaparin

Enoxaparin is safe and effective when used appropriately. There are several factors to consider when prescribing enoxaparin:

- Enoxaparin is not interchangeable with heparin or other LMWHs;
- Enoxaparin should not be administered intramuscularly (IM);
- Appropriate enoxaparin dosing is either fixed (based on a specific indication for use), variable (based on a patient's weight), or a combination of the two. The enoxaparin 30 mg per 0.3 ml and 40 mg per 0.4 ml prefilled syringes are most often used for strength-specific indications that require fixed dosing, such as DVT prophylaxis. Prefilled syringe sizes with larger doses are most often used for indications that require variable dosing based on a patient's weight;
- Enoxaparin may be dosed once a day or twice a day depending on the indication for use;
- Enoxaparin prefilled syringes are available in a variety of syringe volumes and the total milliliters per syringe is based on the strength dispensed; and
- Enoxaparin prescriptions may be written to dispense the quantity in milligrams, prefilled syringes, or vials. However, the prescription must specify the dose and quantity prescribed so the days' supply can be determined and entered correctly on the claim when the prescription is processed.¹³

Resources

Please visit <http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-State/By-State.html> for links to State Medicaid program websites.

The Center for Drug Evaluation and Research (CDER) hosts a website providing health professionals with current information on over-the-counter (OTC) and prescription drugs. Visit <http://www.fda.gov/Drugs/ResourcesForYou/HealthProfessionals> to access drug-related databases, information on drug recalls and alerts, current information on new and generic drug approvals, and information on drug safety and availability.

Section 1927(g)(1)(B) of the Social Security Act identifies the predetermined standards that the State's drug use review program must use to assess data on drug use. Visit http://www.ssa.gov/OP_Home/ssact/title19/1927.htm for information on the compendia.

References

¹ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

² Centers for Disease Control and Prevention. (2011, February 22). Deep Vein Thrombosis/Pulmonary Embolism (DVT/PE): Treatments of DVT and PE. Retrieved August 31, 2011, from <http://www.cdc.gov/ncbddd/dvt/treatments.html>

³ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

⁴ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

⁵ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

⁶ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

⁷ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

⁸ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

⁹ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

¹⁰ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

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¹² Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf

¹³ Lovenox® (enoxaparin) prescribing information. (2011, April 20). Retrieved August 16, 2011, from http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020164s093lbl.pdf



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