

Prior Authorization DRUG Guidelines

LOVENOX

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INDICATIONS AND USAGE

- Lovenox Injection is indicated for the prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism:
 - in patients undergoing abdominal surgery who are at risk for thromboembolic complications;
 - in patients undergoing hip replacement surgery, during and following hospitalization;
 - in patients undergoing knee replacement surgery;
 - in pregnant patients at risk for deep venous thromboses;
 - in medical patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness.
- Lovenox injection is indicated for anticoagulation in conjunction with warfarin in the setting of new onset atrial fibrillation. Lovenox is continued for a minimum of 4 days and until the INR is >2 , which is typically 5-7 days.
- Lovenox Injection is indicated for the prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin.
- Lovenox Injection is indicated for:
 - the inpatient treatment of acute deep vein thrombosis with or without pulmonary embolism, when administered in conjunction with warfarin sodium;
 - the outpatient treatment of acute deep vein thrombosis without pulmonary embolism when administered in conjunction with warfarin sodium.

CONTRAINDICATIONS

- Lovenox Injection is contraindicated in patients with active major bleeding, in patients with thrombocytopenia associated with a positive *in vitro* test for anti-platelet antibody in the presence of enoxaparin sodium, or in patients with hypersensitivity to enoxaparin sodium.
- Lovenox injection is contraindicated in patients with allergies to heparin or pork products.

WARNINGS

- Lovenox Injection is not intended for intramuscular administration.

- Lovenox Injection cannot be used interchangeably (unit for unit) with heparin or other low molecular weight heparins as they differ in manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units, and dosage. Each of these medicines has its own instructions for use.
- Lovenox Injection should not be used in patients with a history of heparin-induced thrombocytopenia.
- Hemorrhage: Lovenox Injection, like other anticoagulants, should be used with extreme caution in conditions with increased risk of hemorrhage, such as bacterial endocarditis, congenital or acquired bleeding disorders, active ulcerative and angiodysplastic gastrointestinal disease, hemorrhagic stroke, or, or ophthalmological surgery, or in patients treated concomitantly with platelet inhibitors.
- Cases of epidural or spinal hematomas have been reported with the associated use of Lovenox Injection and spinal/epidural anesthesia or spinal puncture resulting in long-term or permanent paralysis. The risk of these events is higher with the use of post-operative indwelling epidural catheters or by the concomitant use of additional drugs affecting hemostasis such as NSAIDs. Major hemorrhages including retroperitoneal and intracranial bleeding have been reported. Some of these cases have been fatal.
- Bleeding can occur at any site during therapy with Lovenox Injection. An unexplained fall in hematocrit or blood pressure should lead to a search for a bleeding site.
- Thrombocytopenia can occur with the administration of Lovenox Injection. Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below $100,000/\text{mm}^3$, Lovenox Injection should be discontinued. Cases of heparin-induced thrombocytopenia with thrombosis have also been observed in clinical practice. Some of these cases were complicated by organ infarction, limb ischemia, or death.

Pregnant Women with Mechanical Prosthetic Heart Valves: The use of Lovenox Injection for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves has not been adequately studied. In a clinical study of pregnant women with mechanical prosthetic heart valves given enoxaparin (1 mg/kg bid) to reduce the risk of thromboembolism, 2 of 8 women developed clots resulting in blockage of the valve and leading to maternal and fetal death. Although a causal relationship has not been established these deaths may have been due to therapeutic failure or inadequate anticoagulation. No patients in the heparin/warfarin group (0 of 4 women) died. There also have been isolated postmarketing reports of valve thrombosis in pregnant women with mechanical prosthetic heart valves while receiving enoxaparin for thromboprophylaxis. Women with mechanical prosthetic heart valves may be at higher risk for thromboembolism during pregnancy, and, when pregnant, have a higher rate of fetal loss from stillbirth, spontaneous abortion and premature delivery. Therefore, frequent monitoring of peak and trough anti-Factor Xa levels, and adjusting of dosage may be needed.

Miscellaneous: Lovenox multiple-dose vials contain benzyl alcohol as a preservative. The administration of medications containing benzyl alcohol as a preservative to premature neonates has been associated with a fatal "Gasping Syndrome". Because benzyl alcohol may cross the placenta, Lovenox multiple-dose vials, preserved with benzyl alcohol, should be used with caution in pregnant women and only if clearly needed.

PRECAUTIONS

General: Lovenox Injection should not be mixed with other injections or infusions.

Lovenox Injection should be used with care in patients with a bleeding diathesis, uncontrolled arterial hypertension or a history of recent gastrointestinal ulceration, diabetic retinopathy, and hemorrhage. Lovenox Injection should be used with care in elderly patients who may show delayed elimination of enoxaparin.

If thromboembolic events occur despite Lovenox Injection prophylaxis, appropriate therapy should be initiated.

Mechanical Prosthetic Heart Valves: The use of Lovenox Injection has not been adequately studied for thromboprophylaxis in patients with mechanical prosthetic heart valves and has not been adequately studied for long-term use in this patient population. Isolated cases of prosthetic heart valve thrombosis have been reported in patients with mechanical prosthetic heart valves who have received enoxaparin for thromboprophylaxis. Some of these cases were pregnant women in whom thrombosis led to maternal and fetal deaths. Insufficient data, the underlying disease and the possibility of inadequate anticoagulation complicate the evaluation of these cases. Pregnant women with mechanical prosthetic heart valves may be at higher risk for thromboembolism.

Renal Impairment: In patients with renal impairment, there is an increase in exposure of enoxaparin sodium. All such patients should be observed carefully for signs and symptoms of bleeding. Because exposure of enoxaparin sodium is significantly increased in patients with severe renal impairment (creatinine clearance <30 mL/min), a dosage adjustment is recommended for therapeutic and prophylactic dosage ranges. No dosage adjustment is recommended in patients with moderate (creatinine clearance 30-50 mL/min) and mild (creatinine clearance 50-80 mL/min) renal impairment.

Low-Weight Patients: An increase in exposure of enoxaparin sodium with prophylactic dosages (non-weight adjusted) has been observed in low-weight women (<45 kg) and low-weight men (<57 kg). All such patients should be observed carefully for signs and symptoms of bleeding.

Laboratory Tests: Periodic complete blood counts, including platelet count, and stool occult blood tests are recommended during the course of treatment with Lovenox Injection. When administered at recommended prophylaxis doses, routine coagulation tests such as Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) are relatively insensitive measures of Lovenox Injection activity and, therefore, unsuitable for monitoring. Anti-Factor Xa may be used to monitor the anticoagulant

effect of Lovenox Injection in patients with significant renal impairment. If during Lovenox Injection therapy abnormal coagulation parameters or bleeding should occur, anti-Factor Xa levels may be used to monitor the anticoagulant effects of Lovenox Injection.

Drug Interactions: Unless really needed, agents which may enhance the risk of hemorrhage should be discontinued prior to initiation of Lovenox Injection therapy. These agents include medications such as: anticoagulants, platelet inhibitors including acetylsalicylic acid, salicylates, NSAIDs (including ketorolac tromethamine), dipyridamole, or sulfipyrazone. If co-administration is essential, conduct close clinical and laboratory monitoring.

Pregnancy: Pregnancy Category B:

All pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure. The fetal risk summary below describes Lovenox's potential to increase the risk of developmental abnormalities above background risk.

Fetal Risk Summary

Lovenox is not predicted to increase the risk of developmental abnormalities. Lovenox does not cross the placenta, based on human and animal studies, and shows no evidence of teratogenic effects or fetotoxicity.

Pregnancy alone confers an increased risk for thromboembolism, that is even higher for women with thromboembolic disease and certain high risk pregnancy conditions. While not adequately studied, pregnant women with mechanical prosthetic heart valves may be at even higher risk for thrombosis. Pregnant women with thromboembolic disease, including those with mechanical prosthetic heart valves, and those with inherited or acquired thrombophilias, also have an increased risk of other maternal complications and fetal loss regardless of the type of anticoagulant used.

All patients receiving anticoagulants such as enoxaparin, including pregnant women, are at risk for bleeding. Pregnant women receiving enoxaparin should be carefully monitored for evidence of bleeding or excessive anticoagulation. Consideration for use of a shorter acting anticoagulant should be specifically addressed as delivery approaches.

Hemorrhage can occur at any site and may lead to death of mother and/or fetus. Pregnant women should be apprised of the potential hazard to the fetus and the mother if enoxaparin is administered during pregnancy.

Pediatric Use: Safety and effectiveness of Lovenox Injection in pediatric patients have not been established.

Geriatric Use: Over 2800 patients, 65 years and older, have received Lovenox Injection in pivotal clinical trials. The efficacy of Lovenox Injection in the elderly (≥ 65 years) was similar to that seen in younger patients (< 65 years). The incidence of bleeding complications was similar between elderly and younger patients when 30 mg every 12 hours or 40 mg once a day doses of Lovenox Injection were employed. The incidence of bleeding complications was higher in elderly patients as compared to younger patients when Lovenox Injection was administered at doses of 1.5 mg/kg once a day or 1 mg/kg every 12 hours. The risk of Lovenox Injection-associated bleeding increased with age.

Serious adverse events increased with age for patients receiving Lovenox Injection. Other clinical experience (including postmarketing surveillance and literature reports) has not revealed additional differences in the safety of Lovenox Injection between elderly and younger patients. Careful attention to dosing intervals and concomitant medications (especially antiplatelet medications) is advised. Monitoring of geriatric patients with low body weight (<45 kg) and those predisposed to decreased renal function should be considered

Recommended Dosing Regimen and Authorization Limit

Drug	Dosing Regimen	Authorization Limit
Hip fracture or replacement	<u>Lovenox:</u> 30 mg Q 12 H or 40 mg QD	<u>Lovenox:</u> 14 days
Abdominal surgery	<u>Lovenox:</u> 40 mg QD	<u>Lovenox:</u> 12 days
Knee replacement	<u>Lovenox:</u> 30 mg Q 12 H	<u>Lovenox:</u> 14 days
High risk surgery/major gynecologic surgery or surgery with malignancy	<u>Lovenox:</u> 40 mg QD)	<u>Lovenox:</u> 7-10 days or until discharge
Acute medical illness	<u>Lovenox:</u> 40 mg QD	<u>Lovenox:</u> 7-14 days until illness resolves and/or ambulatory
Acute multiple trauma	<u>Lovenox:</u> 30 mg BID	<u>Lovenox:</u> Hospital discharge unless major impaired mobility
Acute spinal cord injury	<u>Lovenox:</u> <u>30 mg BID or 40 mg QD</u>	<u>Lovenox:</u> <u>Continue to the end of rehabilitation phase of therapy</u>
Embolic stroke	<u>Lovenox:</u> 30 mg BID	<u>Lovenox:</u> Acute phase until ambulatory

Recurrent DVT on oral anticoagulation or oral therapy precluded	<u>Lovenox:</u> 1 mg/kg Q 12 H	Indefinite
Unstable angina/non-Q wave MI	<u>Lovenox:</u> 1 mg/kg Q 12 H	<u>Lovenox:</u> 8-10 days
Acute coronary syndrome	<u>Lovenox:</u> 1 mg/kg Q 12 H	<u>Lovenox:</u> 48 hours
Pregnancy (prophylaxis)	<u>Lovenox:</u> 60 mg QD	<u>Lovenox:</u> 6 weeks post partum
Treatment of VTE	<u>Lovenox:</u> 1 mg/kg Q 12 H	<u>Lovenox:</u> 5-10 days conversion to oral vitamin K antagonist (VKA)
Short-term prophylaxis for transition to /from oral anticoagulation	<u>Lovenox:</u> High-risk of clot: 1 mg/kg Q 12 H Low-risk of clot: 30 mg BID or 40 mg QD	<u>Lovenox:</u> Preoperative 2-3 days following discontinuation of oral VKA, 4 to 5 days post-operatively conversion to VKA
Pediatric patients treatment	<u>Lovenox:</u> < 2 mo 1.5 mg/kg Q12 H > 2 mo 1 mg/kg Q 12 H	Consult literature for appropriate duration based on intended use
Pediatric patients prophylaxis	<u>Lovenox:</u> < 2 mo 0.75 mg/kg Q 12 H > 2 mo 0.5 mg/kg Q 12 H	Consult literature for appropriate duration based on intended use

ADMINISTRATION — Should be administered by deep SubQ injection to the left or right anterolateral and left or right posterolateral abdominal wall. To avoid loss of drug from the 30 mg and 40 mg syringes, do not expel the air bubble from the syringe prior to injection. In order to minimize bruising, do not rub injection site. An automatic injector (Lovenox EasyInjector™) is available with the 30 mg and 40 mg syringes to aid the patient with self-injections. Note: Enoxaparin is available in 100 mg/mL and 150 mg/mL concentrations.

Product Availability Lovenox: Solution for injection, vial: 300 mg/3 ml. Prefilled syringes: 30 mg/0.3 ml, 40 mg/0.4 ml, 60 mg/0.6 ml, 80 mg/0.8 ml, 100 mg/1 ml, 120 mg/0.8 ml, 150 mg/1 ml.

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