

Bon Secours Richmond  
Pharmacy & Therapeutic Committee  
1/2001

Recommendations:

- When ordering LMWH for treatment of DVT/PE, USA, Non-Q wave MI, and other indications requiring 1 mg/kg of enoxaparin, it is recommended that physicians write: enoxaparin 1 mg/kg SC q12 and the patient's weight (if available) on the order. Patient weights will be obtained by nursing when needed.
- Physicians should write the indication on all enoxaparin orders.
- Unfractionated heparin (5000 units q8-12h SC) is recommended to replace enoxaparin (autosubstitution) for medical and general surgery patients requiring DVT prophylaxis, except for orthopedic surgery, acute spinal cord injury, trauma with risk of VTE. Unfractionated heparin is as safe and effective as LMWH, but is substantially less expensive than enoxaparin (\$0.72 versus \$15.67 per day).
- Pharmacists will check all enoxaparin dosage versus indication and weight, and will call the physician as needed for dosage confirmation.
- Standardized weight adjusted dosing of enoxaparin is recommended for treatment of DVT treatment and other indications requiring 1 mg/kg (LMWH during transition to or from oral anticoagulation). This will decrease the potential for incorrect dosages and wastage.

Weight (kg)

25-35 kg	30 mg
36-45 kg	40 mg
46-55 kg	50 mg
56-65 kg	60 mg
66-75 kg	70 mg
76-85 kg	80 mg
86-95 kg	90 mg
96-105 kg	100 mg
106-115 kg	110 mg
116-135 kg	120 mg
136-150 kg	150 mg

- The pharmacy will carry the following sizes of Lovenox® 30 mg, 40 mg, and 60 mg syringes.
- Nurses should combine the contents of multiple Lovenox syringes into one syringe before injecting the patient.
- Appropriate preventive strategies in individual general surgery patients take into account the risk of VTE, the potential benefits of the various agents, and the expense and possible complications incurred by their use.

**Recommended Heparin Doses**

**Prophylaxis**

Indication	Lovenox	Unfractionated Heparin
Patients at risk of VTE	40qd q24h	5000 u q8-12h
Knee/Hip Orthopedic Replacement	30 mg q12h or (40 mg q24h for hip only)	Adjusted Dose Heparin
Abdominal Surgery	40 mg q24h	5000 u q8-12h

**Treatment**

DVT/PE Treatment	1 mg/kg q12h	Adjusted Dose Heparin
USA/Non Q Wave MI	1 mg/kg q12h	Adjusted Dose Heparin
Atrial fibrillation with embolization	1 mg/kg q12h	Adjusted Dose Heparin
Chronic Atrial Fibrillation (previously receiving or transitioning to warfarin)	1 mg/kg q12h	Adjusted Dose Heparin
Peripheral artery embolism	1 mg/kg q12h	Adjusted Dose Heparin

**Surgical Prophylaxis (Lovenox Package Insert)**

	Lovenox 40 mg qd	Heparin 5000 units q8h
<b>Indication</b>		
Abdominal Surgery with Cancer	555	560
VTE(DVT, PE, Death from VTE)	10.1%(56/555)	11.3%(63/560)
DVT only	9.7%(54/555)	10.9%(61/560)
Major Bleeding episodes	4%(23/555)	3%(16/560)
Colorectal Surgery (33% with Cancer)	673	674
VTE (DVT, PE, Death from VTE)	7.1%(48/673)	6.7%(45/674)
DVT only	7%(47/673)	6.5%(44/674)
Major Bleeding episodes	4%(28/673)	3%(21/674)

Chest Guidelines 1998 for Prevention of Venous Thromboembolism	
General Surgery	
<b>Low Risk:</b> Uncomplicated minor surgery in patients less than 40 years old with no clinical risk factors	Early Ambulation
<b>Moderate Risk:</b> General surgery (Major or minor surgery) in patients 40-60 years old without additional risk factors, or Major Surgery in patients < 40 years old with no risk factors, or Minor surgery in patients with risk factors	LDUF (5000 units q12h), LMWH 40 mg qd, IPC, ES
<b>High Risk:</b> Major surgery in patients > 60 years old without additional risk factors or Major surgery in patients 40-60 years old with additional risk factors	(LDUFH (q8h), LMWH, IPC) ± ES
<b>Very High Risk</b> Major surgery in patients > 40 years old plus prior VTE or malignant disease or hypercoagulable	(LDUH (q8h), LMWH 40 mg qd) with IPC
Elective major lower extremity orthopedic surgery, or hip fracture	(Warfarin INR 2-3, LMWH 30 mg q12h, adjusted dose heparin) with (IPC or ES)
Elective neurosurgery	(IPC ± ES), LMWH, LDUFH, (IPC ± ES) + (LMWH or LDUFH)
Acute spinal cord injury	LMWH
Trauma with risk for VTE	LMWH, IPC
Medical Conditions	
<b>High Risk</b> MI	LDUF, Adjusted Dose Heparin
<b>High Risk</b> General medical patients with risk factors for VTE such as CHF or pulmonary infection	LDUH, LMWH
<b>Very High Risk</b> Ischemic stroke and lower extremity paralysis	LDUH, LMWH

**LDUFH:** Low Dose Unfractionated Heparin, **LMWH:** Low Molecular Weight Heparin, **IPC:** Intermittent Pneumatic Compression, **ES:** Graded Compression Elastic Stockings

Risk Factors: age ≥40, prolonged immobility or paralysis, prior VTE, cancer, major surgery (particularly those involving abdomen, pelvis, or lower extremities), obesity, varicose veins, CHF, MI, stroke, fractures of pelvis, hip, or leg; indwelling femoral vein catheter, inflammatory bowel disease, nephrotic syndrome, estrogen use, hypercoagulable states (protein C resistance or deficiency, antithrombin III deficiency, protein S deficiency, dysfibrinogenemia, disorder of plasminogen or plasminogen activation, antiphospholipid antibodies, and lupus anticoagulant, HIT, hyperhomocystinemia, and myeloproliferative disorders). Risk factors are cumulative.

#### Findings:

- LMWH do not require the use of IV pumps, IV poles, or PTT monitoring. They are administered q12-24h by SC injection which decreases nursing time.
- Unfractionated heparin is substantially less expensive than fractionated heparin for hospital therapy when the following are included: medication cost, nursing and pharmacy labor, supplies and equipment and laboratory monitoring (costing 14-37% of an equivalent dose of enoxaparin).
- Conversion of all IV infusion heparin to enoxaparin would cost approximately \$199,730 per year for the Richmond System.
- Numerous errors have occurred with heparin infusions (wrong rate, wrong concentration, PTT not drawn, dose not adjusted per PTT, infusion running empty). Conversion to enoxaparin has the potential to provide safer therapy to the patient.
- The usage of unfractionated heparin has decrease and current accounts for 49% of total daily heparin doses.
- Dalteparin cost approximately 15% less than enoxaparin per kg for treatment, representing a potential yearly cost saving of \$30,000 for BS Richmond. This is not a sufficient savings to undertake a conversion to dalteparin.
- LMWHs have not been directly compared in clinical trials.
- Assessing the relative potency of individual products in terms of activity against a specific coagulation component (factor Xa) has been suggested as a means of reducing product differences. However, accumulating evidence indicates that LMWHs should not be considered bioequivalent because they differ from each other in a number of characteristics based on multiple biological properties, including pharmacokinetics and pharmacodynamics. Hence, the American College of Chest Physicians (ACCP), World Health Organization (WHO), and the FDA caution against extrapolating the properties of one LMWH to another.
- As molecular weight decreases to ≤ 5 kDa, LMWH fractions progressively lose the ability to inhibit thrombin (factor II) and prolong the activated partial thromboplastin time (aPTT). However, they retain the ability to inhibit activated factor X (factor Xa), an action that may have a role in antithrombotic efficacy.
- Specific laboratory assay monitoring—anti-factor Xa activity levels—has been suggested in patients for whom long-term LMWH treatment may be indicated, as well as for patients with characteristics that may influence the distribution or clearance of the drug, such as significant variance from ideal body weight or renal insufficiency.
- The previously proposed theory that anti-factor Xa activity predicts antithrombotic effect, with anti-factor IIa activity predicting hemorrhagic effect, does not provide a complete description of the overall mechanism of LMWH activity. If anti-factor Xa activity were solely responsible for antithrombotic efficacy, the presumption would be that LMWHs with longer half-lives for anti-factor Xa activity could be dosed less frequently. This does not appear to be the case with danaparoid, the heparinoid with the longest relative anti-factor Xa activity half-life.

- LMWHs are primarily cleared by renal excretion, and half-lives increase in patients with renal dysfunction. However, the clinical significance of these findings has been questioned, and specific dosing guidelines and monitoring parameters for the use of individual LMWHs in patients with renal dysfunction have not been determined.
- Although comparative pharmacokinetic and biological activity data for LMWHs are available, controlled trials that directly compare individual LMWHs in clinical settings are generally lacking.
- Bioavailability of LMWH is approximately 90% versus 22-40% for unfractionated heparin.
- Once daily enoxaparin has not been shown to superior to UFH for DVT treatment. There are insufficient clinical trial data to conclude that individual LMWHs are less likely to cause bleeding complications than UFH or warfarin. In fact, the prolonged anticoagulant characteristics of LMWHs, compared with that of standard heparin, may be disadvantageous for certain patients who are at high risk for bleeding.
- Low dose unfractionated heparin is equivalent to LMWH in medical and general surgery DVT prophylaxis.
- Low dose unfractionate heparin (LDUFH) is equally efficacious to LMWH in preventing VTE in general surgery patients. LMWH doses greater than 3400 anti X units/day (34 mg Lovenox) have higher bleeding rates than LDUFH (5000 u q8-12h)
- LMWH should be used with caution in patients with spinal puncture or epidural catheters placed for regional anesthetic and postoperative analgesia.
- Enoxaparin is FDA approved for prophylactic use in general surgery, hip & knee arthorplasty, and for treatment of VTE, and USA. It has more indications than any other currently marketed LMWH.

### FDA-Approved Indications (March 2000) for Available LMWHs

	<b>Enoxaparin</b>	<b>Dalteparin</b>	<b>Danaparoid</b>	<b>Ardeparin</b>	<b>Tinzaparin</b>
General Surgery Prophylaxis	+	+			
Hip Arthroplasty Prophylaxis	+	+	+		
Knee Arthroplasty Prophylaxis	+			+	
Treatment of Venous Thromboembolism (deep venous thrombosis/pulmonary embolism)	+				+
Extended Prophylaxis (postoperatively)	+				
Unstable Angina	+	+			

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