





**Enoxaparin Sodium Injection USP 100 mg/mL Concentration** contains 10 mg enoxaparin sodium (approximate anti-Factor Xa activity of 1000 IU [with reference to the W.H.O. First International Low Molecular Weight Heparin Reference Standard]) per 0.1 mL Water for Injection.

**Enoxaparin Sodium Injection USP 150 mg/mL Concentration** contains 15 mg enoxaparin sodium (approximate anti-Factor Xa activity of 1500 IU [with reference to the W.H.O. First International Low Molecular Weight Heparin Reference Standard]) per 0.1 mL Water for Injection.

The Enoxaparin Sodium Injection USP prefilled syringes and graduated prefilled syringes are preservative-free and intended for use only as a single-dose injection. The multiple-dose vial contains 15 mg benzyl alcohol per 1 mL as a preservative [see *Dosage and Administration (2)* and *How Supplied/Storage and Handling (16)*].

**12. CLINICAL PHARMACOLOGY**

**12.1 Mechanism of Action**  
Enoxaparin is a low molecular weight heparin, which has antithrombotic properties.

**12.2 Pharmacodynamics**  
In humans, enoxaparin given at a dose of 1.5 mg/kg subcutaneously is characterized by a higher ratio of anti-Factor Xa to anti-Factor IIa activity (mean  $\pm$ SD, 14.0:3.1) (based on areas under anti-Factor activity versus time curves) compared to the ratios observed for heparin (mean  $\pm$ SD, 1.22:0.13). Increases up to 1.8 times the control values were seen in the thrombin time (TT) and the activated partial thromboplastin time (aPTT). Enoxaparin at 1 mg/kg dose (100 mg/mL concentration), administered subcutaneously every 12 hours to patients in a large clinical trial resulted in aPTT values of 45 seconds or less in the majority of patients ( $n=1607$ ). A 30 mg intravenous bolus immediately followed by a 1 mg/kg subcutaneous administration at 2 hours prior to surgery and continued for approximately 7 to 10 days after surgery. The efficacy data are provided below (see Table 14).

**12.3 Pharmacokinetics**  
**Pharmacokinetic trials** were conducted using the 100 mg/mL formulation. Maximum anti-Factor Xa and anti-thrombin (anti-Factor IIa) activities occur 3 to 5 hours after subcutaneous injection of enoxaparin. Mean peak anti-Factor Xa activity was 0.16 IU/mL (1.58 mg/mL) and anti-Factor IIa activity was 0.23 mg/mL (2.32 mg/mL) in healthy subjects. Enoxaparin sodium is administered subcutaneously every 12 hours to patients in stable angina receiving 1 mg/kg subcutaneously every 12 hours for 14 days. Mean absolute bioavailability of enoxaparin, after 1.5 mg/kg given subcutaneously, based on anti-Factor Xa activity is approximately 100% in healthy subjects. A 30 mg intravenous bolus immediately followed by a 1 mg/kg subcutaneously every 12 hours provided initial peak anti-Factor Xa levels of 1.16 IU/mL ( $n=16$ ) and average exposure corresponding to 84% of steady-state levels. Steady state is achieved on the second day of treatment.

Enoxaparin pharmacokinetics appear to be linear over the recommended dosage ranges (see *Dosage and Administration (2)*). After repeated subcutaneous administration of 40 mg once daily and 150 mg once daily regimens in healthy volunteers, the steady state is reached on day 2 with an average exposure ratio about 15% higher than after a single dose. Steady-state enoxaparin activity levels are well predicted by single-dose pharmacokinetics. After repeated subcutaneous administration of the 1 mg/kg twice-daily regimen, the steady state is reached from day 4 with mean exposure about 65% higher than after a single dose and mean peak and trough levels of about 1.2 and 0.52 IU/mL, respectively. Based on enoxaparin sodium pharmacokinetics, this difference in steady state is expected and within the therapeutic range. Although the 150 mg/mL concentration of enoxaparin sodium is projected to result in anticoagulant activities similar to those of 100 mg/mL and 200 mg/mL concentrations at the same enoxaparin dose. When a daily 1.5 mg/kg subcutaneous injection of enoxaparin sodium was given to 25 healthy male and female subjects using a 100 mg/mL or a 200 mg/mL concentration for the following pharmacokinetic profiles were obtained (see Table 13).

**Table 13**  
**Pharmacokinetic Parameters\* After 5 Days of 1.5 mg/kg Subcutaneous Once-Daily Doses of Enoxaparin Sodium Using 100 mg/mL or 200 mg/mL Concentrations**

Concentration	Anti-Xa	Anti-IIa	Hepstat	aPTT
100 mg/mL	1.37 ( $\pm 0.23$ )	0.23 ( $\pm 0.05$ )	105 ( $\pm 17$ )	19 ( $\pm 5$ )
200 mg/mL	1.45 ( $\pm 0.22$ )	0.26 ( $\pm 0.05$ )	111 ( $\pm 17$ )	22 ( $\pm 7$ )
90% CI	102%-110%	102%-114%	102%-114%	
$t_{max}$ (h)	100 mg/mL 3 (2-6)	4 (2-5)	2.5 (2-4.5)	3 (2-4.5)
200 mg/mL 3.5 (2-6)	4.5 (2.5-6)	3.3 (2-5)	3 (2-5)	
AUC (ss)	100 mg/mL 14.26 ( $\pm 2.93$ )	1.54 ( $\pm 0.61$ )	1321 ( $\pm 219$ )	
(h*U/mL or h*% sec)	200 mg/mL 15.43 ( $\pm 2.96$ )	1.77 ( $\pm 0.67$ )	1401 ( $\pm 227$ )	
90% CI	105%-112%	103%-109%		

\*Means  $\pm$  SD at Day 5 and 90% Confidence Interval (CI) of the ratio  
\*Median (range)  
Distribution  
The volume of distribution of anti-Factor Xa activity is about 4.3 L.  
Elimination  
Following intravenous dosing, the total body clearance of enoxaparin is 26 mL/min after intravenous dosing of enoxaparin labeled with the gamma-emitter,  $^{99m}Tc$ , 40% of radioactivity and 8 to 20% of anti-Factor Xa activity were recovered in urine in 24 hours. Elimination half-life based on anti-Factor Xa activity was 4.5 hours after a single subcutaneous dose to about 7 hours after repeated dosing. Significant anti-Factor Xa activity persists in plasma for about 12 hours following a 40 mg subcutaneous once a day dose.  
Following subcutaneous dosing, the apparent clearance (CL/F) of enoxaparin is approximately 15 mL/min.  
Metabolism  
Enoxaparin sodium is primarily metabolized in the liver by desulfation and/or depolymerization to low molecular weight species with much reduced biological potency. Renal clearance of active fragments represents about 10% of the administered dose and total renal excretion of active and non-active fragments 40% of the dose.  
Special populations  
Gender  
Apparent clearance and  $A_{sc}$  derived from anti-Factor Xa values following single subcutaneous dosing (40 mg and 80 mg) were slightly higher in males than in females. The source of the gender difference in these parameters has not been conclusively identified; however, body weight may be a contributing factor.  
Geriatric  
Apparent clearance and  $A_{sc}$  derived from anti-Factor Xa values following single and multiple subcutaneous dosing in geriatric subjects were close to those observed in young subjects. Following once a day subcutaneous dosing of 40 mg enoxaparin, the Day 10 mean area under anti-Factor Xa activity versus time curve (AUC) was approximately 15% greater than the mean Day 1 AUC value [see *Dosage and Administration (2)* and *Use in Specific Populations (8.5)*].  
Renal impairment  
A linear relationship between anti-Factor Xa plasma clearance and creatinine clearance at steady state has been observed, which indicates decreased clearance of enoxaparin sodium in patients with reduced renal function. Anti-Factor Xa exposure represented by AUC, at steady state, is marginally increased in patients with creatinine clearance 50 to 80 mL/min and patients with creatinine clearance 30 to  $<50$  mL/min renal impairment after repeated subcutaneous 40 mg once-daily doses. In patients with severe renal impairment (creatinine clearance  $<30$  mL/min), the AUC at steady state is significantly increased on average by 65% after repeated subcutaneous 40 mg once-daily doses [see *Dosage and Administration (2)* and *Use in Specific Populations (8.7)*].  
Hemodialysis  
In a single study, elimination rate appeared similar but AUC was two-fold higher than control population, after a single 0.25 or 0.5 mg/kg intravenous dose.  
Hepatic impairment  
Studies with Enoxaparin Sodium Injection in patients with hepatic impairment have not been conducted and the impact of hepatic impairment on the exposure to enoxaparin is unknown.  
Weight  
After repeated subcutaneous 1.5 mg/kg once daily dosing, mean AUC of anti-Factor Xa activity is marginally higher at steady state in obese healthy volunteers (BMI 30-48 kg/m<sup>2</sup>) compared to non-obese control subjects, while  $A_{sc}$  is not increased.  
When non-weight adjusted dosing was administered, it was found after a single-subcutaneous 40 mg dose, that anti-Factor Xa exposure is 52% higher in low-weight women ( $<45$  kg) and 27% higher in low-weight men ( $<57$  kg) when compared to normal weight control subjects [see *Use in Specific Populations (8.6)*].  
Pharmacokinetic interaction  
No pharmacokinetic interaction was observed between Enoxaparin Sodium Injection and thrombolytics when administered concomitantly.

**13. NONCLINICAL TOXICOLOGY**

**13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**  
No long-term studies in animals have been performed to evaluate the carcinogenic potential of enoxaparin. Enoxaparin was not mutagenic in *in vitro* tests including the Ames test, mouse lymphoma cell forward mutation test, and human lymphocyte chromosomal aberration test, and the *in vivo* rat bone marrow chromosomal aberration test. Enoxaparin was found to have no effect on fertility or reproductive performance of male and female rats at subcutaneous doses up to 20 mg/kg/day or 141 mg/m<sup>2</sup>/day. The maximum human dose in clinical trials was 2.0 mg/kg/day or 78 mg/m<sup>2</sup>/day (for an average body weight of 70 kg, height of 170 cm, and body surface area of 1.8 m<sup>2</sup>).  
**13.2 Animal Toxicology and/or Pharmacology**  
A single subcutaneous dose of 46.4 mg/kg enoxaparin was lethal to rats. The symptoms of acute toxicity were ataxia, decreased motility, dyspnea, cyanosis, and coma.  
**13.3 Reproductive and Developmental Toxicology**  
Teratology studies have been conducted in pregnant rats and rabbits at subcutaneous doses of enoxaparin up to 30 mg/kg/day corresponding to 211 mg/m<sup>2</sup>/day and 410 mg/m<sup>2</sup>/day in rats and rabbits respectively. There was no evidence of teratogenic effects or fetotoxicity due to enoxaparin.  
**14. CLINICAL STUDIES**  
**14.1 Prophylaxis of Deep Vein Thrombosis following Abdominal Surgery in Patients at Risk for Thromboembolic Complications**  
Abdominal surgery patients at risk include those who are over 40 years of age, obese, undergoing surgery under general anesthesia lasting longer than 30 minutes or who have additional risk factors such as malignancy or a history of deep vein thrombosis (DVT) or pulmonary embolism (PE).

In a double-blind, parallel group study of patients undergoing elective cancer surgery of the gastrointestinal, urological, or gynecological tract, a total of 1116 patients were enrolled in the study, and 1115 patients were treated. Patients ranged in age from 32 to 97 years (mean age 67 years) with 52.7% men and 47.3% women. Patients were 98% Caucasian, 1% African Black, 0.4% Asian, and 0.4% others. Enoxaparin Sodium Injection 40 mg subcutaneously, administered once a day, beginning 2 hours prior to surgery and continuing for a maximum of 12 days after surgery, was comparable to heparin 5000 U every 8 hours subcutaneously in reducing the risk of DVT. The efficacy data are provided below (see Table 14).

**Table 14**  
**Efficacy of Enoxaparin Sodium Injection in the Prophylaxis of Deep Vein Thrombosis Following Abdominal Surgery**

Indication	Dosing Regimen	
	Enoxaparin Sodium Injection 40 mg daily subcutaneously n (%)	Heparin 5000 U q8h subcutaneously n (%)
All Treated Abdominal Surgery Patients	555 (100)	560 (100)
Treatment Failures	56 (10.1)	63 (11.3)
Total VTE (%)	95 (CI: 8 to 13)	95 (CI: 9 to 14)
DVT Only (%)	54 (9.7)	61 (10.9)
	95 (CI: 7 to 12)	95 (CI: 8 to 13)

\*VTE = Venous thromboembolic events which included DVT, PE, and death considered to be thromboembolic in origin.  
\*CI = Confidence Interval  
In a second double-blind, parallel group study, Enoxaparin Sodium Injection 40 mg subcutaneously once a day was compared to heparin 5000 U every 8 hours subcutaneously in patients undergoing colorectal surgery (one-third with cancer). A total of 1347 patients were randomized in the study and all patients were treated. Patients ranged in age from 18 to 92 years (mean age 50.1 years) with 54.2% men and 45.8% women. Treatment was initiated approximately 2 hours prior to surgery and continued for approximately 7 to 10 days after surgery. The efficacy data are provided below (see Table 15).

**Table 15**  
**Efficacy of Enoxaparin Sodium Injection in the Prophylaxis of Deep Vein Thrombosis Following Colorectal Surgery**

Indication	Dosing Regimen	
	Enoxaparin Sodium Injection 40 mg daily subcutaneously n (%)	Heparin 5000 U q8h subcutaneously n (%)
All Treated Colorectal Surgery Patients	673 (100)	674 (100)
Treatment Failures	48 (7.1)	45 (6.7)
Total VTE (%)	95 (CI: 5 to 9)	95 (CI: 5 to 9)
DVT Only (%)	47 (7.0)	44 (6.5)
	95 (CI: 5 to 9)	95 (CI: 5 to 8)

\*VTE = Venous thromboembolic events which included DVT, PE, and death considered to be thromboembolic in origin.  
\*CI = Confidence Interval  
**14.2 Prophylaxis of Deep Vein Thrombosis following Hip or Knee Replacement Surgery**  
Enoxaparin sodium injection has been shown to reduce the risk of postoperative deep vein thrombosis (DVT) following hip or knee replacement surgery.

In a double-blind study, Enoxaparin Sodium Injection 30 mg every 12 hours subcutaneously was compared to placebo in patients with hip replacement. A total of 100 patients were randomized in the study and all patients were treated. Patients ranged in age from 41 to 84 years (mean age 67.1 years) with 45% men and 55% women. After hemostasis was established, treatment was initiated 12 to 24 hours after surgery and was continued for 10 to 14 days after surgery. The efficacy data are provided below (see Table 16).

**Table 16**  
**Efficacy of Enoxaparin Sodium Injection in the Prophylaxis of Deep Vein Thrombosis Following Hip Replacement Surgery**

Indication	Dosing Regimen	
	Enoxaparin Sodium Injection 30 mg q12h subcutaneously n (%)	Placebo q12h subcutaneously n (%)
All Treated Hip Replacement Patients	50 (100)	50 (100)
Treatment Failures	5 (10 <sup>1</sup> )	23 (46)
Total DVT (%)	1 (2 <sup>1</sup> )	11 (22)

<sup>1</sup>p value versus placebo = 0.0002  
<sup>2</sup>p value versus placebo = 0.0134

A double-blind, multicenter study compared three dosing regimens of Enoxaparin Sodium Injection in patients with hip replacement. A total of 572 patients were randomized in the study and 560 patients were treated. Patients ranged in age from 31 to 88 years (mean age 64.7 years) with 63% men and 37% women. Patients were 93% Caucasian, 8% Black, < 1% Asian, and 1% others. Treatment was initiated within two days after surgery and was continued for 7 to 11 days after surgery. The efficacy data are provided below (see Table 17).

**Table 17**  
**Efficacy of Enoxaparin Sodium Injection in the Prophylaxis of Deep Vein Thrombosis Following Hip Replacement Surgery**

Indication	Dosing Regimen		
	10 mg daily subcutaneously n (%)	30 mg q12h subcutaneously n (%)	40 mg daily subcutaneously n (%)
All Treated Hip Replacement Patients	161 (100)	208 (100)	199 (100)
Treatment Failures	40 (25)	22 (11 <sup>1</sup> )	27 (14)
Total DVT (%)	17 (11)	8 (4 <sup>1</sup> )	9 (5)

<sup>1</sup>p value versus Enoxaparin Sodium Injection 10 mg once a day = 0.0008  
<sup>2</sup>p value versus Enoxaparin Sodium Injection 10 mg once a day = 0.0188  
There was no significant difference between the 30 mg every 12 hours and 40 mg once a day regimens. In a double-blind study, Enoxaparin Sodium Injection 30 mg every 12 hours subcutaneously was compared to placebo in patients undergoing knee replacement surgery. A total of 132 patients were randomized in the study and 131 patients were treated, of which 99 had total knee replacement and 32 had either unicompartmental knee replacement or tibial osteotomy. The 99 patients with total knee replacement ranged in age from 42 to 85 years (mean age 70.2 years) with 36.4% men and 63.6% women. After hemostasis was established, treatment was initiated 12 to 24 hours after surgery and was continued up to 15 days after surgery. The incidence of proximal and total DVT after surgery was significantly lower for Enoxaparin Sodium Injection compared to placebo. The efficacy data are provided below (see Table 18).

**Table 18**  
**Efficacy of Enoxaparin Sodium Injection in the Prophylaxis of Deep Vein Thrombosis Following Total Knee Replacement Surgery**

Indication	Dosing Regimen	
	Enoxaparin Sodium Injection 30 mg q12h subcutaneously n (%)	Placebo q12h subcutaneously n (%)
All Treated Total Knee Replacement Patients	47 (100)	52 (100)
Treatment Failures	5 (11 <sup>1</sup> )	32 (62)
Total DVT (%)	5 (11 <sup>1</sup> )	32 (62)
	95 (CI: 1 to 21)	95 (CI: 47 to 76)
Proximal DVT (%)	0 (0 <sup>1</sup> )	7 (13)
	95 (Upper CI: 5)	95 (CI: 3 to 24)

<sup>1</sup>p value versus placebo = 0.0001  
<sup>2</sup>p value versus placebo = 0.013  
<sup>3</sup>p value versus placebo = 0.013  
\*CI = Confidence Interval

Additionally, in an open-label, parallel group, randomized clinical study, Enoxaparin Sodium Injection 30 mg every 12 hours subcutaneously in patients undergoing elective knee replacement surgery was compared to heparin 5000 U every 8 hours subcutaneously. A total of 453 patients were randomized in the study and all were treated. Patients ranged in age from 35 to 90 years (mean age 68.5 years) with 43.7% men and 56.3% women. Patients were 92.5% Caucasian, 5.3% Black, and 0.6% others. Treatment was initiated after surgery and continued up to 14 days. The incidence of deep vein thrombosis was lower for Enoxaparin Sodium Injection compared to heparin. At the end of the peri-operative period, all patients underwent bilateral venography. In a double-blind design, those patients with no venous thromboembolic disease were randomized to a post-discharge regimen of either Enoxaparin Sodium Injection 40 mg (n=80) once a day subcutaneously or placebo (n=89) for 3 weeks. A total of 179 patients were randomized in the double-blind phase of the study and all patients were treated. Patients ranged in age from 47 to 87 years (mean age 69.4 years) with 57.5% men and 42.5% women. In this population of patients, the incidence of DVT during extended prophylaxis was significantly lower for Enoxaparin Sodium Injection compared to placebo. The efficacy data are provided below (see Table 19).

**Table 19**  
**Efficacy of Enoxaparin Sodium Injection in the Extended Prophylaxis of Deep Vein Thrombosis Following Hip Replacement Surgery**

Indication (Post Discharge)	Post-discharge Dosing Regimen	
	Enoxaparin Sodium Injection 40 mg daily subcutaneously n (%)	Placebo daily subcutaneously n (%)
All Treated Extended Prophylaxis Patients	90 (100)	89 (100)
Treatment Failures	6 (7 <sup>1</sup> )	18 (20)
Total DVT (%)	95 (CI: 3 to 14)	95 (CI: 12 to 30)
Proximal DVT (%)	5 (6 <sup>1</sup> )	7 (8)
	95 (CI: 2 to 13)	95 (CI: 3 to 16)

<sup>1</sup>p value versus placebo = 0.008  
<sup>2</sup>p value versus placebo = 0.013  
<sup>3</sup>p value versus placebo = 0.537

In a second study, patients undergoing hip replacement surgery were treated, while hospitalized, with Enoxaparin Sodium Injection 40 mg subcutaneously, initiated up to 12 hours prior to surgery. All patients were examined for clinical signs and symptoms of venous thrombosis (VTE) disease. In a double-blind design, patients without clinical signs and symptoms of VTE disease were randomized to a post-discharge regimen of either Enoxaparin Sodium Injection 40 mg (n = 131) once a day subcutaneously or to placebo (n = 131) for 3 weeks. A total of 262 patients were randomized in the study double-blind phase and all patients were treated. Patients ranged in age from 44 to 87 years (mean age 68.5 years) with 43.1% men and 56.9% women. Similar to the first study the incidence of DVT during extended prophylaxis was significantly lower for Enoxaparin Sodium Injection compared to placebo, with a statistically significant difference in both total DVT (Enoxaparin Sodium Injection 21 (16%) versus placebo 45 (34%; p = 0.001) and proximal DVT (Enoxaparin Sodium Injection 8 (6%) versus placebo 28 (21%; p = <0.001).

**14.3 Prophylaxis of Deep Vein Thrombosis in Medical Patients with Severely Restricted Mobility during Acute Illness**  
In a double-blind multicenter, parallel group study, Enoxaparin Sodium Injection 20 mg or 40 mg once a day subcutaneously was compared to placebo in the prophylaxis of deep vein thrombosis (DVT) in medical patients with severely restricted mobility during acute illness (defined as walking distance of <10 meters for 43 days). This study included patients with heart failure (NYHA Class III or IV), acute respiratory failure or complicated chronic respiratory insufficiency (not requiring ventilator support), acute infection (excluding septic shock), or acute rheumatic disorder (acute lumbor or sciatic pain, vertebral compression [due to osteoporosis or tumor], acute arthritic episodes of the lower extremities). A total of 1102 patients were enrolled in the study, and 1073 patients were treated. Patients ranged in age from 40 to 97 years (mean age 73 years) with equal proportions of men and women. Treatment continued for a maximum of 14 days (median duration 7 days). When given at a dose of 40 mg once a day subcutaneously, Enoxaparin Sodium Injection significantly reduced the incidence of DVT as compared to placebo. The efficacy data are provided below (see Table 20).

**Table 20**  
**Efficacy of Enoxaparin Sodium Injection in the Prophylaxis of Deep Vein Thrombosis in Medical Patients with Severely Restricted Mobility During Acute Illness**

Indication	Dosing Regimen		
	Enoxaparin Sodium Injection 20 mg daily subcutaneously n (%)	Enoxaparin Sodium Injection 40 mg daily subcutaneously n (%)	Placebo n (%)
All Treated Medical Patients During Acute Illness	351 (100)	360 (100)	362 (100)
Treatment Failure <sup>1</sup>	43 (12.3)	16 (4.4)	43 (11.9)
Total VTE (%)	43 (12.3)	16 (4.4)	43 (11.9)
	95 (CI: 8 to 15.7)	95 (CI: 2.3 to 6.6)	95 (CI: 8 to 14.6)
Proximal DVT (%)	13 (3.7)	5 (1.4)	14 (3.9)

<sup>1</sup>Treatment failures during therapy, between Days 1 and 14.  
<sup>2</sup>VTE = Venous thromboembolic events which included DVT, PE, and death considered to be thromboembolic in origin.  
<sup>3</sup>CI = Confidence Interval

At approximately 3 months following enrollment, the incidence of venous thromboembolism remained lower in the Enoxaparin Sodium Injection 40 mg treatment group versus the placebo treatment group.

**14.4 Treatment of Deep Vein Thrombosis with or without Pulmonary Embolism**  
In a multicenter, parallel group study, 900 patients with acute lower extremity deep vein thrombosis (DVT) with or without pulmonary embolism (PE) were randomized to an inpatient (hospital) treatment of either (i) Enoxaparin Sodium Injection 1.5 mg/kg once a day subcutaneously, (ii) Enoxaparin Sodium Injection 1 mg/kg every 12 hours subcutaneously, or (iii) heparin intravenous bolus (5000 IU) followed by a continuous infusion (administered to achieve an aPTT of 55 to 85 seconds). A total of 900 patients were randomized in the study and all patients were treated. Patients ranged in age from 18 to 92 years (mean age 60.7 years) with 54.7% men and 45.3% women. All patients also received warfarin sodium dose adjusted according to PT to achieve an International Normalization Ratio [INR] of 2.0 to 3.0, commencing within 72 hours of initiation of Enoxaparin Sodium Injection or standard heparin therapy, and continuing for 90 days. Enoxaparin sodium injection or standard heparin therapy was administered for a minimum of 5 days and until the targeted warfarin sodium INR was achieved. Both Enoxaparin Sodium Injection regimens were equivalent to standard heparin therapy in reducing the risk of recurrent venous thromboembolism (DVT and/or PE). The efficacy data are provided below (see Table 21).

**Table 21**  
**Efficacy of Enoxaparin Sodium Injection in Treatment of Deep Vein Thrombosis with or without Pulmonary Embolism**

Indication	Dosing Regimen <sup>1</sup>		
	Enoxaparin Sodium Injection 1.5 mg/kg daily subcutaneously n (%)	Enoxaparin Sodium Injection 1 mg/kg q12h subcutaneously n (%)	Placebo aPTT Adjusted Intravenous Therapy n (%)
All Treated DVT Patients with or without PE	298 (100)	312 (100)	290 (100)
Treatment Failures	13 (4.4)	9 (2.9 <sup>2</sup> )	12 (4.1)
Total VTE (%)	11 (3.7)	7 (2.2)	8 (2.8)
Proximal DVT (%)	9 (3.0)	6 (1.9)	7 (2.4)
PE (%)	2 (0.7)	2 (0.6)	4 (1.4)

<sup>1</sup>All patients were also treated with warfarin sodium commencing within 72 hours of Enoxaparin Sodium Injection or standard heparin therapy.  
<sup>2</sup>VTE = venous thromboembolic event (DVT and/or PE).  
<sup>3</sup>The 95% Confidence Interval for the treatment differences for total VTE were: Enoxaparin Sodium Injection once a day versus heparin (3.0 to 3.5); Enoxaparin Sodium Injection every 12 hours versus heparin (4.2 to 1.7).

Similarly, in a multicenter, open-label, parallel group study, patients with acute proximal DVT were randomized to Enoxaparin Sodium Injection or heparin. Patients who could not receive outpatient therapy were excluded from entering the study. Outpatient inclusion criteria included the following: inability to receive outpatient heparin therapy because of associated comorbid conditions or potential for non-compliance and inability to attend follow-up visits as an outpatient because of geographic inaccessibility. Eligible patients could be treated in hospital, but ONLY Enoxaparin Sodium Injection patients were permitted to go home on therapy (72%). A total of 501 patients were randomized in the study and all patients were treated. Patients ranged in age from 19 to 96 years (mean age 57.8 years) with 60.5% men and 39.5% women. Patients were randomized to either Enoxaparin Sodium Injection 1 mg/kg every 12 hours subcutaneously or heparin intravenous bolus (5000 IU) followed by a continuous infusion administered to achieve an aPTT of 60 to 85 seconds (in-patient treatment). All patients also received warfarin sodium as described in the previous study. Enoxaparin Sodium Injection or standard heparin therapy was administered for a minimum of 5 days. Enoxaparin Sodium Injection was equivalent to standard heparin therapy in reducing the risk of recurrent venous thromboembolism. The efficacy data are provided below (see Table 22).

**Table 22**  
**Efficacy of Enoxaparin Sodium Injection in Treatment of Deep Vein Thrombosis**

Indication	Dosing Regimen <sup>1</sup>	
	Enoxaparin Sodium Injection 1 mg/kg q12h subcutaneously n (%)	Heparin aPTT Adjusted Intravenous Therapy n (%)
All Treated DVT Patients	247 (100)	254 (100)
Patient Outcome		
Total VTE (%)	13 (5.3 <sup>2</sup> )	17 (6.7)
DVT Only (%)	11 (4.5)	14 (5.5)
Proximal DVT (%)	10 (4.0)	12 (4.7)
PE (%)	2 (0.8)	3 (1.2)

<sup>1</sup>All patients were also treated with warfarin sodium commencing on the evening of the second day of Enoxaparin Sodium Injection or standard heparin therapy.  
<sup>2</sup>VTE = venous thromboembolic event (deep vein thrombosis [DVT] and/or pulmonary embolism [PE]).  
<sup>3</sup>The 95% Confidence Interval for the treatment difference for total VTE was: Enoxaparin Sodium Injection versus heparin (5.6 to 9.7).

**14.5 Prophylaxis of Ischemic Complications in Unstable Angina and Non-Q-Wave Myocardial Infarction**  
In a multicenter, double-blind, parallel group study, patients who recently experienced unstable angina or non-Q-wave myocardial infarction were randomized to either Enoxaparin Sodium Injection 1 mg/kg every 12 hours subcutaneously or heparin intravenous bolus (5000 IU) followed by a continuous infusion (adjusted to achieve an aPTT of 55 to 85 seconds). A total of 3171 patients were enrolled in the study, and 3107 patients were treated. Patients ranged in age from 25 to 94 years (mean age 64 years), with 33.4% of patients female and 66.6% male. Race was distributed as follows: 89.8% Caucasian, 4.8% Black, 2.0% Asian, and 3.5% other. All patients were also treated with aspirin 100 to 325 mg per day. Treatment was initiated within 24 hours of the event and continued until clinical stabilization, revascularization procedures, or hospital discharge, with a maximal duration of 8 days of therapy. The combined incidence of the triple endpoint of death, myocardial infarction, or recurrent angina was lower for Enoxaparin Sodium Injection compared with heparin therapy at 14 days after initiation of treatment. The lower incidence of the triple endpoint was sustained up to 30 days after initiation of treatment. These results were observed in an analysis of both all-randomized and all-treated patients. The efficacy data are provided below (see Table 23).

**Table 23**  
**Efficacy of Enoxaparin Sodium Injection in the Prophylaxis of Ischemic Complications in Unstable Angina and Non-Q-Wave Myocardial Infarction (combined endpoint of death, myocardial infarction, or recurrent angina)**

Indication	Dosing Regimen <sup>1</sup>		
	Enox		