1. NAME OF THE MEDICINAL PRODUCT

Lomoh-20

Lomoh-40

Lomoh-60

Lomoh-80

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Lomoh-20

Composition per syringe;

Enoxaparin Sodium Ph.Eur. 20 mg

Water for Injection USP q.s. to 0.2 ml

Lomoh-40

Composition per syringe;

Enoxaparin Sodium Ph.Eur. 40 mg

Water for Injection USP q.s. to 0.4 ml

Lomoh-60

Composition per syringe;

Enoxaparin Sodium Ph.Eur. 60 mg

Water for Injection USP q.s. to 0.6 ml

Lomoh-80

Composition per syringe;

Enoxaparin Sodium Ph.Eur. 80 mg

Water for Injection USP q.s. to 0.8 ml

3. PHARMACEUTICAL FORM

Injectable for subcutaneous or Intravascular use

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Lomoh 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 medical patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness.

Lomoh Injection is indicated for the prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin.

Lomoh 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;
- prevention of thrombus formation in extra-corporeal circulation during hemodialysis.

4.2 Posology and method of administration

All patients should be evaluated for a bleeding disorder before administration of Lomoh Injection, unless the medication is needed urgently. Since coagulation parameters are unsuitable for monitoring Lomoh Injection activity, routine monitoring of coagulation parameters is not required.

Adult Dosage:
Abdominal surgery: In patients undergoing abdominal surgery who are at risk for thromboembolic complications, the recommended dose of Lomoh Injection is 40 mg once a day administered by SC injection with the initial dose given 2 hours prior to surgery. The usual duration of administration is 7 to 10 days; administration up to 12 days has been well tolerated.

Hip or knee replacement surgery: In patients undergoing hip or knee replacement surgery, the recommended dose of Lomoh Injection is 30 mg every 12 hours administered by SC injection. Provided that hemostasis has been established, the initial dose should be given 12 to 24 hours after surgery. For hip replacement surgery, a dose of 40 mg once a day SC, given initially 12 (±3) hours prior to surgery, may be considered. Following the initial phase of thromboprophylaxis in hip replacement surgery patients, continued prophylaxis with Lomoh Injection 40 mg once a day administered by SC injection for 3 weeks is recommended. The usual duration of administration is 7 to 10 days; administration up to 14 days has been well tolerated.

Medical patients during acute illness: In medical patients at risk for thromboembolic complications due to severely restricted mobility during acute illness, the recommended dose of Lomoh Injection is 40 mg once a day administered by SC injection. The usual duration of administration is 6 to 11 days; administration up to 14 days has been well tolerated.

Unstable angina and non-Q-wave myocardial infarction: In patients with unstable angina or non-Q-wave myocardial infarction, the recommended dose of Lomoh Injection is 1 mg/kg administered SC every 12 hours in conjunction with oral aspirin therapy (100 to 325 mg once daily). Treatment with Lomoh Injection should

be prescribed for a minimum of 2 days and continued until clinical stabilization. The usual duration of treatment is 2 to 8 days; administration up to 12.5 days has been well tolerated.

Treatment of deep vein thrombosis with or without pulmonary embolism: In outpatient treatment, patients with acute deep vein thrombosis without pulmonary embolism who can be treated at home, the recommended dose of Lomoh Injection is 1 mg/kg every 12 hours administered SC. In inpatient (hospital) treatment, patients with acute deep vein thrombosis with pulmonary embolism or patients with acute deep vein thrombosis without pulmonary embolism (who are not candidates for outpatient treatment), the recommended dose of Lomoh Injection is 1 mg/kg every 12 hours administered SC or 1.5 mg/kg once a day administered SC at the same time every day. In both outpatient and inpatient (hospital) treatments, warfarin sodium therapy should be initiated when appropriate (usually within 72 hours of Lomoh Injection). Lomoh Injection should be continued for a minimum of 5 days and until a therapeutic oral anticoagulant effect has been achieved (International Normalization Ratio 2.0 to 3.0). The average duration of administration is 7 days; administration up to 17 days has been well tolerated.

Prevention of thrombus formation in extra-corporeal circulation during hemodialysis: The recommended dose of Enoxaparin sodium is 1 mg/kg. For patients with a high risk of hemorrhage the dose should be reduced to 0.5 mg/kg for double vascular access or 0.75 mg/kg for single vascular access. During hemodialysis, Enoxaparin sodium should be introduced into the arterial line of the circuit at the beginning of the dialysis session. The effect of this dose is usually sufficient for a 4-hour session. However, if fibrin rings are found, a further dose of 0.5 to 1 mg/kg may be given.

Renal Impairment: Although no dose adjustment is recommended in patients with moderate (creatinine clearance 30-50 mL/min) and mild (creatinine clearance 50-80 mL/min) renal impairment, all such patients should be observed carefully for signs and symptoms of bleeding. A dosage adjustment is required for patients with severe renal impairment (creatinine clearance <30 mL/min), since enoxaparin sodium exposure is increased significantly in this patient population. The following dosage

adjustments are recommended: prophylactic dose ranges: 20 mg once daily; therapeutic dose ranges: 1 mg/kg once daily.

Hepatic impairment: Caution should be used in hapatically impaired patients.

Elderly patients: No dosage adjustment is necessary unless kidney function is impaired.

Children: Enoxaparin sodium is not recommended in children.

Lomoh Injection is a clear, colorless to pale yellow sterile solution, and as with other parenteral drug products, should be inspected visually for particulate matter and discoloration prior to administration. Lomoh Injection is administered by SC injection in prophylactic and curative treatment and by intravascular route during hemodialysis. It must not be administered by intramuscular injection. Lomoh Injection is intended for use under the guidance of a physician. Patients may self-inject only if their physician determines that it is appropriate and with medical follow-up, as necessary. Proper training in subcutaneous injection technique should be provided.

Subcutaneous injection technique: Patients should be lying down and Lomoh Injection administered by deep SC injection. To avoid the loss of drug, do not expel the air bubble from the syringe before the injection. Administration should be alternated between the left and right anterolateral and left and right posterolateral abdominal wall. The whole length of the needle should be introduced into a skin fold held between the thumb and forefinger; the skin fold should be held throughout the injection. To minimize bruising, do not rub the injection site after completion of the injection.

4.3 Contraindications

Lomoh 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. Patients with known hypersensitivity to heparin or pork products should not be treated with Lomoh Injection.

4.4 Special warnings and precautions for use

Warnings:

Lomoh Injection is not intended for intramuscular administration. Lomoh 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. Lomoh Injection should be used with extreme caution in patients with a history of heparin-induced thrombocytopenia.

Hemorrhage: Enoxaparin 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 shortly after brain, spinal, 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 Enoxaparin 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 Enoxaparin Injection. An unexplained fall in hematocrit or blood pressure should lead to a search for a bleeding site.

Thrombocytopenia: Thrombocytopenia can occur with the administration of Enoxaparin Injection. Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/mm3, Lomoh 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.

Percutaneous coronary revascularization procedures: To minimize the risk of bleeding following vascular instrumentation during the treatment of unstable angina, the vascular access sheath for instrumentation should remain in place for 6

to 8 hours following a dose of Lomoh Injection. The next scheduled dose should be given no sooner than 6 to 8 hours after sheath removal.

Pregnant Women with Mechanical Prosthetic Heart Valves: The use of Enoxaparin Injection for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves has not been adequately studied. There also have been isolated postmarketing reports of valve thrombosis in pregnant women with mechanical prosthetic heart valves while receiving Enoxaparin for thromboprophylaxis. Although a causal relationship has not been established these deaths may have been due to therapeutic failure or inadequate anticoagulation. 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.

Precautions:

General: Lomoh Injection should not be mixed with other injections or infusions. Lomoh 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. Lomoh Injection should be used with care in elderly patients who may show delayed elimination of Enoxaparin. If thromboembolic events occur despite Lomoh Injection prophylaxis, appropriate therapy should be initiated.

Mechanical Prosthetic Heart Valves: The use of Enoxaparin 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 (see dosage and administration). 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 Enoxaparin 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 Enoxaparin Injection activity and, therefore, unsuitable for monitoring. Anti-Factor Xa may be used to monitor the anticoagulant effect of Lomoh Injection in patients with significant renal impairment. If during Lomoh Injection therapy abnormal coagulation parameters or bleeding should occur, anti-Factor Xa levels may be used to monitor the anticoagulant effects of Lomoh Injection. If a significant decrease of platelet count (30 to 50 %) is observed, the treatment must be discontinued and patient switched to another therapy.

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

Geriatric: The efficacy of Enoxaparin Injection in the elderly (>65 years) is similar to that seen in younger patients (<65 years). The risk of Enoxaparin Injection-associated bleeding increases with age. Serious adverse events increase with age for patients receiving Enoxaparin Injection. There are no additional differences in the safety of Enoxaparin 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.

4.5 Interaction with other medicinal products and other forms of interaction

Unless really needed, agents which may enhance the risk of hemorrhage should be discontinued prior to initiation of Lomoh Injection therapy. These agents include medications such as: anticoagulants, platelet inhibitors including acetylsalicylic acid (and derivatives), NSAIDs (including ketorolac, tromethamine, ticlopidine, clopidogrel), dipyridamole, or sulfinpyrazone, dextran 40, glucocorticoids, other antiplatelet agents including glycoprotein IIb/IIIa antagonists. If co-administration is essential, conduct close clinical and laboratory monitoring.

4.6 Pregnancy and lactation

Pregnancy: Category B. There are no adequate and well-controlled studies in pregnant women. Teratology studies of Enoxaparin in pregnant rats and rabbits showed no evidence of teratogenic effects or fetotoxicity due to Enoxaparin. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

All pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure. 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. 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.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Lomoh Injection is administered to nursing women.

4.7 Effects on ability to drive and use machines

Enoxaparin has no effect on the ability to drive and operate machines

4.8 Undesirable effects

Hematomas (epidural hematoma, spinal hematoms, angiography-related hematoma, abdominal wall hematomas, psoas hematoma) have been reported following subcutaneous injection of Enoxaparin. Intrahepatic hemorrhage, lumbar plexopathy have occurred in patients treated with Enoxaparin.

When spinal or epidural anesthesia is used in conjunction with low molecular weight heparin or heparinoids, there is a risk of neuraxial hematomas that can result in long-term or permanent paralysis. This risk is increased by the use of indwelling catheters for analgesia, traumatic or repeated epidural/spinal puncture, and the use of drugs that affect hemostasis (non-steroidal anti-inflammatory agents, platelet inhibitors, or other anticoagulants) There have been many reports of epidural or spinal hematoma formation in patients with concurrent Enoxaparin therapy and spinal/epidural anesthesia or spinal puncture. This risk is increased by the use of concomitant drugs which affect hemostasis.

Thrombocytosis is a rare side effect of Enoxaparin therapy. In case reports, platelet counts have increased up to 1200 cells per cubic millimeter after several weeks of treatment. Platelet counts have returned to normal following discontinuation of the drug

Asymptomatic increases in liver function tests (AST and ALT) greater than three times the upper limit of normal have been reported in patients treated with

Enoxaparin These increases are reversible and rarely associated with increases in bilirubin.

Hypersensitivity reactions, persistent erythema, erythematous macules, erythema with peeling have occurred after subcutaneous Enoxaparin and certoparin, as well as unfractionated heparin.

Permanent paralysis is a potential complication due to when bleeding within the spinal column occurs from the use of low molecular weight heparins and heparinoid. Bleeding or hematomas within the spinal column may result when the heparin product is used concurrently with spinal or epidural anesthesia, or spinal puncture. Increased risk occurs with 1) catheters placed in the spinal canal to administer pain medication, 2) by the use of other drugs affecting blood clotting mechanism, such as non steroidal anti-inflammatory drugs, platelet inhibitors, or other anticoagulants, or by 3) traumatic or repeated epidural or spinal puncture. Clinicians should consider fully the potential benefit versus risk before neuraxial intervention in patients anticoagulated or in those patients scheduled for anticoagulation for thromboprophylaxis.

Pain, local irritation, local reactions at the injection site (i.e., skin necrosis, nodules, inflammation, oozing), systemic allergic reactions (i.e., pruritus, urticaria, anaphylactoid reactions), vesiculobullous rash, rare cases of hypersensitivity, cutaneous vasculitis, purpura may occur following subcutaneous injection of Enoxaparin. Thrombocytosis, thrombocytopenia with thrombosis, anemia, blood coagulation disorder (bleeding, drop in hematocrit), hyperkalemia, very rare cases of hyperlipidemia, spontaneous splenic rupture resulting in shock have been reported with use of Enoxaparin injection.

4.9 Overdose

Accidental overdosage following administration of Enoxaparin Injection may lead to hemorrhagic complications. Injected Lomoh Injection may be largely neutralized by the slow i.v. injection of protamine sulfate (1% solution). The dose of protamine sulfate should be equal to the dose of Lomoh Injection injected: 1 mg protamine sulfate should be administered to neutralize 1 mg Lomoh Injection, if Enoxaparin sodium was administered in the previous 8 hours. An infusion of 0.5 mg protamine

per 1 mg of Enoxaparin sodium may be administered if Enoxaparin sodium was administered greater than 8 hours previous to the protamine administration, or if it has been determined that a second dose of protamine is required. The second infusion of 0.5 mg protamine sulfate per 1 mg of Lomoh Injection may be administered if the aPTT measured 2 to 4 hours after the first infusion remains prolonged. After 12 hours of the Enoxaparin sodium injection, protamine administration may not be required. However, even with higher doses of protamine, the aPTT may remain more prolonged than under normal conditions found following administration of heparin. In all cases, the anti-Factor Xa activity is never completely neutralized (maximum about 60%). Particular care should be taken to avoid overdosage with protamine sulfate. Administration of protamine sulfate can cause severe hypotensive and anaphylactoid reactions. Because fatal reactions, often resembling anaphylaxis, have been reported with protamine sulfate, it should be given only when resuscitation techniques and treatment of anaphylactic shock are readily available. A single SC dose of 46.4 mg/kg Enoxaparin was lethal to rats. The symptoms of acute toxicity were ataxia, decreased motility, dyspnea, cyanosis, and coma.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Enoxaparin is a low molecular weight heparin which has antithrombotic properties. Low molecular weight heparins are fragments or fractions of conventional (unfractionated) heparin that produce anticoagulation when administered subcutaneously. In humans, Enoxaparin given subcutaneously (SC) is characterized by a higher ratio of anti-Factor Xa to anti-Factor IIa activity compared to the ratios observed for heparin. Increases of up to 1.8 times the control values are seen in the thrombin time (TT) and the activated partial thromboplastin time (aPTT).

5.2 Pharmacokinetic properties

Enoxaparin pharmacokinetics appear to be linear over the recommended dosage ranges. Bioavailability of Enoxaparin is 100% and time to peak concentration is 3 to 5 hours after subcutaneous injection. The volume of distribuiton of anti-Factor Xa activity in normal volunteers is about 4.3 liters. Animal studies suggest preferential

accumulation of Enoxaparin in the kidney, liver, and spleen. The primary route of elimination of Enoxaparin is thought to be renal, largely through glomerular filtration. Anti-Factor Xa exposure, at steady-state is marginally increased in mild (CrCl 50 to 80 mL/min) and moderate (CrCl 30 to 50 mL/min) renal dysfunction after repeated subcutaneous dosages. In patients with severe renal impairment (CrCl less than 30 mL/min) the exposure, at steady-state is increased by an average of 65% after multiple doses given once daily subcutaneously. Enoxaparin sodium is primarily metabolized in the liver by desulfation and/or depolymerization to lower molecular weight species with much reduced biological potency. Elimination half-life of Enoxaparin is 4.5 hours after single subcutaneous dose (range 3 to 6 hours) and 7 hours after repeated dosing.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to the information included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

1. Sodium Hydroxide
2. Water for Injection
3. Nitrogen Gas

6.2 Incompatibilities

None of the In-active ingredients of the formulation have been known to exhibit incompatibility with the Active Ingredients.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25^{o}C. Do not freeze.

6.5 Nature and contents of container

Enoxaparin Sodium injection (20 mg/0.2 ml, 40 mg/0.4 ml, 60 mg/0.6 ml and 80 mg/0.8 ml) is filled in 1 ml pre graduated glass syringe.

1 ml pre filled graduated glass syringe is inserted in an overprinted blister. One such blister is packed in an overprinted carton bearing all batch details along with a pack insert.

6.6 Instructions for use, handling and disposal

Store below 25°C. Do not freeze.

Immediately dispose of the syringe in the nearest sharp container.

7. MARKETING AUTHORISATION HOLDER

Emcure Pharmaceuticals Ltd.

T-184, MIDC Bhosari, Pune-411026, Maharashtra, India.

8. MARKETING AUTHORISATION NUMBER(S)

Shall be provided when available.

9.DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not Applicable.

10. DATE OF REVISION OF THE TEXT

Not Applicable.

11. LEGAL CATEGORY

For Prescription use only