SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

1.1 Product Name: Enoxaparin Sodium Injection USP

1.2 Strength: 20 mg/0.2 mL, 40 mg/0.4 mL, 60 mg/0.6 mL & 80 mg/0.8 mL of Enoxaparin Sodium USP

1.3 Pharmaceutical Dosage Form: Sterile solution for Injection.

2. Qualitative and quantitative composition

2.1 Qualitative Declaration

In terms of the active substance(s)

Sterile solution for injection – 0.5 mL and 1.0 mL PFS

Each PFS contains 20 mg/0.2 mL, 40 mg/0.4 mL, 60 mg/0.6 mL & 80 mg/0.8 mL of Enoxaparin Sodium USP.

INN : Enoxaparin Sodium USP

Chemical Name : Since Enoxaparin Sodium is a heterogeneous mixture, a separate Chemical name may not be given.

Quantitative Declaration (Qualitative and Quantitative formula for unit)

S. No.	Ingredients	Grade	Qty / Unit				Function
			20 mg/ 0.2 mL	40 mg/ 0.4 mL	60 mg/ 0.6 mL	80 mg/ 0.8 mL	
1.	Enoxaparin Sodium	USP	20 mg	40 mg	60 mg	80 mg	Active Ingredient
2.	Water for Injection	USP	q.s. to 0.2 mL	q.s. to 0.4 mL	q.s. to 0.6 mL	q.s. to 0.8 mL	Solvent

3. Pharmaceutical Form

Sterile solution for Injection

4. Clinical Particulars

4.1 Indications

- Prophylaxis of venous thromboembolic disease (prevention of blood clot formation in the veins), in particular after certain procedures.
- Prevention of thrombus formation in the extra-corporal circulation during hemodialysis.

- Treatment of established deep vein thrombosis.
- Treatment of unstable angina and non-Q-wave myocardial infarction during the acute stage, in combination with aspirin.

4.2 Posology and method of administration

Method of administration:

1 mg (0.01 mL) of Enoxaparin corresponds approximately to 100 anti-Xa I.U**.** Enoxaparin should be injected by deep subcutaneous route in prophylactic and curative treatment and by intravascular route during haemodialysis.

Do not inject intramuscularly.

Subcutaneous administration technique:

The prefilled syringes are ready-to-use. **The air bubble from the syringe should not be expelled before the injection.** The subcutaneous injection should preferably be made when the patient is lying down. Enoxaparin is administered in the subcutaneous cellular tissue of the anterolateral or posterolateral abdominal wall, alternately on the left and the right side.

The injection itself consists in introducing the needle perpendicularly and not tangentially, throughout its entire length into a fold of skin held between the thumb and index finger. The skin fold should be held throughout the injection.

Prophylaxis of venous thrombosis:

In the case of a surgery with a moderate thrombogenic risk and when patients do not present high thrombo-embolism risk, the recommended dosage is 20 mg (0.2mL) once daily by a single subcutaneous injection. In the case of a surgery with a high thrombogenic risk (hip and knee surgery) and/or in patients with a high risk of thrombo-embolism, the dosage should be 40 mg(0.4 ml)-once daily by a single subcutaneous injection. In general surgery, the first injection should be given 2 hours before the surgical procedure. In orthopaedic surgery, the first injection is to be given 12 hours preoperatively. A higher prophylactic dosage may be envisaged when the risk of thrombo-embolism linked to the type of surgery and/or to the patient's history is increased.

Enoxaparin treatment is usually prescribed for an average period of 7 to 10 days.

Longer treatment duration may be appropriate in certain cases and the treatment should be continued for as long as there is a risk of venous thrombo-embolism and until the patient is ambulatory.

Prevention of extra corporal thrombus during Hemodialysis:

The recommended dose is 1mg/kg. Enoxaparin should be introduced in 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; in the event fibrin rings are found, a further dose of 0.5 to 1 mg/kg may be given.

Treatment of established deep vein thrombosis:

A dose of 1 mg/kg should be given subcutaneously every 12 hours. The duration of the treatment should not exceed a period of 10 days.

Treatment of unstable angina and non-Q-wave myocardial infarction:

A dose of 1 mg/kg should be given subcutaneously every 12 hours. The recommended treatment should be prescribed for a period of 2 to 8 days, until clinical stabilization of the patient. Enoxaparin should be administered concurrently with aspirin (100 to 325 mg daily per oral route).

- **Elderly:** No dosage adjustment is necessary in preventative therapy. In curative therapy measurement of anti-Xa activity is recommended.
- **Children:** Enoxaparin is not recommended for children.
- **Renal impairment:** No dosage adjustment is necessary at prophylactic do whereas dosage adjustment is necessary and the monitoring of anti-Xa activity is recommended at curative doses.
- **Patients under 40 kg and over 100 kg weight:** Particular clinical surveillance is necessary in order to adjust dosage if necessary. In all cases, strictly follow the physician's prescription.

4.3 Contra-indications

Enoxaparin sodium Injection should not be used in the following situations:

- Hypersensitivity (allergy) to Enoxaparin, heparin or other low molecular weight heparins.
- Major clotting disorders.

- History of thrombocytopenia (in the past, marked fall in platelet count) with Enoxaparin or with another Heparin.
- Active gastro-intestinal ulcer or organic lesion likely to bleed.
- Acute infectious endocarditis (inflammation of the inner lining of the heart), except when affecting a mechanical valve replacement.

4.4 Special warnings and precautions for use

WARNINGS:

Do not inject intramuscularly.

Keep out of reach of children.

Low molecular weight heparins should not be used interchangeably since they differ in their molecular weights, specific anti- Xa activities and dosage. Very careful attention and compliance with the specific mode of use of each product are absolutely essential. Enoxaparin is to be used with extreme caution in patients with history of heparin induced thrombocytopenia.

Spinal/Epidural anesthesia:

As with other anticoagulants, there have been cases of neuraxial hematomas reported with the concurrent use of enoxaparin sodium and spinal/epidural anesthesia. These may result in long-term or permanent paralysis. The risk of these events is higher with the use of post-operative indwelling epidural catheters or with concomitant use of drugs affecting hemostasis such as NSAIDs, platelet inhibitors or other anticoagulants. The risk also appears to be increased by traumatic or repeated neuraxial punctures.

When scheduling or using epidural or spinal anesthesia/analgesia with enoxaparin, placement and removal of the catheter is best performed prior to enoxaparin administration. Otherwise it should occur when anticoagulant activity of enoxaparin is low. If an indwelling catheter remains in place for greater than 24 hours after surgery, the timing of catheter removal is extremely important; it should be removed 24 hours after the most recent dose of enoxaparin sodium. The subsequent enoxaparin sodium dose should be given no sooner than 2 hours after catheter removal. Extreme vigilance and frequent monitoring of the patient’s neurological status is required. If signs of neuraxial hematoma are suspected urgent diagnosis and treatment including spinal cord decompression are necessary.

This drug should only be taken under medical supervision.

Never suddenly discontinue treatment with out consulting your physician.

PRECAUTIONS FOR USE:

Enoxaparin injection procedure should be seriously observed. Monitoring of platelet count level is necessary regardless of the therapeutic indication and the dosage administered. It is recommended that the platelet count be measured before the initiation of the treatment and regularly thereafter during treatment. If a significant decrease of the platelet count (30 to 50% of the initial count) is observed, the treatment should be discontinued. Enoxaparin should be used with caution in case of renal or hepatic insufficiency, history of peptic ulcer or any organic lesion likely to bleed, hemorrhagic vascular cerebral stroke, uncontrolled severe arterial hypertension, diabetic retinopathy; shortly after neuro or ophthalmologic surgery and in case of spinal/epidural anesthesia.

In case of doubt you must consult your physician or pharmacist for advice.

4.5 Interaction with other medicaments and other forms of interaction

In order to avoid possible interactions with other drugs you must inform your Physician or Pharmacist about any other current treatment.

Not recommended combinations: (substances increasing the risk of hemorrhage): acetylsalicylic acid (and derivatives) at analgesic and antipyretic doses. Non steroidal anti-inflammatory drugs (general route), Ticlopidine, Dextran 40 (Parenteral use).

Combinations to be used with caution: oral anticoagulant, thrombolytic drugs, acetylsalicylic acid at anticoagulant platelet doses (in the treatment of unstable angina and non-Q wave myocardial infarction), glucocorticoids (general route).

4.6 Pregnancy and lactation

In case of pregnancy or lactation you always have to ask your physician or pharmacist for advice before the beginning of the treatment. As a precautionary measure, enoxaparin should not be use during pregnancy whereas lactation is not contraindicated.

4.7 Effects on ability to drive and use machines

Enoxaparin Sodium has no effect on the ability to drive machines.

4.8 Undesirable effects

Like any active product, this drug may induce undesirable effects to a greater or lesser degree.

- Hemorrhage (bleeding): this may occur during treatment with ant anticoagulant: your physician should be informed immediately.
- Bluish marks at injection sites.
- Localized or general allergic reactions.
- Thrombocytopenia (abnormally low platelet count level): your physician should be informed immediately.
- Rare incidences of severe skin rash at injection sites: consult your physician.
- Risk of osteoporosis (bone demineralization leading to bone fragility.
- Increased blood level of certain enzymes.

Cases of neuraxial hematomas with the concurrent use of enoxaparin and spinal/epidural anesthesia or spinal puncture which may have resulted in varying degrees of neurological injuries including long term or permanent paralysis have been reported.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

Enoxaparin Sodium USP is an Anti - coagulant.

Mechanism of action and Pharmacodynamic effects:

Enoxaparin is a low molecular weight heparin with a high anti-Xa activity (100 I.U. /mg), and with a low anti-II or anti thrombin activity (28 I.U. /mg). At doses required for various indications, enoxaparin does not increase bleeding time. At preventive doses, enoxaparin causes no notable modification of APTT. It neither influences platelet aggregation nor binding of fibrinogen to platelets.

5.2 Pharmacokinetic properties

The pharmacokinetic parameters have been studied in terms of the time course of plasma anti-Xa activity.

Bioavailability: After subcutaneous injection, Enoxaparin is rapidly and completely absorbed. The bioavailability of Enoxaparin is close to 95%.

Distribution: After subcutaneous injection, the maximum plasma activity is obtained 3 hours after the administration.

The anti-Xa activity is located in the vascular space

Biotransformation: Enoxaparin is primarily metabolized in the liver.

Elimination: Following intravenous (IV) dosing, the total body clearance of Enoxaparin is 26 mL/min. After IV dosing of Enoxaparin labeled with the gamma-emitter, 99mTc, 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 SC dose to about 7 hours after repeated dosing. Significant anti-Factor Xa activity persists in plasma for about 12 hours following a 40 mg SC once a day dose.

Following SC dosing, the apparent clearance (CL/F) of Enoxaparin is approximately 15 mL/min.

Excretion: Enoxaparin is eliminated in the urine. In the elderly, the elimination is slightly decreased.

5.3 Preclinical safety data

No information available

6 Pharmaceutical particulars

6.1 List of excipients

Water for Injection USP

6.2 Incompatibilities

The excipients have no deleterious effect on the chemical stability of the active ingredient. This has been demonstrated by the stability studies carried out on the finished product.

6.3 Shelf-life

36 months

6.4 Special precautions for storage

Store below 30 °C and keep out of reach of children.

6.5 Nature and contents of the container

Enoxaparin Sodium Injection USP is filled in 0.5 mL and 1.0 mL USP Type I clear glass Pre Fillable Syringes and stoppered with Plunger stoppers.

6.6 Instructions for use/handling

Enoxaparin Sodium Injection USP is for intra-venous injection and is supplied as a single-use, ready to use, sterile solution in 0.5 mL and 1.0 mL prefilled syringe. The contents of the syringe are sterile and must be used immediately once the container has been opened.