For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Biocon Biologics

℞ Low molecular weight Heparin

Enoxaparin sodium injection IP 40mg/0.4mL /60mg/0.6mL

DYNALIX®40/60 डाइनैलिक्स 40/60

COMPOSITION
DYNALIX® 40
Each pre-filled syringe contains:
Enoxaparin Sodium IP 40mg
(Porcine derived) (Equivalent to 4000 IU
anti-factor Xa activity)
Water for Injections IP q.s. to 0.4mL

DYNALIX® 60
Each pre-filled syringe contains:
Enoxaparin Sodium IP 60mg
(Porcine derived) (Equivalent to 6000 IU
anti-factor Xa activity)
Water for Injections IP q.s. to 0.6mL

ATC Code : B01AB05

Clinical Pharmacology:
Enoxaparin Sodium is a low molecular weight heparin with a high anti-Xa activity (100 IU/mg), and low anti-IIa. At doses required for the various indications, Enoxaparin Sodium does not increase bleeding time. At preventive doses Enoxaparin Sodium causes no notable modification of activated Partial Thromboplastin Time (aPTT). It neither influences platelet aggregation nor binding of fibrinogen to platelets.

The pharmacokinetic parameters have been studied in terms of the time course of plasma anti-Xa activity and also by anti-IIa activity at the recommended dosage ranges. The absolute bioavailability of Enoxaparin Sodium after subcutaneous administration is close to 100%. The mean maximum plasma anti-Xa activity is observed 3 to 5 hours after subcutaneous injection. Enoxaparin Sodium pharmacokinetic appears to be linear over the recommended dosage ranges. Even if a difference in steady-state has been reported between single or repeated administration, this difference is expected and within the therapeutic ranges. The mean maximum plasma anti-IIa activity is observed approximately 3 to 4 hours following subcutaneous injection. Enoxaparin Sodium is primarily metabolized in the liver. The elimination half-life of anti-Xa activity is approximately 4 hours after a single administration to about 7 hours after repeated administration. Renal clearance of active fragments represents about 10% of the administrated dose and total renal excretion 40% of the dose. In the elderly, since renal function is know to decline with age, the elimination may be reduced. In patients with severe renal impairment (creatinine clearance < 30ml/min), the AUC is significantly increased after repeated subcutaneous administration of 4000 anti-Xa IU once daily. In a single study, elimination rate appeared similar in patients undergoing dialysis.

Therapeutic indications:
Enoxaparin Sodium is indicated for:
- Prophylaxis of venous thromboembolic disease (prevention of blood clot formation in the veins), in particular those which may be associated with orthopedic or general surgery,
- Prophylaxis of venous thromboembolic disease in medical patients bedridden due to acute illnesses, including cardiac insufficiency, respiratory failure, severe infection, rheumatic diseases.
- Treatment of deep vein thrombosis, with or without pulmonary embolism,
- Treatment of unstable angina and non-Q-wave myocardial infarction, administered concurrently with aspirin.

Prophylaxis of Deep Vein Thrombosis

- **Enoxaparin is indicated for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE):**
- 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

Treatment of Acute Deep Vein Thrombosis Enoxaparin 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

Administration:
Strictly follow the recommended dosage unless directed otherwise by the physician.

Prophylaxis of venous thromboembolic disease in surgical patients. In patients with a moderate thromboembolic risk (e.g. abdominal surgery) the recommended dose of Enoxaparin Sodium is 4000 anti-Xa IU (0.4 ml) once daily by subcutaneous injection. In general surgery, the first injection should be given 2 hours before the surgical procedure. In patients with a high risk of thromboembolism (e.g. orthopedic surgery) the recommended doses of Enoxaparin Sodium given by subcutaneous injection is 4000 anti-Xa IU (0.4 ml) once daily initiated 12 hours preoperatively. Enoxaparin Sodium treatment is usually prescribed for an average period of 7 to 10 days. Longer treatment duration may be appropriate in some patients and the treatment should be continued for as long as there is a risk of venous thromboembolism and until the patient is ambulatory. Continued therapy with 4000 anti-Xa IU once daily for 3 weeks following the initial therapy has been proven to be beneficial in orthopedic surgery.
Prophylaxis of venous thromboembolic disease in medical patients. The recommended dose of Enoxaparin Sodium is 4000 anti-Xa IU (0.4 ml) once daily by subcutaneous injection, Treatment with Enoxaparin Sodium is prescribed for a minimum of 6 days and continued until-the return of full ambulation, for a maximum of 14 days.

Treatment of deep vein thrombosis with or without pulmonary embolism Enoxaparin Sodium can be administered subcutaneously either as a single daily injection of 150 anti-Xa IU/kg or as twice daily injections of 100 anti-Xa IU/kg. In patients with complicated thromboembolic disorders, a dose of 100 anti-Xa IU/kg twice daily is recommended. Enoxaparin Sodium treatment is usually prescribed for an average period of 10 days. Oral anticoagulant therapy should be initiated when appropriate and Enoxaparin Sodium treatment should be continued until a therapeutic anticogulant effect has been achieved.

Treatment of unstable angina and non-Q-wave myocardial infarction. The recommended dose of Enoxaparin Sodium is 100 anti-Xa IU/kg every 12 hours by subcutaneous injection, administered concurrently with oral aspirin (100 to 325 mg once daily). Treatment with Enoxaparin Sodium in these patients should be prescribed for a minimum of 2 days and continued until clinical stabilization. The usual duration of treatment is 2 to 8 days.

Special population
Elderly: No dosage adjustment is necessary, unless for kidney function is impaired.
Children: Enoxaparin Sodium is not recommended in children.
Renal impairment: A dosage adjustment is required for patient with severe renal impairment (Creatinine clearance < 30 ml/min), since Enoxaparin Sodium exposure is significantly increased in this patient population. The following dosage adjustments are recommended:
Prophylactic dose ranges: 2000 anti-Xa IU once daily; Therapeutic dose range: 100 anti-Xa IU/kg once daily.

Moderate and mild renal impairment: Careful clinical monitoring is recommended.
Hepatic impairment: Caution should be used in hepatic impaired patients.
Methods of administration: Enoxaparin Sodium should be injected by deep subcutaneous route in prophylactic and curative treatment.

DO NOT ADMINISTER BY THE INTRAMUSCULAR ROUTE.
The pre-filled syringes are ready-to-use. The air bubble from the syringes should not be expelled before the injection. The subcutaneous injection should preferably be made when the patient is lying down. Enoxaparin Sodium is administered in the subcutaneous 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.

Contraindications: Enoxaparin Sodium must not be used in the following situations:
- In patients with known hypersensitivity (allergy) to either Enoxaparin Sodium, heparin or other low molecular weight heparin,
- In patients with active major bleeding and conditions with a high risk of uncontrolled hemorrhage including recent hemorrhagic stroke.

Warning and precautions
Warnings
- Low Molecular weight Heparins should not be used to interchangeably since they differ in their manufacturing process, molecular weights specific anti-Xa activities, units and dosage. Very careful attention and compliance with the specific instructions on use of each product are absolutely essential.
- 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 resulting in long-term or permanent paralysis. These events are rare with Enoxaparin Sodium dosage regimens of 4000 anti-Xa IU once daily or lower. The risk is greater with high doses of Enoxaparin Sodium, the use of post-operative indwelling epidural catheters or with concomitant use of

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drugsaffecting hemostasis such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).
The risk also appears to be increased by traumatic or repeated neuraxial puncture during epidural or spinal anesthesia, the placement and removal of the catheter is best performed when the anticoagulant effect of Enoxaparin Sodium is low: 10 to 12 hours after administration of 4000 anti-Xa IU or less daily doses of Enoxaparin
Sodium or 24 hours following the administration of higher dose (100 anti-Xa IU/kg twice daily or 150 anti-Xa IU/kg once daily). The subsequent administration 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.
- Heparin-induced thrombocytopenia
  Enoxaparin Sodium is to be used with extreme caution in patients with a history of heparin-induced thrombocytopenia with or without thrombosis.
- Percutaneous coronary revascularisation procedures.
  To minimize the risk of bleeding following the vascular instrumentation during the treatment of unstable angina, the vascular access sheath should remain in place for 6 to 8 hours following a dose of Enoxaparin Sodium. The next scheduled dose should be given no sooner than 6 to 8 hours after sheath removal.
- Prosthetic heart valves
  There have been no adequate studies to access the safe and effective use of Enoxaparin Sodium in preventing thromboembolism in patients with prosthetic heart valves. The use of Enoxaparin Sodium cannot be recommended for this purpose.
- Laboratory tests
  At doses used for prophylaxis of venous thromboembolism, Enoxaparin Sodium doses not influence bleeding time and global blood coagulation tests significantly, nor doses it affect platelet aggregation or binding of fibrinogen to platelets. At higher doses, increases in aPTT (activated Partial Thromboplastin Time) and ACT (Activated Clotting Time) may occur.

Precautions
Enoxaparin Sodium should be used with a caution in conditions with increased potential for bleeding, such as impaired hemostasis, history of peptic ulcer, recent ischemic stroke, uncontrolled severe arterial hypertension, diabetic retlnopathy and recent neuro or opthalmologic surgery (see Interaction).
- Hemorrhage in the elderly
  No increases in bleeding is observed in the elderly as prophylactic doses while at therapeutic doses bleeding complications may be observed particularly in patients 80 years os age and older. Careful monitoring is recommended.
- Renal impairment
  In patient with renal impairment, there is an increases in exposure of Enoxaparin Sodium which increases the risk of bleeding. Therefore, in patients with severe renal impairment, a dosage adjustment is recommended for prophylactic and therapeutic dose ranges (see how should this drug be used). Although no dosage adjustment is recommended in patients with moderate and mild renal impairment, careful monitoring is advised.
- Low weight
  In low weight patients (women < 45 kg and men < 57 kg), an increase in exposure of Enoxaparin Sodium with prophylactic doses have been observed which may lead to a higher risk of bleeding. Therefore, careful monitoring is recommended.

  Monitoring of platelet count level is necessary regardless of the therapeutic indication and the dosage administered. It is recommended that the platelet counts be measured before the initiation of the treatment and regular thereafter during treatment. If a significant decreases of the platelet count (30 to 50% of the initial count) is observed, the treatment must be discontinued and the patient switched to another therapy.

Overdose:
Accidental over dosage after subcutaneous administration of massive doses of Enoxaparin Sodium may lead to bleeding complications. Neutralization can be obtained by slow intravenous injection of protamine (1 mg protamine can be used to neutralize the anticoagulant effect of about 1 mg Enoxaparin Sodium). However the anti-Xa activity of Enoxaparin Sodium is never completely neutralized (maximum about 60%).

Interactions
In order to avoid possible interactions with other medicines, inform your physician about any other current treatment.

It is recommended that agents which affect hemostasis should be discontinued prior to Enoxaparin Sodium therapy unless strictly indicated. These agents include medications such as: acetylsalicylic acid (and derivatives), NSAIDs (general route) including ketorolac, ticlopidine, clopidogrel, dextran 40 (parenteral use), glucocorticoids (general route), thrombolytics and anticoagulants, other anti platelet agents including glycoprotein IIb/IIIa antagonists. As with other Low Molecular Weight Heparins, if the combination is indicated, Enoxaparin Sodium should be used with careful clinical and laboratory monitoring when appropriate.

Pregnancy and lactation: In humans, there is no evidence that Enoxaparin Sodium crosses the placental barrier. Enoxaparin Sodium should be used during pregnancy only if the physician has established a clear need. Enoxaparin Sodium is not recommended for use in pregnant women with prosthetic heart valves.
As a precaution, lactating mothers receiving Enoxaparin Sodium should be advised to avoid breast-feeding.

Undesirable effects: Please tell your physician, if you experience any adverse effect with the use of this product.

Hemorrhage (bleeding): This may occur during treatment with any anticoagulants in the presence of associated risk factors such as:

Major hemorrhage including retroperitoneal and intracranial bleeding has been reported. Some of these cases have been lethal. Cases of neuraxial hematomas with the concurrent use of Enoxaparin Sodium and spinal/epidural anesthesia or spinal puncture which have resulted in varying degrees of neurologic injuries including long term or permanent paralysis have been reported (see Warnings and Precautions).

Thrombocytopenia: Mild and transient thrombocytopenia (abnormally low platelet count level). In rare cases, immuno allergic throbocytopenia with thrombosis. In some cases thrombosis was complicated by organ infarction or limb ischemia.

Local reactions: Pain, hematoma and mild local irritation may follow the subcutaneous injection of Enoxaparin Sodium. Rarely, hard inflammatory nodules have been observed at the injection site. They resolve after a few days and should not cause treatment discontinuation. Exceptional cases of skin necrosis (skin lesion including irreversible damages) at the injection site have been reported with heparins and Low molecular Weight Heparins. These phenomena are usually preceded by purpura or erythematous plaques, infiltrated and painful. Treatment must be discontinued.

Others: Although rare, cutaneous (bullous eruptions) or systemic allergic reactions including anaphylactoid reactions may occur.

Asymptomatic and reversible increases in platelet counts and liver enzyme levels (transaminases) have been reported.

Storage
Store below 25° C. Store protected from light.
Do not refrigerate or freeze.
Keep out of reach of children.

Shelf life : Please refer carton/label.

Special precautions for disposal and other handling :
Dissolve or mix material with a suitable combustible solvent and Material should be disposed of in keeping with all local and national legislation.

Presentation
DYNALIX® 40: One pre-filled syringe in a blister pack, such 1 blister packed in a carton with pack insert.
DYNALIX® 60: One pre-filled syringe in a blister pack, such 1 blister packed in a carton with pack insert.

Marketed by:
Biocon Biologics Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

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To report adverse events and/or product complaints visit our website **www.biocon.com** or call toll free No.: **1800 102 9465** or e mail us at **drugsafety@biocon.com**