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

Rx

Enoxaparin Sodium Injection IP 60mg/0.6 ml.

(Low Molecular Weight Heparin)

Axorin 60 Injection

60mg/0.6ml. Pre-filled Syringe
Subcutaneous route Intravascular
route during haemodialysis.
(6000 Anti-factor Xa I.U./0.6mL)

Composition :
Each Pre-filled Syringe contains :
Enoxaparin Sodium IP 60 mg
(6000 Anti-factor Xa units)
Water for Injections IP q.s.

Properties
Pharmaco-therapeutic class: Antithrombotic agent/heparin group (B: blood and blood forming organs).
Enoxaparin sodium is a low molecular weight heparin with a high anti-Xa activity (100 IU/mg), and low anti-IIa or anti thrombin activity (28 IU/mg). 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 platelet.
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 bio-availability 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 is primarily metabolized in the liver. The elimination half-life of anti-Xa activity is approximately 4 hours after single administration to about 7 hours after repeated administration. Renal clearance of active fragments represents about 10% of the administered dose and total renal excretion 40% of the dose. In the elderly, since renal function is known to decline with age, the elimination may be reduced. In patients with severe renal impairment (creatinine clearance < 30 ml/min), the AUC is significantly increased after repeated subcutaneous administration of 4000 anti-Xa IU once daily. In a single study, elimination rate appeared is similar in patients undergoing dialysis.

When should this drug be used (Therapeutic indications)
Solution for injection containing 2000 anti-Xa IU and 4000 anti-Xa IU
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 orthopaedic or general surgery.
- Prophylaxis of venous thromboembolic disease in medical patients bedridden due to acute illness including cardiac insufficiency, respiratory failure, severe infections, rheumatic diseases.

Solution for injection containing 6000 anti-Xa IU and 8000 anti-Xa IU
Enoxaparin sodium is indicated for:
- Treatment of deep vein thrombosis, with or without pulmonary embolism.
- Treatment of unstable angina and non-Q-wave myocardial infraction, administered concurrently with aspirin.
- Prevention of thrombus formation in extra corporeal circulation during hemodialysis.

How should this drug be used
Strictly follow the recommended dosage unless directed otherwise by the physician
Prophylaxis of venous thromboembolic disease in surgical patients
In patients with moderate thromboembolism risk (e.g. abdominal surgery) the recommended dose of Enoxaparin sodium 2000 anti-Xa IU (0.2 ml or 4000 anti-Xa IU (0.4ml) once daily by subcutaneous injection. In general surgery, the first injection should be given 2 hours before the surgical procedure. In patients with the high risk of thromboembolism (e.g. orthopaedic surgery) the recommended dose of enoxaparin sodium given by subcutaneous injection is 4000 anti-Xa IU (0.4 ml) once daily initiated 12 hours preoperatively. For special recommendations concerning dosing interval for spinal/epidural anesthesia and precutaneous coronary revascularization procedures, see warnings. 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 thromboembolism and until the patient is ambulatory. Continued therapy with 4000 anti-Xa IU once daily for three weeks following the inital therapy has been proven to be beneficial in orthopaedic surgery.
Prophylaxis of venous thromboembolic disease in medical patients
The recommended dose of Enoxaparin sodium 4000 anti-Xa IU (0.4ml) once daily by subcutaneous injection. Treatment with Enoxaparin sodium is prescribed for a minimum of 6 days and continues 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 injection 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 appreciated and Enoxaparin sodium treatment should be continued until a therapeutic anticoagulant effect has been achieved (International Normalization Ratio 2 to 3).
Treatment of unstable angina and non Q-wave myocardial infraction
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.
Prevention of thrombus formation in extra corporeal circulation
The recommended dose of Enoxaparin sodium is 100 anti-Xa IU/kg. For patients with high risk of hemorrhage, the dose should be reduced to 50 anti-Xa IU-kg for double vascular access or 75 anti-Xa Iu/kg for single vascular access. During haemodialysis 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 hours session. However, if fibrin rings are found, a further dose of 50 to 100 anti-Xa IU/kg may be given.
Special population
Elderly: No dosage adjustment is necessary, unless kidney function is impaired(see warnings and precautions).
Children: Enoxaparin sodium is not recommended for children.
Renal Impairment: See warning & precautions and properties.
Severe renal impairment: A dosage adjustment is required for patients with severe renal impairment (creatinine clearance<30ml/min). Since enoxaparin sodium exposure is significantly increasing in this patient population. The following dosage adjustments are recommended: Prophylactic dosage ranges: 2000 anti-Xa IU once daily: Therapeutic dose ranges: 100 anti-Xa IU/kg once daily
Moderate and mild renal impairment: Careful clinical monitoring is recommended.
Hepatic impairment: Caution should be used in haptically impaired patients.
Method of administration
Enoxaparin sodium should be injected by deep subcutaneous route in prophylactic and curative treatment and by intra-vascular route during hemodialysis. DO NOT ADMINISTER BY THE INTRAMUSCULAR ROUTE.
The pre-filled syringes are ready to use. The air bubble from the syringe should not be expelled before the injection. The subcutaneous injection should preferably made when the patient is lying down. Enoxaparin sodium is administered in the subcutaneous tissue of the anterolateral or posteriolateral 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.
When should this drug not to be used (Contra Indications)
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 heparins.
In patients with active major bleeding and conditions with a high risk or uncontrolled hemorrhage including recent hemorrhagic stroke.

120X180 MM BACK

Warnings and Precautions
Warnings
- Low molecular heparins should not be used 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 in use of each product are absolutely essential.
- Spinal/Epidural anesthesia
  As with other anticoagulant, 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 drugs affecting homeostasis such as Non Steroidal Anti-Inflammatory Drugs (NSAIDS) (see interactions). 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 the 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 doses (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 neuroxial hematoma are suspected urgent diagnosis and treatment including spinal cord decompression are necessary.
- Heparin-induced thrombocytopnia
  Enoxaparin sodium is to be used with extreme caution in patients with a history of heparin-induced thrombocytopenia with or without thrombosis.
- Precutaneous coronary revascularization procedures
  To minimize the risk of bleeding following the vascular instrumentation during the treatment of unstable angina, the vascular acess 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 assess 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 does not influence bleeding time and global blood coagulation tests significantly, nor does it affect platelet aggregation or binding of fibrinogen to platelet. At higher doses, increases in aPTT (Activated Partial Thromboplastin Time) and ACT (Activated Clotting Time) may occur.

Precautions
- Enoxaparin sodium should be used with caution in conditions with increased potential for bleeding, such as impaired hemostasis, history of peptic ulcer, recent ischemic stroke, uncontrolled severe arterial hypertension, diabetic retinopathy and recent neuro or ophthalmologic surgery (see interactions)
- Hemorrhage in elderly
  No increase in bleeding is observed in the elderly at prophylactic doses while at therapeutic doses bleeding complications may be observed particularly in patients 80 years of age and older. Careful monitoring is recommended.
- Renal impairment
  In patients with renal impairment, there is an increase 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 < 57kg), an increase in exposure of enoxaparin sodium with prophylactic doses has been observed which may lead to a higher risk of bleeding. Therefore, careful monitoring is recommended.
- Monitoring of platelet count 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 regularly thereafter during treatment. If a significant decrease of the platelet count (30 to 50% of the initial count) is observed, the treatment must be discontinued and the patient is switched to another therapy.

Overdose
Accidental over dosage after extra corporeal or 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 protaine can be used to) neutralize the anticoagulant effect of about 1 mg enoxaparin sodium 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 or pharmacist about any other current treatment.
It is recommended that agents which affect homeostasis should be discontinued prior to enoxaparin sodium therapy unless strictly indicated. These agents include medications such as: acetylsalicylic acid (and derivatives). NSAIDS (generals route) including ketorolac, ticlopidine, clopidogrel, dextran 40 (parentral use), gluccocorticoids (general route), thrombolytics and anticoagulants. 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 (see warnings). As a precaution, lactating mothers receiving enoxaparin sodium should be advised to avoid breast-feeding.
Undesirable effects
Please tell your physician or pharmacist , if you experience any adverse effect with the use of this product
- Hemorrhage (bleeding). This may occur during treatment with only anticoagulants in the presence of associated risk factors such as; organic lesions liable to bleed, invasive procedures or the use of medications affecting hemostasis (blood coagulation) (see interactions). Major hemorrhage including retroperitoneal and intracranial bleeding has been reported. Some of theses 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 thrombocytopenla with thrombosis (formation of clot in veins). In some cases thrombosis was complicated by organ Infraction (tissue death by lack of oxygen) or limb ischemia (deficiency of blood supply).
- Local reactions : Pain, hematoma (bluish marks) 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 lesions including Irreversible damages) at the injection site have been reported with heparins and low molecular weight heparins. These phenomena are usually precede by purpura (small hemorragia in the skin) or orythemalous plaques (red inflammatory rash), Infiltrated and painful. Treatment must be discontinued.
- Others: Although rare, cutaneous (bullous eruptions) or systemic allergic reactions may occur. Asymptometic 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.
Expiry date
Do not use later than date of expiry indicated on the outer packaging. Keep out of reach of children.
Presentation
Enoxaparin pre-filled syringe is available in a monocarton.

Marketed by
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