Product: Enoxaparin sodium [Clexane]
Strengths: 2000 IU (equivalent to 20 mg)/0.2 mL Solution for Injection (SC) (BR-799); 4000 IU (equivalent to 20 mg)/0.4 mL Solution for Injection (SC) (BR-797); 6000 IU (equivalent to 20 mg)/0.6 mL Solution for Injection (SC) (BR-798)
Presentation: 0.2 mL or 0.4 mL in 0.5 mL pre-filled syringe with needle per Box of 2's; 0.6 mL in 1 mL pre-filled syringe with needle per Box of 2's
I: Prophylaxis of venous thrombo-embolic disease, in those associated with orthopedic or general surgery, and in medical patients bedridden due to acute illnesses including cardiac insufficiency, respiratory failure, severe infections, rheumatic diseases. For the treatment of deep vein thrombosis with or without pulmonary embolism and prevention of thrombus formation in extra corporeal circulation during hemodialysis. Used in the treatment of unstable angina and non-Q-wave myocardial infarction, administered concurrently with aspirin, and of acute ST-segment Elevation Myocardial Infarction (STEMI) including patients to be managed medically or with subsequent Percutaneous Coronary Intervention (PCI).
D: In patients with a moderate risk of thrombo-embolism, the recommended dose is 20 mg or 40 mg once daily by subcutaneous injection. In patients with a high risk of thrombo-embolism, the recommended dose is 40 mg once daily, initiated 12 hours prior to surgery or 30 mg twice daily, initiated 12 to 24 hours after surgery. For the prophylaxis of venous thrombo-embolism in medical patients, the recommended dose is 40 mg once daily and for the treatment of deep vein thrombosis with or without pulmonary embolism, it can be administered as a single injection of 1.5 mg/kg or as twice daily injections of 1 mg/kg. In patients with complicated thrombo-embolic disorders, a dose of 1 mg/kg administered twice daily is recommended. For the prevention of extra corporeal thrombus during hemodialysis, the recommended dose 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. Dose adjustment is done for patients with renal impairment.
C: Hypersensitivity to enoxaparin sodium, heparin or its derivatives including other low molecular weight heparins. Active major bleeding and conditions with a high risk of uncontrolled hemorrhage, including recent hemorrhagic stroke.
W/P: Cases of neuraxial hematoma have been reported with the concurrent use of enoxaparin sodium and spinal or epidural anaesthesia resulting in long term paralysis which are rare with enoxaparin sodium dosage regimens 40 mg once daily or lower. The risk is greater with higher enoxaparin sodium dosage regimen, use of post-operative indwelling catheters or the concomitant use of additional drugs affecting hemostasis such as NSAIDs. The risk also appears to be increased by traumatic or repeated neuraxial puncture or in patients with a history of spinal surgery or spinal deformity. Enoxaparin sodium is to be used with extreme caution in patients with a history of heparin-induced thrombocytopenia without circulating antibodies. To minimize the risk of bleeding following the vascular instrumentation during the treatment of unstable angina, non-Q-wave myocardial infarction and acute ST-segment elevation myocardial infarction, adhere precisely to the intervals recommended between doses. At doses used for prophylaxis of venous thrombo-embolism, enoxaparin sodium does not influence bleeding time and global blood coagulation tests significantly, nor does it affect platelet aggregation or binding of fibrinogen to platelets. Do not administer by the intramuscular route. Since exposure of enoxaparin sodium is significantly increased in patients with severe renal impairment, a dosage adjustment is recommended for therapeutic and prophylactic dosage ranges. The risk of antibody-mediated heparin-induced thrombocytopenia also exists with Low Molecular Weight Heparins. If a confirmed significant decrease of the platelet count is observed, enoxaparin sodium treatment must be immediately discontinued, and the patient switched to another therapy.
Int: 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: systemic salicylates, acetylsalicylic acid, and NSAIDs including ketorolac, dextran 40, ticlopidine, clopidogrel, systemic glucocorticoids, thrombolytics and anticoagulants, and other anti-platelet agents including glycoprotein IIb/IIIa antagonists. If the combination is indicated, enoxaparin sodium should be used with careful clinical and laboratory monitoring when appropriate.
AE: Hemorrhage, Thrombocytopenia, Thrombocytosis, Allergic reaction, Urticaria, Pruritus, Erythema, Injection site pain and hematoma
PK: The pharmacokinetic parameters of enoxaparin sodium have been studied primarily in terms of the time course of plasma anti-Xa activity and by anti-IIa activity, at the recommended dosage ranges after single and repeated subcutaneous administration and after single intravenous administration. The quantitative determination of anti-Xa and anti-IIa pharmacokinetic activities was conducted by validated amidolytic methods with specific substrates and an enoxaparin standard calibrated against the international standard for LMWHs (NIBSC). The absolute bioavailability of enoxaparin sodium after subcutaneous injection, based on anti-Xa activity, is close to 100%. The volume of distribution of enoxaparin sodium anti-Xa activity is about 5 liters and is close to the blood volume. Enoxaparin sodium is primarily metabolized in the liver by desulfation and/or depolymerization to lower molecular weight species with much reduced biological potency. Enoxaparin sodium is a low clearance drug with a mean anti-Xa plasma clearance of 0.74 L/h after a 1.5 mg/kg 6-hour intravenous infusion.
PD: Enoxaparin sodium is a Low Molecular Weight Heparin with a mean molecular weight of approximately 4,500 daltons. Enoxaparin sodium is obtained by alkaline depolymerization of heparin benzyl ester. In the in vitro purified system, enoxaparin sodium has a high anti-Xa activity and low anti-IIa or anti thrombin activity. These anticoagulant activities are mediated through anti-thrombin III (ATIII) resulting in anti-thrombotic activities in humans. Beyond its anti-Xa/IIa activity, further anti-thrombotic and anti-inflammatory properties of enoxaparin have been identified in healthy subjects and patients as well as in non-clinical models. These include ATIII-dependent inhibition of other coagulation factors like factor VIIa, induction of endogenous Tissue Factor Pathway Inhibitor (TFPI) release as well as a reduced release of von Willebrand factor (vWF) from the vascular endothelium into the blood circulation. These factors are known to contribute to the overall anti-thrombotic effect of enoxaparin.