

ENOXA Médís® 2000 anti-Xa UI/0,2 ml - ENOXa Médís® 4000 anti-Xa UI/0,4 ml

ENOXA Médís® 6000 anti-Xa UI/0,6 ml - ENOXa Médís® 8000 anti-Xa UI/0,8 ml

Enoxaparin sodium

FORMS AND PRESENTATIONS:

ENOXA Médís 2000 UI anti-Xa 0,2 ml; Enoxaparin sodium 20 mg/0,2 ml, injectable solution, box of 02 pre-filled syringes.
ENOXA Médís 4000 UI anti-Xa 0,4 ml; Enoxaparin sodium 40 mg/0,4 ml, injectable solution, box of 02 pre-filled syringes.
ENOXA Médís 6000 UI anti-Xa 0,6 ml; Enoxaparin sodium 60 mg/0,6 ml, injectable solution, box of 02 pre-filled syringes.
ENOXA Médís 8000 UI anti-Xa 0,8 ml; Enoxaparin sodium 80 mg/0,8 ml, injectable solution, box of 02 pre-filled syringes.

COMPOSITION PER PRE-FILLED SYRINGE:

Table with 4 columns: Quantity per syringe, ENOXa Médís 2000 UI anti-Xa 0,2 ml, ENOXa Médís 4000 UI anti-Xa 0,4 ml, ENOXa Médís 6000 UI anti-Xa 0,6 ml, ENOXa Médís 8000 UI anti-Xa 0,8 ml. Rows include Active compound, Excipients, and WFI.

PHARMACOLOGICAL PROPERTIES:

Pharmaco-therapeutic class: Antithrombotic agent/heparin group. Enoxaparin sodium is a low molecular weight heparin with a high anti-Xa activity (100 IU/mg), and low anti-IIa or anti-IIIa activity (28 times 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.

THERAPEUTIC INDICATIONS:

- ENOXA Médís 2000 UI anti-Xa: Prophylactic Treatment of the venous thrombo-embolic disease in surgery, at the risk moderate or high. Prevention of the coagulation of the circuit of extracorporeal circulation during the hemodialysis.
ENOXA Médís 4000 anti-Xa UI: Prophylaxis of venous thrombo-embolic disease in surgery, at the risk moderate or high. Prophylaxis of venous thrombo-embolic disease in medical patients bedridden due to acute illness.
ENOXA Médís 6000 anti-Xa UI and ENOXa Médís 8000 anti-Xa UI: Prevention of the coagulation of the circuit of extracorporeal circulation during the hemodialysis.

Enoxaparin sodium is indicated for:
- Patients with a moderate thromboembolism risk (e.g. abdominal surgery)
- Treatment of acute myocardial infarction with ST segment elevation in combination with thrombolytic therapy in eligible or not a secondary coronary angioplasty patients.

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 heparins.
- In patients with active major bleeding and conditions with a high risk of uncontrolled hemorrhage including recent hemorrhagic stroke.

DOSE AND MODE OF ADMINISTRATION:

Strictly follow the recommended dosage unless directed otherwise by the doctor.
Prophylaxis of venous thromboembolic disease in surgical patients:
- In patients with a moderate thromboembolism risk (e.g. abdominal surgery) the recommended dose of Enoxaparin sodium is 2000 anti-Xa IU (0,2 ml) or 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 thromboembolism risk (e.g. orthopedic 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. 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.

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 to 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 anticoagulant effect has been achieved (International Normalisation Ratio 2 to 3).

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.

Prevention of thrombus formation in extra corporeal circulation during hemodialysis:

The recommended dose of Enoxaparin sodium is 100 anti-Xa IU/kg. For patients with a high risk of hemorrhage, the dose should be reduced to 80 anti-Xa IU/kg for double vascular access or 75 anti-Xa IU/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 50 to 100 anti-Xa IU/kg may be given.

Special population:

- Elderly: No dosage adjustment is necessary, unless kidney function is impaired.
-Children: Enoxaparin sodium is not recommended in children.
-Renal impairment: Severe renal impairment: A dosage adjustment is required for patients 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 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 hepatically impaired patients.

Mode of administration:

Enoxaparin sodium should be injected by deep subcutaneous route in a subcutaneous and curative treatment and by intravenous route during hemodialysis.

DO NOT ADMINISTER BY THE INTRAMUSCULAR ROUTE.

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 and occur regardless of whether the catheter is inserted into the epidural or subarachnoid space. 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, through the skin into a fold of skin between the thumb and index finger. The skin fold should be held throughout the injection.

WARNING AND PRECAUTIONS OF USE:

- Spinal/Epidural anesthesia:
- Low Molecular Weight 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 on use of each product are absolutely essential.
- 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 and occur regardless of whether the catheter is inserted into the epidural or subarachnoid space. 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, through the skin into a fold of skin between the thumb and index finger. The skin fold should be held throughout the injection.
- Percutaneous coronary revascularisation procedures: To minimize the risk of bleeding following the vascular instrumentation during the treatment of unstable angina, the vascular access should be closed 6 to 8 hours after sheath removal. The next scheduled dose should be given no sooner than 6 to 8 hours after sheath removal. The site of the procedure should be observed for signs of bleeding or hematoma formation.
- Pregnant women with mechanical prosthetic heart valves: The use of Enoxaparin sodium in pregnant women with mechanical prosthetic heart valves has not been adequately studied. Pregnant women with mechanical prosthetic heart valves may be at a higher risk for thromboembolism.

-Laboratory tests:
- As 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 platelets. At higher doses, increases in aPTT (activated Partial Thromboplastin Time) and ACT (Activated Clotting Time) may occur. Increases in aPTT and ACT are not linearly correlated with increasing Enoxaparin sodium anti-thrombotic activity and therefore these tests are unsuitable and unreliable for monitoring Enoxaparin sodium therapy.

-Precautions of use:
- Bleeding: As with other anticoagulants, bleeding may occur at any site. 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, concomitant use of medications affecting hemostasis.

-Mechanical prosthetic heart valves: The use of Enoxaparin sodium for thromboprophylaxis in patients with mechanical prosthetic heart valves has not been adequately studied.

-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. Although no dosage adjustment is recommended in patients with moderate and mild renal impairment, careful monitoring is advised.

-Low weight patients: In low weight patients (women < 45 kg and men < 57 kg), 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: The risk of antibody-mediated heparin-induced thrombocytopenia also exists with Low Molecular Weight Heparins. Signs of thrombocytopenia may occur, it usually appears between the 5th and the 21st day following the beginning of Enoxaparin sodium treatment. Therefore, 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 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 switched to another therapy.

-Overdose: Accidental overdose after intravenous, extra corporeal or subcutaneous administration of massive doses of Enoxaparin sodium may lead to bleeding complications. Neutralization may be obtained by slow intravenous injection of protamine; however the anti-Xa activity of Enoxaparin sodium is never completely neutralized (maximum about 60%). 1 mg protamine can be used to neutralize the anticoagulant effect of about 1 mg Enoxaparin sodium. 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. After 12 hours of the Enoxaparin sodium injection, protamine administration may not be required.

PREGNANCY AND LACTATION:

In humans, there is no evidence that Enoxaparin sodium crosses the placental barrier during the second trimester. There is no information available concerning the first and the third trimesters. As there are no adequate and well-controlled studies in pregnant women, Enoxaparin sodium should be used during pregnancy only if the doctor has established a clear need. Pregnant women with mechanical prosthetic heart valves may be at a higher risk for thromboembolism.

As a precaution, lactating mothers receiving Enoxaparin sodium should be advised to avoid breast-feeding.

DRUG INTERACTIONS:

In order to avoid possible interactions with other medicines, inform your doctor or pharmacist about any other current treatment. It is recommended that agents which affect hemostasis should be discontinued prior to Enoxaparin sodium therapy (unless strictly indicated) 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 aggregation 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.

ADVERSE EFFECTS:

-Hemorrhage (bleeding): This may occur during treatment with any anticoagulants in the presence of associated risk factors such as: Organic lesions liable to bleed; invasive procedures or the use of medications affecting hemostasis (e.g. aspirin).
-Local reactions: 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.

-Thrombocytopenia: mild and transient thrombocytopenia (abnormally low platelet count level). In rare cases, immuno-allergic thrombocytopenia with thrombosis (formation of clot in the veins). In some cases thrombosis was complicated by organ infarction (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, which are not cystic enclosures of Enoxaparin sodium, 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 (small hemorrhage in the skin) or erythematous plaques (red inflammatory rash), infiltrated and painful. Treatment must be discontinued.

-Others: Although rare, cutaneous (blisters eruptions) or systemic allergic reactions including anaphylactoid reactions may occur. Very rare cases of hypersensitivity cutaneous vasculitis (blood vessel inflammation) have been reported. Asymptomatic and reversible increases in platelet counts and liver enzyme levels (transaminases) have been reported.

DELIVERY CONDITIONS:

List I - Only on medical prescription.
SPECIAL PRECAUTIONS OF STORAGE: Do not store above 25°C.

PRESENTATIONS AND M.A. NUMBERS:

Table with 3 columns: Specialities, M.A., Presentations. Rows include ENOXa Médís® 2000 anti-Xa UI/0,2 ml, ENOXa Médís® 4000 anti-Xa UI/0,4 ml, ENOXa Médís® 6000 anti-Xa UI/0,6 ml, ENOXa Médís® 8000 anti-Xa UI/0,8 ml.

Marketing Authorisation Holder and Manufacturer:

LES LABORATOIRES MEDIS
Tunis road - KM 7 - BP 206 - 8000 Nabeul - Tunisia
Tel: (+216) 72 23 80 06. Fax: (+216) 72 23 50 16.
E-mail: contact@labmedis.com
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This is a drug
- A drug is a specific product used to prevent, cure or relieve a disease.
- A drug is a product acting on your health and its use should be under medical supervision and be appropriate for you.
- Strictly respect the doctor's prescription and the instructions.
- Follow your pharmacist's advice by this drug : its administration must be done according to the instructions.
- Do not stop the drug's intake without consulting your doctor.
- Do not expect the prescription or increase the dosage without consulting your doctor.

هذا دواء
- الدواء منتج طبي يستخدم للوقاية من المرض، أو علاجه، أو تخفيف أعراضه.
- الدواء منتج طبي يستخدم لصحتك ويجب استخدامه تحت إشراف طبي.
- يجب احترام وصفة الطبيب بدقة والتوجيهات.
- اتبع نصيحة الصيدلي عند تناول هذا الدواء : يجب أن يتناول الدواء وفقاً للتعليمات.
- لا تتوقف عن تناول الدواء دون استشارة الطبيب.
- لا تتوقع وصفة الطبيب أو زيادة الجرعة دون استشارة الطبيب.

KEEP ANY DRUG OUT OF THE REACH OF CHILDREN.