1000 mm (Length)

700 mm (Height)

Abbreviated Package Insert
See Product Monograph for complete Product Information
PrELONOX
Enoxaparin sodium
Solution for Injection, 100 mg/mL, Subcutaneous or Intravenous Use
30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/mL
Pre-filled syringes
USP
Anticoagulant/Antithrombotic Agent

1 INDICATIONS

Elonox (enoxaparin sodium) is indicated for:

- The prophylaxis of thromboembolic disorders (deep vein thrombosis) in patients undergoing:
  - orthopedic surgery of the hip or knee. In addition, Elonox is indicated in hospital or after hospital discharge for long-term prevention of venous thromboembolic diseases following hip replacement surgery.
  - high risk abdominal, gynecological, or urological surgeries;
  - colorectal surgery.
- The prophylaxis of deep vein thrombosis (DVT) in medical patients who are at moderate risk of DVT and who are bedridden due to moderate to severe acute cardiac insufficiency (NYHA Class III or IV heart failure), acute respiratory failure revealing or complicating chronic respiratory insufficiency not requiring ventilatory support and acute respiratory infections (excluding septic shock), who require short-term prophylaxis of deep vein thrombosis.
- The prevention of thrombus formation in the extra-corporeal circulation during hemodialysis.

Elonox is also indicated for:

- The treatment of deep vein thrombosis, with or without pulmonary embolism.
- The treatment of unstable angina or non-Q-wave myocardial infarction, concurrently with ASA.
- Treatment of acute ST-segment Elevation Myocardial Infarction (STEMI), including patients to be managed medically or with subsequent Percutaneous Coronary Intervention (PCI).

Indications have been granted on the basis of similarity between Elonox and Elonox HP and the reference biologic drug Lovenox and Lovenox HP.

1.1 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (≥ 75 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety and a brief discussion can be found in 7.1.4 Geriatrics.

2 CONTRAINDICATIONS

Enoxaparin sodium is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container, or to other low molecular weight heparins and/or heparin. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

- Enoxaparin is contraindicated in patients with history of confirmed or suspected immunologically-mediated heparin-induced thrombocytopenia (delayed-onset severe thrombocytopenia), within the past 100 days, or in patients in whom an *in vitro* platelet-aggregation test in the presence of enoxaparin is positive (circulating antibodies) (see 7 WARNINGS AND PRECAUTIONS, Heparin-induced thrombocytopenia, and 9 DRUG INTERACTIONS).
- Enoxaparin is also not indicated in the following situations:
  - Acute or subacute bacterial endocarditis.
  - Active bleeding.
  - Major blood clotting disorders.
  - Active gastric or duodenal ulcer.
  - Hemorrhagic cerebrovascular accident (except if there are systemic emboli).
  - Severe uncontrolled hypertension.
  - Diabetic or hemorrhagic retinopathy.
  - Other conditions or diseases involving an increased risk of hemorrhage.
  - Injuries to and operations on the brain, spinal cord, eyes and ears.
  - Spinal/epidural anesthesia is contraindicated where repeated treatment doses of enoxaparin sodium (1 mg/kg every 12 hours or 1.5 mg/kg once daily) are required, due to an increased risk of bleeding.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Elonox must not be administered by the intramuscular route.

Subcutaneous injection
Elonox is administered by subcutaneous injection for the prevention of venous thromboembolic disease, treatment of deep vein thrombosis, treatment of unstable angina and non-Q-wave myocardial infarction and treatment of acute ST-segment Elevation Myocardial Infarction.

For subcutaneous use Elonox should not be mixed with other injections or infusions.

Intravenous bolus injection
For acute ST-segment Elevation Myocardial Infarction, treatment is to be initiated with a single intravenous bolus injection immediately followed by a subcutaneous injection.

4.2 Recommended Dose and Dosage Adjustment

Prophylaxis in patients at risk of venous thromboembolism following hip or knee surgery (e.g. orthopedic surgery)
The recommended dose of Elonox is 30 mg (3 000 IU) every 12 hours administered by subcutaneous injection. Provided that hemostasis has been established, the initial dose should be given 12 to 24 hours after surgery. The usual duration of treatment is from 7 to 14 days.

Treatment should be continued for as long as the risk of DVT persists. Continued therapy with Elonox 40 mg once daily for 3 weeks following the initial phase of thromboprophylaxis in hip replacement surgery patients has been proven to be beneficial.

Prophylaxis in patients at risk of thromboembolism following abdominal or colorectal surgery
In patients undergoing abdominal surgery who are at risk for thromboembolic complications, the recommended dose of Elonox is 40 mg (4 000 IU) once daily administered by subcutaneous injection, with the initial dose given 2 hours prior to surgery (see 7 WARNINGS AND PRECAUTIONS, General, Selection of General Surgery Patients). The usual duration of treatment is from 7 to 10 days for a maximum of 12 days.

Patients at high risk for thromboembolic complications following high risk abdominal, gynecological or urological and colorectal surgery, for cancer, who are not at risk of bleeding may benefit from an extended prophylaxis up to 4 weeks.

Prophylaxis in Medical Patients
In medical patients at risk for deep vein thrombosis due to severely restricted mobility during acute illness (see 7 WARNINGS AND PRECAUTIONS, General, Selection of Medical Patients), the recommended dose of Elonox is 40 mg (4 000 IU) once daily by subcutaneous injection. The usual duration of administration is 6 to 11 days.

Treatment of Deep Vein Thrombosis, with or without Pulmonary Embolism
Elonox can be administered subcutaneously either as 1.5 mg/kg once daily or as twice daily injections of 1 mg/kg.

The 1.5 mg/kg once daily dose is the equivalent of 150 IU/kg and should be given at the same time every day. The single daily dose should not exceed 18 000 IU. The expected plasma anti-Xa levels during subcutaneous treatment, when enoxaparin is used as the reference standard, would be < 0.3 IU anti-Xa/mL before injection and < 1.7 IU anti-Xa/mL 3 - 4 hours post injection. The measurement of plasma anti-Xa circulating activities depends on the experimental conditions of the assay, particularly on the reference standard used.

In patients with complicated thromboembolic disorders (i.e. with increased risk of recurrent venous thromboembolism (VTE) such as obese patients, cancer patients or patients with symptomatic PE), a dose of 1 mg/kg administered twice daily is recommended. This is the equivalent of 100 IU/kg. The expected plasma anti-Xa levels during subcutaneous treatment, when enoxaparin is used as the reference standard, would be < 0.3 IU anti-Xa/mL before injection and < 1.15 IU anti-Xa/mL 3 - 4 hours post injection.

Oral anticoagulant therapy should be initiated as soon as possible, and Elonox should be continued until a therapeutic anticoagulant effect has been achieved (INR: 2 to 3), in general for approximately 7 days.

Treatment of Unstable Angina or non-Q-wave Myocardial Infarction
The recommended dose of Elonox is 1 mg/kg every 12 hours by subcutaneous injection. This is the equivalent of 100 IU/kg. The maximum dose should not exceed 10 000 IU/12 hours. The expected plasma anti-Xa levels during subcutaneous treatment would be < 0.3 IU anti-Xa/mL before injection and < 1.15 IU anti-Xa/mL 3 - 4 hours after injection. Treatment should continue for a minimum of 2 days until clinical stabilization has been achieved, in general, for up to 8 days. The effect of the short-term treatment was sustained over a one-year period.

Concomitant therapy with acetylsalicylic acid (ASA) (100 to 325 mg once daily) is recommended (see 7 WARNINGS AND PRECAUTIONS, Peri-Operative considerations-Percutaneous coronary revascularisation procedures).

Treatment of acute ST-segment Elevation Myocardial Infarction
In patients with acute-ST-segment elevation myocardial infarction, the recommended dose of Elonox injection is a **single intravenous bolus of 30 mg** plus a 1 mg/kg subcutaneous dose followed by 1 mg/kg administered subcutaneously every 12 hours (maximum 100 mg for each of the first two subcutaneous doses only, followed by 1 mg/kg subcutaneous dosing for the remaining doses). For dosage in patients ≥ 75 years of age, see section below entitled Geriatrics. When administered in conjunction with a thombolytic (fibrin specific or non-fibrin specific), Elonox injection should be given between 15 minutes before and 30 minutes after the start of fibrinolytic therapy. All patients should receive acetylsalicylic acid (ASA) as soon as they are identified as having STEMI and maintained with 75 to 325 mg once daily unless contraindicated. The recommended duration of Elonox injection treatment is 8 days or until hospital discharge, whichever comes first.

For patients managed with Percutaneous Coronary Intervention (PCI):
If the last Elonox subcutaneous administration was given less than 8 hours before balloon inflation, no additional dosing is needed. If the last Elonox subcutaneous administration was given more than 8 hours before balloon inflation, an intravenous bolus of 0.3 mg/kg of Elonox injection should be administered (see 7 WARNINGS AND PRECAUTIONS, Peri-Operative considerations - Percutaneous coronary revascularisation procedures).

Prevention of thrombus formation in the extra corporeal circulation during hemodialysis
In patients with chronic renal failure, undergoing hemodialysis and that are not at high risk of hemorrhage, the following dosage is recommended:

- Optimization of dosage is required for each individual patient (different clotting stimuli are produced by different dialysis circuits and membranes, and there is inter-patient variability).
- A starting dose of enoxaparin, ranging from 0.5 - 1.0 mg/kg, can be administered into the arterial line of the circuit at the beginning of the dialysis session. The effect of this dose range is usually sufficient for a 4-hour session. This dose range recommendation stem from results in published clinical studies (see 14 CLINICAL TRIALS).
- Doses in subsequent dialysis session can be adjusted, based on the outcome of the previous dialysis.

Geriatrics (≥ 75 years of age)
For treatment of acute ST-segment Elevation Myocardial Infarction in geriatric patients ≥ 75 years of age, do not use an initial intravenous bolus. Initiate dosing with 0.75 mg/kg subcutaneously every 12 hours (maximum 75 mg for each of the first two subcutaneous doses only, followed by 0.75 mg/kg subcutaneous dosing for the remaining doses). No dose adjustment is necessary for other indications in geriatric patients unless kidney function is impaired.

Use in Patients with Renal Impairment
All patients with renal impairment treated with low molecular weight heparins should be monitored carefully.

Exposure to enoxaparin increases with degree of renal impairment. In patients with renal impairment, the increased exposure to enoxaparin has been shown to increase risk of bleeding (see 10.3 Pharmacokinetics, Special Populations and Conditions, Renal Insufficiency).

For the prevention of thrombus formation in the extra corporeal circulation during hemodialysis, see 4 DOSAGE AND ADMINISTRATION, Prevention of thrombus formation in the extra corporeal circulation during hemodialysis.

A dosage adjustment is required for patients with severe renal impairment (creatinine clearance < 30 mL/min) since enoxaparin exposure is significantly increased in this patient population. The following dosage adjustments are recommended for prophylaxis and treatment in patients with **severe** renal impairment:

- For prophylaxis in conjunction with hip or knee orthopedic surgery, the recommended dosage is **30 mg (3 000 IU) once daily**
- For prophylaxis in conjunction with abdominal or colorectal surgery, or for prophylaxis in medical patients at risk of DVT, the recommended dosage is **20 mg (2 000 IU) or 30 mg (3 000 IU) once daily** based on individual risk/benefit assessment
- For treatment of deep vein thrombosis, with or without pulmonary embolism, the recommended dosage is **1 mg/kg once daily**
- For treatment of unstable angina or non-Q-wave myocardial infarction, the recommended dosage is **1 mg/kg once daily**.
- For treatment of acute ST-segment Elevation Myocardial Infarction, the recommended dosage is **30 mg-single intravenous bolus plus a 1 mg/kg subcutaneous dose followed by 1 mg/kg administered subcutaneously once daily**. (Maximum 100 mg for first subcutaneous dose only)
- For treatment of acute ST-segment Elevation Myocardial Infarction in geriatric patients ≥ 75 years of age, the recommended dosage is **1 mg/kg administered subcutaneously once daily (no initial bolus)**. (Maximum 100 mg for first subcutaneous dose only)

Dosage adjustment may also need to be considered in patients who have renal characteristics close to those of patients with severe renal impairment.

Spinal/epidural anesthesia
For patients receiving spinal/epidural anesthesia see 7 WARNINGS AND PRECAUTIONS, Peri-Operative considerations section.

Pediatrics
Health Canada has not authorized an indication for pediatric use.

4.4 Administration

Subcutaneous Injection Technique
The subcutaneous injection of Elonox should be carried out with the patient sitting or lying down in a comfortable position. Inject in the subcutaneous tissue of the anterolateral and posterolateral abdominal girdle, alternatively on the left and right sides. With the thickness of skin held between the operator's thumb and finger, introduce the entire length of the needle vertically into the skin.

Arterial line injection:
Elonox is administered through the arterial line of a dialysis circuit for the prevention of thrombus formation in the extra-corporeal circulation during hemodialysis.

It must not be administered by the intramuscular route.

The Elonox pre-filled disposable syringe is ready for immediate use.

Intravenous (Bolus) Injection Technique
Elonox should be administered through an intravenous line. Elonox should not be mixed or co-administered with other medications. To avoid the possible mixture of Elonox with other drugs, the intravenous access chosen should be flushed with a sufficient amount of saline or dextrose solution prior to and following the intravenous bolus administration of Elonox to clear the port of drug. Elonox may be safely administered with normal saline solution (0.9%) or 5% dextrose in water.

Initial 30 mg bolus
The initial 30 mg bolus can be administered, using enoxaparin sodium pre-filled syringes. When graduated pre-filled syringes are used, expel the excessive volume if needed, to retain only 30 mg (0.3 mL) in the syringe. The 30 mg dose can then be directly injected into the intravenous line.

Additional bolus for Percutaneous Coronary Intervention (PCI) when last subcutaneous administration was given more than 8 hours before balloon inflation
For patients being managed with PCI, an additional intravenous bolus of 0.3 mg/kg is to be administered if last subcutaneous administration was given more than 8 hours before balloon inflation (see 4.2 Recommended Dose and Dosage Adjustment, For patients managed with Percutaneous Coronary Intervention (PCI)).

In order to assure the accuracy of the small volume to be injected, it is recommended to dilute the drug.

For example, to obtain a 3 mg/mL solution, using a 60 mg enoxaparin sodium pre-filled syringe, it is recommended to use a 50 mL infusion bag (i.e. using either normal saline solution (0.9%) or 5% dextrose in water) as follows:

Withdraw 30 mL from the infusion bag with a syringe and discard the liquid. Inject the complete contents of the 60 mg enoxaparin sodium pre-filled syringe into the 20 mL remaining in the bag. Gently mix the contents of the bag. Withdraw the required volume of diluted solution with a syringe for administration into the intravenous line.

After dilution is completed, the volume to be injected can be calculated using the following formula [Volume of diluted solution (mL) = Patient weight (kg) x 0.1] or using the table below.

The dilution should be prepared immediately before use.

Table 1. Volume to be injected through intravenous line after dilution is completed

Weight [kg]	Required dose (0.3 mg/kg) [mg]	Volume to inject when diluted to a final concentration of 3 mg/mL [mL]
45	13.5	4.5
50	15	5
55	16.5	5.5
60	18	6
65	19.5	6.5
70	21	7
75	22.5	7.5
80	24	8
85	25.5	8.5
90	27	9
95	28.5	9.5
100	30	10

Care should be taken to ensure use of the correct formulation, either Elonox (100 mg/mL concentration) or Elonox HP (150 mg/mL concentration), when using these products.

Important: When the Elonox dose to be given is equivalent to the full amount of the pre-filled syringe, no attempt should be made to expel air prior to giving the injection. If the graduated syringes (60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/mL, 120 mg/0.8 mL, 150 mg/mL) are used and the dose of Elonox has to be adjusted, it is necessary to expel the air bubble and any excess drug solution.

Under normal conditions of use, enoxaparin sodium does not modify global clotting tests of activated partial thromboplastin time (aPTT), prothrombin time (PT) and thrombin clotting time (TT). Therefore treatment cannot be monitored with these tests. The plasma levels of the drug can be verified by measuring anti-Xa and anti-IIa activities.

4.5 Missed Dose

Patients should be instructed to take the missed dose as soon as it is remembered, unless it is almost time for the next dose. In this case, the missed dose should be skipped and the normal dosing schedule should be resumed. The patient should be instructed not to double the dose.

5 OVERDOSAGE

Accidental overdosage following administration of Elonox (enoxaparin sodium) may lead to hemorrhagic complications. Elonox should be immediately discontinued, at least temporarily, in cases of significant excess dosage. In more serious cases, protamine should be administered.

The anticoagulant effect of enoxaparin sodium is inhibited by protamine. This effect may be largely neutralized by slow intravenous injection of protamine sulfate. However, even with higher doses of protamine, the aPTT may remain prolonged to a greater extent than usually seen with unfractionated heparin. Anti-factor Xa activity is never completely neutralized (maximum about 60%).

In the event that prompt reversal of the anticoagulant effects of enoxaparin is required at any time after Elonox dosing, the following table is provided as a guide for initial use of protamine. Attending health professionals confronted with a potential overdosage of enoxaparin should always use their best clinical judgment in determining the appropriate dosing regimen of protamine to be administered.

Table 2. Neutralization of enoxaparin by protamine

	Time since Elonox dose		
	≤ 8 hours	> 8 hours and ≤ 12 hours	> 12 hours
Protamine dose	1 mg protamine per 1 mg enoxaparin	0.5 mg protamine per 1 mg enoxaparin	May not be required

A second infusion of 0.5 mg protamine per 1 mg Elonox may be administered if the aPTT measured 2 to 4 hours after the first infusion remains prolonged.

Particular care should be taken to avoid overdosage with protamine sulfate. Administration of protamine sulfate can cause severe hypotensive and anaphylactoid reactions. Because fatal reactions, often resembling anaphylaxis, have been reported with protamine sulfate, it should be given only when resuscitation equipment and treatment of anaphylactic shock are readily available.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 3. Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous injection & Intravenous injection	Solution for injection – 100 mg/mL enoxaparin sodium Pre-filled syringes with protective shield: 30 mg/0.3 mL 40 mg/0.4 mL 60 mg/0.6 mL 80 mg/0.8 mL 100 mg/mL Solution for injection HP – 150 mg/mL enoxaparin sodium Pre-filled syringes with protective shield: 120 mg/0.8 mL 150 mg/mL	water for injection

Elonox (enoxaparin sodium) 100 mg/mL is available in pre-filled syringes offered with a system that shields the needle after injection:

- Single dose 30 mg/0.3 mL pre-filled syringes 27 G ½ Inch in packs of 10 syringes per carton, 2 pre-filled syringes with protective shield per blister, each in individual blister pack.
- Single dose 40 mg/0.4 mL pre-filled syringes 27 G ½ Inch in packs of 10 syringes per carton, 2 pre-filled syringes with protective shield per blister, each in individual blister pack.
- Single dose 60 mg/0.6 mL pre-filled syringes 27 G ½ Inch in packs of 10 syringes per carton, 2 pre-filled syringes with protective shield per blister, each in individual blister pack.
- Single dose 80 mg/0.8 mL pre-filled syringes 27 G ½ Inch in packs of 10 syringes per carton, 2 pre-filled syringes with protective shield per blister, each in individual blister pack.
- Single dose 100 mg/mL pre-filled syringes 27 G ½ Inch in packs of 10 syringes per carton, 2 pre-filled syringes with protective shield per blister, each in individual blister pack.

The 60 mg/0.6 mL, 80 mg/0.8 mL, and the 100 mg/mL syringes are imprinted with a graduation scale of 1.0 mL with major increments of 0.1 mL and minor increments of 0.025 mL.

Elonox HP (enoxaparin sodium) 150 mg/mL (High Potency) is available in pre-filled syringes offered with a system that shields the needle after injection:

- Single dose 120 mg/0.8 mL pre-filled syringes 27 G ½ Inch in packs of 10 syringes per carton, 2 pre-filled syringes with protective shield per blister, each in individual blister pack.
- Single dose 150 mg/mL pre-filled syringes 27 G ½ Inch in packs of 10 syringes per carton, 2 pre-filled syringes with protective shield per blister, each in individual blister pack.

The 120 mg/0.8 mL, and the 150 mg/mL syringes are imprinted with a graduation scale of 1.0 mL with major increments of 0.1 mL and minor increments of 0.02 mL.

Each Elonox presentation has a solution pH of 5.5 - 7.5 with an approximate anti-Factor Xa activity of 100 IU per 1 mg of drug (with reference to the W.H.O. First International Low Molecular Weight Heparin Reference Standard).

Composition
Elonox (enoxaparin sodium) pre-filled syringe: each syringe contains 100 mg/mL of enoxaparin sodium in water for injection. The solution in the pre-filled syringe is preservative-free and intended for use as a single-dose injection.

Elonox HP (enoxaparin sodium) pre-filled syringe: each syringe contains 150 mg/mL of enoxaparin sodium in water for injection. The solution in the pre-filled syringe is preservative-free and intended for use as a single-dose injection.

The pH of the syringe solution is 5.5 - 7.5 with an approximate anti-Factor Xa activity of 100 IU per 1 mg of drug (with reference to the W.H.O. First International Low Molecular Weight Heparin Reference Standard).

Description
Elonox (enoxaparin sodium) is a low molecular weight heparin fragment, which is obtained by controlled depolymerization of natural heparin from porcine intestinal mucosa. It possesses antithrombotic action. Enoxaparin is composed of molecules with and without a specially characterized pentasaccharide, the antithrombin binding site that is essential for high affinity binding to the plasma protein antithrombin (formerly referred to as antithrombin III). With a molecular weight range of 3 800 - 5 000 daltons (versus 15 000 daltons for heparin), the enoxaparin molecule is too small to bind simultaneously to thrombin and antithrombin, the primary anticoagulant factor in blood.

7 WARNINGS AND PRECAUTIONS

General

Elonox (enoxaparin sodium) must NOT be administered by the intramuscular route.

Elonox cannot be used interchangeably (unit for unit) with unfractionated heparin (UFH) or other low molecular weight heparins (LMWHs) as they differ in their manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units and dosages. Special attention and compliance with instructions for use of each specific product is required during any change in treatment.

Determination of anti-Xa levels in plasma is the only method available for monitoring enoxaparin sodium activity. The effect of enoxaparin sodium on global clotting tests such as aPTT, PT and TT is dose-dependent. At lower doses, used in prophylaxis, enoxaparin sodium does not prolong these tests. At higher doses, aPTT prolongation is observed but treatment cannot be monitored with these tests.

Measurement of peak anti-Xa levels at about 4 hours post-dose should be considered in patients at higher risk of bleeding and receiving Elonox, such as the elderly, patients with renal impairment or the extremes of body weight, during pregnancy, or for children. At treatment doses, peak anti-Xa levels should generally be maintained at no more than 1.5 IU/mL in these patients (see 10 CLINICAL PHARMACOLOGY, and 7 WARNINGS AND PRECAUTIONS, Monitoring and Laboratory Tests).

Selection of General Surgery Patients

Risk factors associated with postoperative venous thromboembolism following general surgery include history of venous thromboembolism, varicose veins, obesity, heart failure, malignancy, previous long bone fracture of a lower limb, bed rest for more than 5 days prior to surgery, predicted duration of surgery of more than 30 minutes, age 60 years or above.

Selection of Orthopedic Surgery Patients

Major orthopedic surgery carried out on the lower extremities is associated with a higher risk of VTE, and a notable percentage of patients will develop a thrombosis if they are not given prophylaxis.

Factors shown to predispose patient to VTE following major orthopedic surgery include a history of VTE, current obesity, delayed mobilization, advanced age or cancer. Other risk factors that might be clinically important include congestive heart failure, chronic obstructive pulmonary disease (COPD) as well as female gender.

High risk period for VTE lasts up to 3 months after hip surgery, therefore thromboprophylaxis should start as soon as possible and continue for up to 28 to 35 days after surgery.

Selection of Medical Patients

The risk factors for the development of thrombosis in the individual medical patient are important in determining whether thromboprophylaxis is appropriate. In one clinical trial, enoxaparin sodium 40 mg once daily reduced the risk of the development of deep vein thrombosis (DVT) from 14.9% to 5.5% during the short term risk period in bedridden patients. Careful consideration should be given to the selection of patients. Patients at high risk of developing DVT or other thrombosis (such as patients with a malignant disease, a history of thrombophilia and known deficiency in antithrombin III, protein C or protein S, or APC resistance) are not candidates for therapy with Elonox 40 mg once daily because this dose may be inadequate for those patients. Furthermore, Elonox should not be given for thromboprophylaxis in medical patients who are bedridden due to infections with septic shock. Medical patients who require short term thromboprophylaxis for the risk of DVT due to severely restricted mobility during acute illness including moderate to severe heart failure, acute respiratory failure revealing or complicating chronic respiratory insufficiency not requiring ventilatory support, and acute respiratory infections may be selected for thromboprophylaxis with Elonox 40 mg once daily.

The safety and efficacy of enoxaparin sodium 40 mg once daily following hospital discharge has not been established in the medical patient population. In the clinical trial mentioned above, thromboembolic events were not common following discontinuation of enoxaparin sodium 40 mg at discharge. However, a significant number of patients did require antithrombotic therapy following discharge; specifically 13.63%. During the 3-month period following discharge, less than 1% of events were serious and included deep vein thrombosis, pulmonary embolism and death which is considered to be thromboembolic in origin. Therefore, the physician should consider whether thromboprophylaxis post-discharge would be necessary for the individual patient.

Elonox at a dose of 40 mg once daily should not be given for thromboprophylaxis other than deep vein thrombosis (DVT) prevention or in medical patients who, in the opinion of the attending health professional, would be at a higher risk of thromboembolism (such as patients with a malignant disease, a history of thrombophilia and known deficiency in antithrombin III, protein C or protein S, or APC resistance). Furthermore, Elonox should not be given for thromboprophylaxis in medical patients who are bedridden due to infections with septic shock. Patients with severe COPD complicated by right heart failure are candidates for another form of thromboprophylaxis. Enoxaparin sodium at a dose of 40 mg once daily has been studied in medical patients who require short term thromboprophylaxis to prevent the development of DVT while they are bedridden (6 to 11 days). If, in the opinion of the attending health professional, longer thromboprophylaxis is necessary, then consideration should be given to a thromboprophylactic agent, which has been proven effective.

Patients with Extreme Body Weight

Safety and efficacy of low molecular weight heparins in high weight (e.g. > 120 kg) and low weight (e.g. < 45 kg) patients have not been fully determined. Individualised clinical and laboratory monitoring is recommended in these patients (see also 10.3 Pharmacokinetics, Special Population and Conditions, Obesity/Low-Weight Patients).

- Low-weight patients – prophylactic treatment
  An increase in exposure of enoxaparin sodium with prophylactic dosages (non-weight adjusted) has been observed in low-weight women (< 45 kg) and low-weight men (< 57 kg), which may lead to a higher risk of bleeding. Therefore, careful clinical monitoring is advised in these patients (see 10.3 Pharmacokinetics, Special Population and Conditions, Low-Obesity/Low-Weight Patients).
- Obese patients – prophylactic treatment
  Obese patients are at higher risk for thromboembolism. The safety and efficacy of prophylactic doses in obese patients (BMI > 30 kg/m^2) has not been fully determined and there is no consensus for dose adjustment. These patients should be observed carefully for signs and symptoms of thromboembolism (see 10.3 Pharmacokinetics, Special Population and Conditions, Obesity/Low-Weight Patients).

Cardiovascular

Acute Coronary Disease

When thrombolytic treatment is considered appropriate in patients with unstable angina, non-Q-wave myocardial infarction and acute ST-segment Elevation Myocardial Infarction, the concomitant use of an anticoagulant such as enoxaparin sodium may increase the risk of bleeding.

Patients with Prosthetic Heart Valves

Cases of prosthetic valve thrombosis have been reported in patients who have received low molecular weight heparins for thromboprophylaxis. Some of these patients were pregnant women in whom thrombosis led to maternal and/or fetal deaths. Pregnant women are at higher risk of thromboembolism (see 7.1.1 Pregnant Women).

Gastrointestinal
Elonox should be used with caution in patients with gastrointestinal ulceration.

Hematologic

Hemorrhage

Bleeding may occur in conjunction with unfractionated heparin or low molecular weight heparin use. As with other anticoagulants, Elonox should be used with extreme caution in patients at increased risk of hemorrhage. Bleeding can occur at any site during therapy with enoxaparin sodium. An unexpected drop in hematocrit or blood pressure should lead to a search for a bleeding site (see 8.1 Adverse Reaction Overview, Bleeding).

Thrombocytopenia

Thrombocytopenia of any degree should be monitored closely.

Heparin-induced thrombocytopenia (HIT)

Heparin-induced thrombocytopenia can occur with the administration of Elonox. Its incidence is unknown at present.

Use of enoxaparin sodium in patients with a history of immune mediated HIT within the past 100 days or in the presence of circulating antibodies is contraindicated (see 2 CONTRAINDICATIONS). Circulating antibodies may persist several years.

Enoxaparin sodium is to be used with extreme caution in patients with a history (more than 100 days) of heparin-induced thrombocytopenia without circulating antibodies. The decision to use enoxaparin sodium in such a case must be made only after a careful benefit risk assessment and after non-heparin alternative treatments are considered.

Platelets

Platelet counts should be determined prior to the commencement of treatment with Elonox and, subsequently, twice weekly for the duration of therapy.

Caution is recommended when administering Elonox to patients with congenital or drug induced thrombocytopenia, or platelet defects.

Hepatic/Biliary/Pancreatic
Elonox should be used with caution in patients with hepatic insufficiency.

Immune
During Elonox administration, special caution is necessary in rapidly developing thrombocytopenia and severe thrombocytopenia (< 100 000/mcL). A positive or indeterminate result obtained from *in vitro* tests for antiplatelet antibody in the presence of enoxaparin or other low molecular weight heparins and/or heparin would contraindicate enoxaparin sodium.

Monitoring and Laboratory Tests
Enoxaparin sodium has only a moderate prolonging effect on clotting time assays such as aPTT or thrombin time. For lab monitoring of effect, anti-Xa methods are recommended. Prolongation of aPTT during therapy with enoxaparin sodium to the same extent as with unfractionated heparin should only be used as a criteria of overdose. Dose increases aimed at prolonging aPTT to the same extent as with unfractionated heparin could cause overdose and bleeding.

Enoxaparin sodium is administered subcutaneously, and therefore, the individual patient's antifactor Xa activity level will not remain within the range that would be expected with unfractionated heparin by continuous intravenous infusion throughout the entire dosing interval. In patients treated with enoxaparin 1 mg/kg twice daily for proximal deep vein thrombosis, mean peak plasma anti-Xa levels were 0.91 IU/mL. In patients given enoxaparin 1 mg/kg twice daily for acute treatment of unstable angina, peak anti-Xa activity levels were 1 - 1.1 IU/mL. At steady-state in patients given a 1.5 mg/kg once a day regimen for treatment of DVT, mean peak activity was 1.7 IU anti-Xa/mL. The steady-state is practically achieved at the second or the third dose depending on the dosage regimen, once or twice daily, respectively. Elonox should be administered as directed (see 4 DOSAGE AND ADMINISTRATION).

As with all anti-thrombotic agents, there is a risk of systemic bleeding with enoxaparin sodium administration. Consequently, therapy should not be started before primary hemostasis has been established and preferably no sooner than 12 hours after surgery (see 4 DOSAGE AND ADMINISTRATION). Care should be taken with enoxaparin sodium use in high dose treatment of newly operated patients.

After treatment is initiated, patients should be carefully monitored for bleeding complications. This may be done by regular physical examination of the patients, close observation of the surgical drain and periodic measurements of hemoglobin, and anti-factor Xa determinations.

With normal prophylactic doses, enoxaparin sodium does not modify global clotting tests of activated partial thromboplastin time (aPTT), prothrombin time (PT) and thrombin clotting time (TT). Therefore, treatment cannot be monitored with these tests.

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 antithrombotic activity and therefore are unsuitable and unreliable for monitoring enoxaparin activity.

Peri-Operative Considerations

Spinal/Epidural Hematomas

There have been cases of epidural hematomas reported with the use of low molecular weight heparins (LMWH) and spinal/epidural anesthesia or spinal puncture procedures, resulting in long term or permanent paralysis. The risk of these events is greater with higher Elonox dosage regimens, use of post-operative indwelling catheters or the concomitant use of additional drugs affecting hemostasis such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other drugs affecting coagulation including glycoprotein IIb/IIIa antagonists. The risk of spinal hematoma appears to be increased by traumatic or repeated epidural or spinal puncture, history of spinal surgery or spinal deformity. Elonox should be given after spinal/epidural anesthesia only if the anesthesiologist considers the spinal/epidural puncture as uncomplicated. Consideration should be given to delaying the next dose for 24 hours if the puncture induced trauma.

The concomitant use of a neuraxial blockade and of an anticoagulant therapy is a clinical decision that should be made after careful assessment of the benefits and risks to the individual patient, in the following situations:

- In patients already treated with anticoagulants, the benefits of a neuraxial blockade must be carefully balanced against the risks.
- In patients planned to undergo elective surgery with neuraxial blockade, the benefits of anticoagulant therapy must be carefully balanced against the risks.

To reduce the potential risk of bleeding associated with the concurrent use of enoxaparin sodium and epidural or spinal anesthesia/analgesia, or spinal puncture procedures, the pharmacokinetic profile of the drug should be considered (see 10 CLINICAL PHARMACOLOGY). Placement and removal of the catheter is best performed when the anticoagulant effect of enoxaparin is low; however, the exact timing to reach a sufficiently low anticoagulant effect in each patient is not known. In the case of patients with spinal lumbar puncture, spinal anesthesia or epidural anesthesia, a minimum of 12 hours should elapse between the Elonox injection at prophylactic doses or for 24 hours at treatment doses, and the insertion or removal of the spinal/epidural catheter or needle. A specific recommendation for timing of a subsequent LMWH dose after catheter removal cannot be made. The timing of the next dose must be based on a benefit-risk assessment considering both the risk for thrombosis and the risk for bleeding in the context of the procedure and patient risk factors.

If anticoagulation is administered in the setting of epidural/spinal anesthesia or spinal puncture procedures, continuous monitoring must be exercised to detect any signs and symptoms of neurological impairment such as midline back pain, sensory and motor deficits (numbness or weakness in lower limbs), bowel and/or bladder dysfunction (see 8 ADVERSE REACTIONS). Patients should be instructed to inform their physician immediately if they experience any of the above signs or symptoms. If signs or symptoms of spinal hematoma are suspected, urgent diagnosis and treatment including spinal cord decompression should be initiated immediately.

For patients with creatinine clearance < 30 mL/minute, additional clinical considerations are necessary, given that elimination of enoxaparin is more prolonged; consideration should be given to doubling the timing of removal of a catheter.

Percutaneous coronary revascularisation procedures

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 Elonox injection doses. It is important to achieve hemostasis at the puncture site after PCI. In case a closure device is used, the sheath can be removed immediately. If a manual compression method is used, it is recommended to remove the sheath 6 hours after the last intravenous/subcutaneous injection. If the treatment with enoxaparin sodium is to be continued, 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 (see 4.2 Recommended Dose and Dosage Adjustment, Treatment of Unstable Angina or non-Q-wave Myocardial Infarction and Treatment of acute ST-segment Elevation Myocardial Infarction).

Renal
Elonox should be used with caution in patients with renal insufficiency.

Elonox dosage should be reduced in patients with severely impaired renal function (see 10.3 Pharmacokinetics, Special Populations and Conditions, Renal Insufficiency, and 4.2 Recommended Dose and Dosage Adjustment, Use in Patients with Renal Impairment).

Patients with impaired renal function should be carefully monitored because half-life for anti-Xa activity after administration of low molecular weight heparin may be prolonged in this patient population (see 4.2 Recommended Dose and Dosage Adjustment, Use in Patients with Renal Impairment).

In patients with renal impairment, there is an increase in exposure to enoxaparin which increases the risk of bleeding. Since exposure to enoxaparin is significantly increased in patients with severe renal impairment (creatinine clearance < 30 mL/min), a dosage adjustment is recommended for both therapeutic and prophylactic dosage ranges (see 10.3 Pharmacokinetics, Special Populations and conditions, Renal Insufficiency, and 4.2 Recommended Dose and Dosage Adjustment, Use in Patients with Renal Impairment).

7.1 Special Populations

7.1.1 Pregnant Women

Teratogenic effects: As with other low molecular weight heparins, Elonox should not be used in pregnant women unless the therapeutic benefits to the patients outweigh the possible risks. There have been reports of congenital anomalies in infants born to women who received low molecular weight heparin during pregnancy including cerebral anomalies, limb anomalies, hypospadias, peripheral vascular malformation, fibrotic dysplasia and cardiac defects. A causal relationship has not been established nor has the incidence been shown to be higher than in the general population.

Non-teratogenic effects: There have been post-marketing reports of fetal death when pregnant women received low molecular weight heparins. Causality for these cases has not been established. Pregnant women receiving anticoagulants, including enoxaparin sodium, are at increased risk for bleeding. Hemorrhage can occur at any site and may lead to death of mother and/or fetus. Pregnant women receiving Elonox should be carefully monitored. Pregnant women and women of child-bearing potential should be informed of the potential hazard to the fetus and the mother if Elonox is administered during pregnancy.

There are also post-marketing reports of prosthetic valve thrombosis in pregnant women with prosthetic heart valves while receiving low molecular weight heparins for thromboprophylaxis. These events led to maternal death or surgical interventions.

Pregnant women with prosthetic heart valves appear to be at exceedingly high risk of thromboembolism. An incidence of thromboembolism approaching 30% has been reported in these patients, in some cases even with apparent adequate anticoagulation at treatment doses of low molecular weight heparins or unfractionated heparin. Any attempt to anticoagulate such patients should normally only be undertaken by medical practitioners with documented expertise and experience in this clinical area.

7.1.2 Breast-feeding

It is not known whether enoxaparin sodium is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Elonox is administered to nursing women.

7.1.3 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Geriatrics (≥ 75 years of age): Elderly patients (especially patients eighty years of age and older) receiving low molecular weight heparins are at increased risk of bleeding. Careful attention to dosing and concomitant medications, especially anti-platelet preparations, is advised. Close monitoring of elderly patients with low body weight (eg. < 45 kg) and those predisposed to decreased renal function is recommended.

For treatment of acute ST-segment Elevation Myocardial Infarction in geriatric patients, the incidence of bleeding complications was higher in patients ≥ 65 years of age as compared to younger patients (< 65 years). Patients ≥ 75 years of age did not receive a 30 mg intravenous bolus prior to the normal dosage regimen and had their subcutaneous dose adjusted to 0.75 mg/kg every 12 hours (see 4.2 Recommended Dose and Dosage Adjustment, Treatment of acute ST-segment Elevation Myocardial Infarction, Geriatrics (≥ 75 years of age)).

In the clinical study for treatment of acute STEMI, with adjustment in dose for patients ≥ 75 years of age, there was no evidence of difference in efficacy between patients ≥ 75 years of age (n = 1241) and patients less than 75 years of age (n = 9015).

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

It is recommended that agents which affect hemostasis should be discontinued prior to Elonox therapy unless strictly indicated. If the combination is indicated, Elonox should be used with careful clinical and laboratory monitoring when appropriate.

Elonox should be used with caution in patients receiving oral anticoagulants, platelet inhibitors, non-steroidal anti-inflammatories and thrombolytic agents because of increased risk of bleeding. Aspirin, unless contraindicated, is recommended in patients treated for unstable angina or non-Q-wave myocardial infarction and acute ST-segment Elevation Myocardial Infarction (see 4 DOSAGE AND ADMINISTRATION).

9.7 Drug-Laboratory Test Interactions

Since enoxaparin sodium use may be associated with a rise in hepatic transaminases, this observation should be considered when liver function tests are assessed (see 8.5 Post Market Adverse Reactions, Liver).

11 STORAGE, STABILITY AND DISPOSAL

Store at 15°C to 25°C. Protect from heat.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

PATIENT MEDICATION INFORMATION
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PrELONOX
Enoxaparin sodium
Solution for Injection, 100 mg/mL

Read this carefully before you start taking **Elonox** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Elonox**.

***Elonox** is a biosimilar biologic drug (biosimilar) to the reference biologic drug Lovenox. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.*

What is Elonox used for?
Elonox is used:

- To prevent the formation of deep vein thrombosis (blood clots), which can occur as a complication of orthopedic surgery such as hip or knee surgery or of intra-abdominal (inside the body cavity below diaphragm which contains stomach, intestines, liver, and other organs) surgeries;
- To prevent the formation of deep vein thrombosis in medical patients who are at risk of thromboembolic (blockage of blood vessel by a blood clot) complications due to severely restricted mobility during acute illnesses (cardiac insufficiency [reduced ability of heart to pump blood], respiratory failure or severe chest infections);
- To treat the deep vein thrombosis with or without pulmonary embolism (blockage of blood vessel in the lungs);
- To treat the unstable angina and non-Q-wave myocardial infarction (death of a part of the heart muscle that does not involve full thickness of the heart wall), concurrently with acetylsalicylic acid (ASA);
- To treat the acute ST-segment Elevation Myocardial Infarction (STEMI), a particular form of heart attack. This indication includes patients to be managed medically or those with subsequent Percutaneous Coronary Intervention (PCI), a procedure that opens up a coronary artery (blood vessel that brings blood and oxygen to the heart muscle) and restores blood flow;
- To prevent clotting in the extra-corporeal circulation during hemodialysis.

How does Elonox work?
Elonox is an anti-thrombotic drug. This means that Elonox helps to prevent blood clots from forming in patients who have either undergone surgery or are suffering from a medical condition that limits their mobility. It can also treat existing blood clots in deep veins or in unstable coronary artery disease (Unstable Angina or non Q-wave Myocardial Infarction).

What are the ingredients in Elonox?

Medicinal ingredients: Enoxaparin sodium.

Non-medicinal ingredients: Water for injection.

Elonox comes in the following dosage forms:
Elonox 100 mg/mL is available in pre-filled syringes offered with a system that shields the needle after injection:

- Single dose 30 mg/0.3 mL pre-filled syringes with protective shield
- Single dose 40 mg/0.4 mL pre-filled syringes with protective shield
- Single dose 60 mg/0.6 mL pre-filled syringes with protective shield
- Single dose 80 mg/0.8 mL pre-filled syringes with protective shield
- Single dose 100 mg/mL pre-filled syringes with protective shield

Do not use Elonox if you have:

- a known allergy to Elonox or any of its constituents;
- a known allergy to any other low molecular weight heparins and/or heparin;
- thrombocytopenia (a severe decrease in the number of platelets in the blood);
- History (within the past 100 days) of heparin-induced thrombocytopenia (HIT) (a blood clotting disorder caused by heparin).
- bacterial endocarditis (bacterial infection inside of the heart);
- active bleeding;
- a major clotting disorder;
- gastric or duodenal ulcer (defect of the internal walls of the stomach or small intestine);
- cerebrovascular accident (except if there are systemic emboli);
- severe uncontrolled hypertension (high blood pressure);
- eye problems due to diabetes (diabetic retinopathy) or hemorrhage (bleeding);
- a tendency to bleeding regardless of the reason;
- injury or surgery on the brain, spinal cord, eyes and ears;
- kidney problems;
- liver problems;
- spinal/epidural anesthesia is contraindicated where repeated treatment doses of Elonox (1 mg/kg every 12 hours or 1.5 mg/kg once daily) are required, due to an increased risk of bleeding;
- other conditions or diseases involving an increased risk of bleeding;

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Elonox. Talk about any health conditions or problems you may have, including if you:

- have prosthetic (artificial) heart valve,
- have a stroke (cerebrovascular accident),
- have a known allergy to Elonox or any of its constituents, or to other low molecular weight heparins and/or heparin,
- have thrombocytopenia (a severe decrease in the number of platelets in the blood), a history of heparin-induced thrombocytopenia (HIT) (a blood clotting disorder caused by heparin).
- have bacterial endocarditis (bacterial infection inside of the heart),
- have a major clotting disorder,
- have gastric or duodenal ulcer (defect of the internal walls of the stomach or small intestine),
- have hypertension (high blood pressure),
- have a tendency to bleeding regardless of the reason,
- have an injury or had surgery (spinal surgery with spinal/epidural anesthesia) involving the central nervous system, eyes or ears,
- have a spinal defect (or deformity),
- have kidney problems,
- have liver problems,
- have eye problems due to diabetes or hemorrhage (bleeding).

It is important that you provide your doctor with an accurate history of any serious illnesses you may have had in the past or any current medical conditions, as these may influence the action of Elonox.

You should also inform your doctor at once if you are pregnant or if you are breast-feeding, so he can evaluate the possible risks to you and the infant.

Other warnings you should know about:
Certain medications may intensify the anticoagulant effect (increase the anti-clotting effect) of Elonox. Therefore, it is important for you to advise your doctor of all drugs that you are presently taking.

It is necessary that you follow the instructions of your doctor or nurse carefully. Only give yourself the injections prescribed and do so the entire time period specified by your doctor.

Do not take any drugs other than those prescribed by your doctor while you are taking Elonox.

If you need to consult with another doctor or see your dentist, be absolutely sure to tell them that you are being treated with Elonox.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Elonox:

- Drugs that affect blood clotting. These agents include medication such as:
  - Acetylsalicylic acid (ASA), salicylates, and non-steroidal anti-inflammatories (e.g. diclofenac, ibuprofen, ketorolac);
  - Prednisolone;
  - Dextran, vitamin K antagonists, clopidogrel, ticlopidine and dipyridamole.

How to take Elonox:
Elonox is a prescription drug and must be used as directed. Usually it is administered as a subcutaneous injection, which means the injection is made just under the surface of the skin. For some conditions, Elonox may be administered as an intravenous (IV) injection. Elonox must NOT be administered by the intramuscular route.

Usual dose:

Hip or Knee Replacement Surgery: While you are in the hospital, your doctor or a nurse will give your first injection within 24 hours after your operation, so as to prevent blood clots from forming. After that, your doctor or a nurse will give you 2 subcutaneous injections every day (one injection every 12 hours) while you are in hospital.

In case of hip replacement surgery, after completing the treatment with 2 subcutaneous injections per day, your doctor may ask you to take 1 subcutaneous injection every day for the following days at home or in hospital for an additional 3 weeks.

Abdominal or Colorectal Surgery: While you are in the hospital, your doctor or a nurse will give your first injection 2 hours prior to surgery. After that, your doctor or a nurse will give you 1 subcutaneous injection once a day while you are in hospital, your doctor may ask you to continue to take 1 subcutaneous injection every day for up to 4 weeks.

Medical Patients: While you are in the hospital, your doctor or a nurse will give you 1 subcutaneous injection once a day. The usual duration of administration is 6 to 11 days.

Treatment of Deep Vein Thrombosis, with or without Embolism: while you are in the hospital, your doctor or a nurse will give you 1 subcutaneous injection once or twice daily for about 10 days.

Treatment of Unstable Angina or Non-Q-Wave Myocardial Infarction: while you are in the hospital, your doctor or a nurse will give you 2 subcutaneous injections every day (one injection every 12 hours) along with oral ASA (100 to 325 mg once daily) for a minimum of 2 days.

Treatment of acute ST-segment Elevation Myocardial Infarction (STEMI): while you are in the hospital, your doctor or a nurse will give you a single intravenous (IV) injection followed by 2 subcutaneous injections every day (one injection every 12 hours) along with oral ASA (75 to 325 mg once daily) for a minimum of 8 days, unless contraindicated.

It is possible that after you go home, you may need to continue your injections of Elonox for a few days.

Prevention of thrombus formation in the extra-corporeal circulation during hemodialysis: while you are in the hospital, your doctor or a nurse will inject Elonox 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.

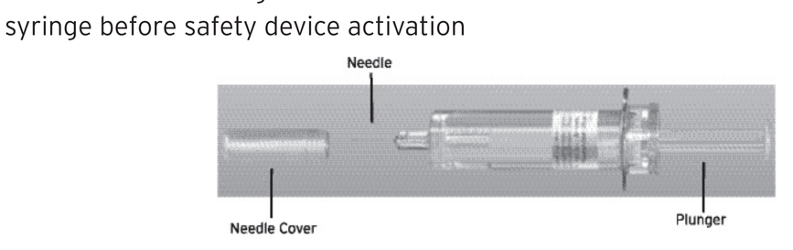
Instructions for self-injection of Elonox
Your doctor may want you to continue your Elonox injections at home for a few days. **If so, he or a nurse will show you how to administer your Elonox injections before you are released from hospital. It is essential that you follow these instructions exactly. If you have questions, be sure you ask your doctor or nurse to provide the explanations you require.**

Proper subcutaneous (under the skin) injection of Elonox is essential to prevent pain and bruising at the injection site.

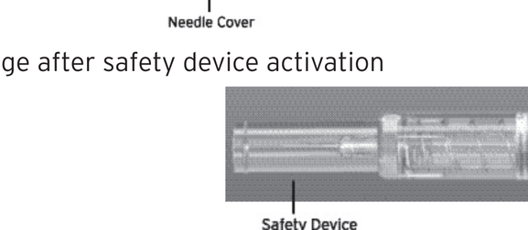
When at home, there is nothing for you to prepare. The syringe is pre-filled with the exact amount of drug required. Do not press on the plunger prior to injection.

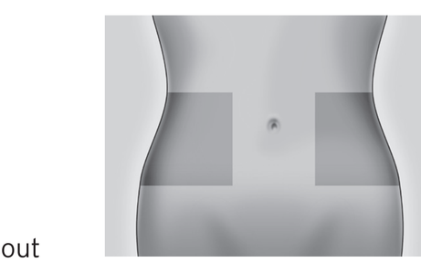
Elonox solution should be inspected visually for clarity, particulate matter, precipitation, discolouration, and leakage prior to administration. Do not use if solution shows haziness, particulate matter, discolouration or leakage.

Pre-filled syringe before safety device activation



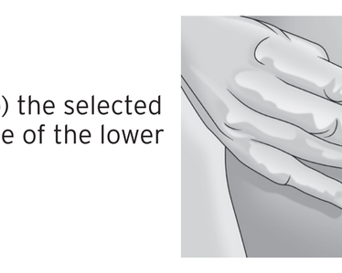
Pre-filled syringe after safety device activation

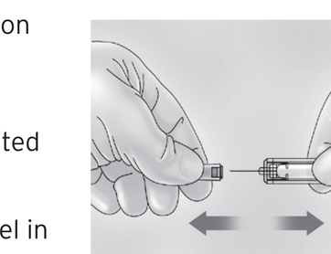




The recommended site for injection is into the fat of the lower abdomen. This should be at least 5 centimeters away from your belly button and out towards your sides.

Prior to injection, wash your hands and cleanse (do not rub) the selected site for injection with an alcohol swab. Select a different site of the lower abdomen for each injection.

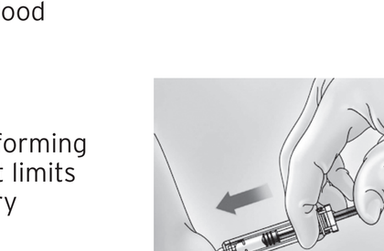




Remove the needle cover by pulling it straight off the syringe. If adjusting the dose is required, the dose adjustment must be done prior to injecting Elonox.

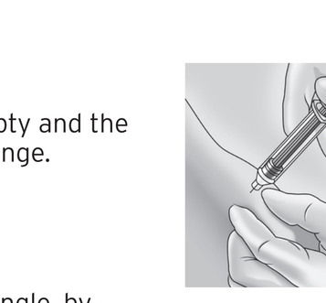
NOTE: To avoid the loss of drug when using the 30 and 40 mg pre-filled syringes, do not expel the air bubble from the syringe before the injection.

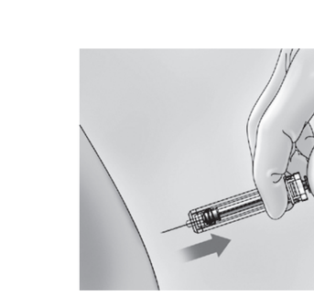
Sit or lie down in a comfortable position and gather a fold of skin with your thumb and forefinger.



Then holding the syringe at a right angle to the skin folded between your thumb and forefinger, insert the needle as far as it will go. Hold the skin fold throughout the injection process. Once the needle has been inserted, the syringe should not be moved.

Push the plunger to inject Elonox. Be sure the syringe is empty and the plunger is pushed all the way down before removing the syringe.

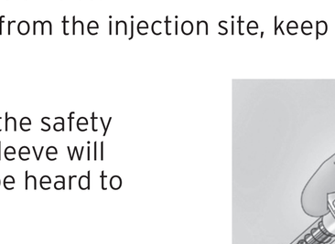




Remove the needle at a right angle, by pulling it straight out. You can now release the skin fold and apply light pressure to the skin at the injection site for several seconds with an alcohol swab. This action will help lessen any oozing of Elonox or bleeding. Do not rub the injection site.

Once the syringe is removed from the injection site, keep your finger on the plunger rod.

Orient the needle away from you and others, and activate the safety system by firmly pushing the plunger rod. The protective sleeve will automatically cover the needle and an audible "click" will be heard to confirm shield activation.



NOTE:

- The safety system can only be activated once the syringe has been emptied.
- Activation of the safety system must be done only after removing the needle from your skin.
- Do not replace the needle shield after injection.
- The safety system should not be sterilized.

Activation of the safety system may cause minimal splatter of fluid. For optimal safety activate the system while orienting it downwards away from yourself and others.

You should then safely dispose of the syringe and needle with its protective sleeve, so they remain out of reach of children.

Overdose:
Accidental overdosage may result in hemorrhaging, which cannot be treated at home. Therefore, if you suspect that you have used too much Elonox, call your doctor immediately even if you do not yet observe any unusual symptoms. Your doctor can then make arrangements to bring you to hospital for observation and/or treatment.

If you think you, or a person you are caring for, have taken too much Elonox, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If you miss a dose of this medication by a few hours, take it as soon as you remember. However if you are close to the time of the next dose, skip the missed dose and proceed with the regular dosing schedule. Do not double doses. If you are unsure about how to proceed contact your doctor or your pharmacist.

What are possible side effects from using Elonox?
These are not all the possible side effects you may have when taking Elonox. If you experience any side effects not listed here, tell your healthcare professional.

Administration of Elonox may result in bleeding which can have serious or life-threatening consequences. Hemorrhagic strokes (bleeding inside of the brain) and serious intra-abdominal bleeding (bleeding into the body cavity below diaphragm which contains stomach, intestines, liver, and other organs) have been reported. Elonox is generally well tolerated when used according to directions of use.

During your hospital stay or when using Elonox at home, it is important that you notify your doctor immediately if you notice any of the following symptoms which may be a sign of an underlying complication:

- Bleeding or oozing from the surgical wound;
- Any other bleeding episodes, for example, at the site of the injection, nosebleeds, blood in the urine or if you cough or throw up blood, or have bloody stools;
- Bleeding gums while brushing teeth;
- Spontaneous bruising (a bruise not caused by a blow or any apparent reason);
- Purplish or reddish discolouration or pain around the injection site;
- Skin discolouration as caused by ruptured blood vessels;
- Pain or swelling in any part of your leg, foot or hip;
- Dizziness;
- Headache;
- Rapid or unusual heart beat;
- Chest pain or shortness of breath;
- Vomiting;
- Confusion;
- Abdominal pain.

Talk to you doctor or pharmacist if you experience other side effects such as:

- Changes in the results of blood tests done to check how your liver is working during treatment with Elonox.
- Signs of liver problems such as loss of appetite, dark urine, light-colored stools, yellowing of the skin or eyes (jaundice).
- If you have an allergic reaction. The signs may include: skin rash, angioedema (swelling of lips, face, throat and tongue, breathing difficulties) and anaphylactic/anaphylactoid reactions including shock.
- Long term use of Elonox (greater than 3 months) may increase your risk of bone thinning (osteoporosis).
- Some patients may experience hair loss. The hair usually grows back once the treatment is discontinued.
- If you have had a spinal puncture or a spinal anesthetic and notice tingling, numbness and muscular weakness, particularly in the lower part of your body, or if you have problems controlling your bowels and/or bladder.

This is not a complete list of side effects. For any unexpected effects while taking Elonox, contact your doctor or pharmacist.

Reporting Side Effects
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store at 15°C to 25°C. Protect from heat. Keep out of reach and sight of children.

If you want more information about Elonox:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website (https://www.fresenius-kabi.com/en-ca); or by calling 1-877-821-7724.

FRESENIUS KABI

This leaflet was prepared by:
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Toronto, ON M9W 0C8
Questions or concerns? 1-877-821-7724
Last Revised October 26, 2022

20002902

350 mm

60 mm

60 mm

Printer to remove dieline

Elonox Injection English (EN) Insert (Front) Program: InDesign CC21	Fresenius Kabi Canada Ltd. Dieline: 700 mm x 1000 mm By: Haider Al-Baldawi	**Version:** 3 **Date:** November 1, 2022 **Part No.:** 20002902
Fonts: Interstate Arial	**Text Specification:** Text: 10 points on 11 points Product Name: 10 points	**Colour Specification:** Black C

Pharmacodes to be incorporated on artwork prior to printing.
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Folded sizes: 95(L) x 60(H) mm
Substrate: 40GSM Bible Paper
Pharma code: 2902