

HEPAXANE 2,000 IU (20 mg)/0.2 mL solution for injection in pre-filled syringe
HEPAXANE 4,000 IU (40 mg)/0.4 mL solution for injection in pre-filled syringe
HEPAXANE 6,000 IU (60 mg)/0.6 mL solution for injection in pre-filled syringe
HEPAXANE 8,000 IU (80 mg)/0.8 mL solution for injection in pre-filled syringe
HEPAXANE 10,000 IU (100 mg)/1 mL solution for injection in pre-filled syringe

enoxaparin sodium

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, or pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What HEPAXANE is and what it is used for
2. What you need to know before you use HEPAXANE
3. How to use HEPAXANE
4. Possible side-effects
5. How to store HEPAXANE
6. Contents of the pack and other information

1. What HEPAXANE is and what it is used for

HEPAXANE contains the active substance called enoxaparin sodium that is a low molecular weight heparins (LMWH).

HEPAXANE works in two ways.

- 1) Stopping existing blood clots from getting any bigger. This helps your body to break them down and stop them causing you harm.
- 2) Stopping blood clots forming in your blood.

HEPAXANE can be used to:

- Treat blood clots that are in your blood
- Stop blood clots forming in your blood in the following situations:
 - Before and after an operation
 - When you have an acute illness and face period of limited mobility
 - When you have unstable angina (a condition when not enough blood gets to your heart)
 - After a heart attack
- Stop blood clots forming in the tubes of your dialysis machine (used for people with severe kidney problems)

2. What you need to know before you use HEPAXANE

Do not use HEPAXANE

- If you are allergic to enoxaparin sodium or any of the other ingredients of this medicine (listed in Section 6.). Signs of an allergic reaction include: rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- If you are allergic to heparin or other Low Molecular Weight Heparins such as nadroparin, tinzaparin or dalteparin
- If you have had a reaction to heparin that caused a severe drop in the number of your clotting cells (platelets) - this reaction is called heparin-induced thrombocytopenia - within the last 100 days or if you have antibodies against enoxaparin in your blood
- If you are bleeding heavily or have a condition with a high risk of bleeding (such as stomach ulcer, recent surgery of the brain or eyes), including recent bleeding stroke.
- If you are using HEPAXANE to treat blood clots in your body and going to receive spinal or epidural anaesthesia or lumbar puncture within 24 hours.

Warnings and precautions

HEPAXANE should not be used interchangeably with other medicines belonging to the group of low molecular weight heparins. This is because they are not exactly the same and do not have the same activity and instructions for use.

Talk to your doctor or pharmacist before using HEPAXANE if:

- you have ever had a reaction to heparin that caused a severe drop in the number of your platelets
- you are going to receive spinal or epidural anaesthesia or lumbar puncture (see Operations and Anaesthetics); a delay should be respected between HEPAXANE use and this procedure
- you have had a heart valve fitted
- you have endocarditis (an infection of the inner lining of the heart)
- you have history of gastric ulcer
- you have had a recent stroke
- you have high blood pressure
- you have diabetes or problems with blood vessels in the eye caused by diabetes (called diabetic retinopathy)
- you have had an operation recently on your eyes or brain
- you are elderly (over 65 years old) and especially if you are over 75 years old
- you have kidney problems
- you have liver problems
- you are underweight or overweight
- you have high level of potassium in your blood (this may be checked with a blood test)
- you are currently using medicines which affect bleeding (see section below – Other medicines You may have a blood test before you start using this medicine and at intervals while you are using it; this is to check the level of the clotting cells (platelets) and potassium in your blood.

Other medicines and HEPAXANE

Tell your doctor or pharmacist if you are taking or may take/use any other medicines.

- Warfarin - used for thinning the blood
- Aspirin (also known as acetylsalicylic acid or ASA), clopidogrel or other medicines - used to stop blood clots from forming (see also in section 3, "Changing of anticoagulant medicine")
- Dextran injection - used as a blood replacer
- Ibuprofen, diclofenac, ketorolac or other medicines as non-steroidal anti-inflammatory agents which are used to treat pain and swelling in arthritis and other conditions.
- Prednisolone, dexamethasone or other medicines - used to treat asthma, rheumatoid arthritis and other conditions.
- Medicines which increase potassium level in your blood such as potassium salts, water pills, some medicines for heart problems.

Operations and anaesthetics

If you are going to have a spinal puncture or an operation where an epidural or spinal anaesthetic is used, tell your doctor that you are using HEPAXANE See "Do not use HEPAXANE". Also tell your doctor if you have any problem with your spine or if you have ever had spinal surgery.

Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
If you are pregnant and have a mechanical heart valve, you may be at an increased risk of developing blood clots. Your doctor should discuss this with you.
If you are breastfeeding or to plan to breast-feed, you should ask your doctor for advice before taking this medicine.

Driving and using machines

HEPAXANE does not affect the ability to drive and operate machinery.

HEPAXANE contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

3. How to use HEPAXANE

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Having this medicine

- Your doctor or nurse will normally give you HEPAXANE. This is because it needs to be given as an injection.
- When you go home you may need to continue to use HEPAXANE and give it to yourself (see below instructions on how to do this).
- HEPAXANE is usually given by injection underneath the skin (subcutaneous).
- HEPAXANE can be given by injection into your vein (intravenous) after certain types of heart attack or operation.
- HEPAXANE can be added to the tube leaving the body (arterial line) at the start of the dialysis session.

Do not inject HEPAXANE into a muscle.

How much will be given to you

- Your doctor will decide how much HEPAXANE to give you. The amount will depend on the reason it is being used
- If you have problems with your kidneys, you may be given a smaller amount of HEPAXANE.

- 1) Treating blood clots that are in your blood
 - The usual dose is 150 IU (1.5 mg) for every kilogram of your weight each day or 100 IU (1mg) for every kilogram of your weight twice a day.
 - Your doctor will decide how long you should receive HEPAXANE
- 2) Stopping blood clots forming in your blood in the following situations:
 - a) Operation or periods of limited mobility due to an illness
 - The dose will depend on how likely you are to develop a clot. You will be given 2,000 IU (20 mg) or 4,000 IU (40 mg) of HEPAXANE each day.
 - If you are going to have an operation, your first injection will be usually given 2 hours or 12 hours before your operation.
 - If you have restricted mobility due to illness, you will normally be given 4,000 IU (40mg) of HEPAXANE each day.
 - Your doctor will decide how long you should receive HEPAXANE.
 - b) After you have had a heart attack
HEPAXANE can be used for two different types of heart attack called STEMI (ST segment elevation myocardial infarction) or Non STEMI (NSTEMI). The amount of HEPAXANE given to you will depend on your age and the kind of heart attack you have had.

NSTEMI type of heart attack:

- The usual amount is 100 IU (1mg) for every kilogram of weight, every 12 hours.
- Your doctor will normally ask you to take aspirin (acetylsalicylic acid) as well.
- Your doctor will decide how long you should receive HEPAXANE.

STEMI type of heart attack if you are under 75 years old:

- An initial dose of 3,000 IU (30mg) of HEPAXANE will be given as an injection into your vein.
- At the same time, you will also be given HEPAXANE as an injection underneath your skin (subcutaneous injection). The usual dose is 100 IU (1mg) for every kilogram of your weight, every 12 hours.
- Your doctor will normally ask you to take aspirin (acetylsalicylic acid) as well.
- Your doctor will decide how long you should receive HEPAXANE.

STEMI type of heart attack if you are aged 75 years or older:

- The usual dose is 75 IU (0.75mg) for every kilogram of your weight, every 12 hours.
- The maximum amount of HEPAXANE given for the first two injections is 7,500 IU (75mg).
- Your doctor will decide how long you should receive HEPAXANE.

For patients have an operation called Percutaneous Coronary Intervention (PCI):

Depending on when you were last given HEPAXANE, your doctor may decide to give an additional dose of HEPAXANE before a PCI operation. This is by injection into your vein.

3) Stopping blood clots from forming in the tubes of your dialysis machine

- The usual dose is 100 IU (1 mg) for every kilogram of your weight
- HEPAXANE is added to the tube leaving the body (arterial line) at the start of the dialysis session. This amount is usually enough for a 4 hour session. However, your doctor may give you a further dose of 50 IU to 100 IU (0.5 to 1mg) for every kilogram of your weight, if necessary.

Method of administration

The pre-filled syringe is ready for immediate use.

This medicine must not be administered by the intramuscular route.

Injection through the arterial line of the extracorporeal circuit

In order to prevent blood clots forming in the tubes of your dialysis machine, this medicine will be given by an injection into the tube leaving the body (arterial line).

Intravenous injection technique (for acute STEMI indication only)

In the treatment of acute STEMI, treatment should begin with a single rapid injection into your vein (intravenous injection), immediately followed by an injection underneath the skin (subcutaneous injection).

Subcutaneous injection (injection underneath the skin) technique

This medicine is usually given by injection underneath the skin (subcutaneous).

Injection is best done when the patient is in the supine position by deep subcutaneous injection. The administration should be alternated between the left and right anterolateral or posterolateral abdominal wall. The whole length of the needle should be introduced vertically into a skin fold held between the thumb and index finger. The skin fold should not be released until the injection is complete. Do not rub the injection site after administration.

If you use pre-filled 20 mg and 40 mg syringe, do not remove the air bubble from the syringe prior to injection, as this may result in a reduction of the dose.

The pre-filled syringe is intended for single use only.

Do not use this medicine if you notice any visible change in the appearance of the solution.

How to give yourself an injection of HEPAXANE

If you are able to give HEPAXANE to yourself, your doctor or nurse will show you how to do this. Do not try to inject yourself if you have not been trained how to do so. If you are not sure what to do, talk to your doctor or nurse immediately.

Before injecting yourself with HEPAXANE

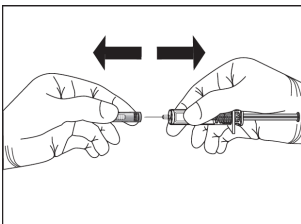
- Check the expiry date on the medicine. Do not use if the date has passed
- Check the syringe is not damaged and the medicine in it is a clear solution. If not, use another syringe
- Do not use this medicine if you notice any change in the appearance of the product.
- Make sure you know how much you are going to inject
- Check your abdomen to see if the last injection caused any redness, change in skin colour, swelling, oozing or is still painful, if so talk to your doctor or nurse
- Decide where you are going to inject the medicine. Change the place where you inject each time from the right to the left side of your stomach. HEPAXANE should be injected just under the skin on your stomach, but not too near the belly button or any scar tissue (at least 5 cm away from these)

The pre-filled syringe is intended for single use only, one-time use only and are available with a system that shields the needle after injection.

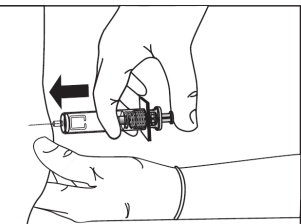
Instructions on injecting yourself with HEPAXANE:

Patients should be lying down and HEPAXANE administered by deep SC injection. Administration should be alternated between the left and right anterolateral and left and right posterolateral abdominal wall. The whole length of the needle should be introduced into a skin fold held between the thumb and forefinger; the skin fold should be held throughout the injection. To minimize bruising, do not rub the injection site after completion of the injection. HEPAXANE pre-filled syringes and graduated pre-filled syringes are for single, one-time use only and are available with a system that shields the needle after injection. Remove the pre-filled syringe from the blister packaging by peeling at the arrow as directed on the blister. Do not remove by pulling on the plunger as this may damage the syringe.

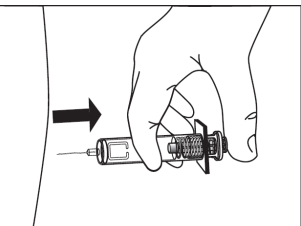
- 1) Remove the needle shield by pulling it straight off the syringe.



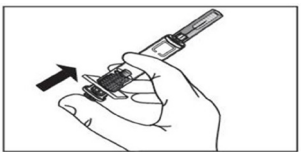
- 2) Gently pinch the cleaned area of your abdomen between your forefinger and thumb to make a fold in the skin. Make sure you hold the skin fold throughout the injection. Insert the full length of the needle into the skin fold and inject the medicine by pushing the plunger to the bottom of the syringe.



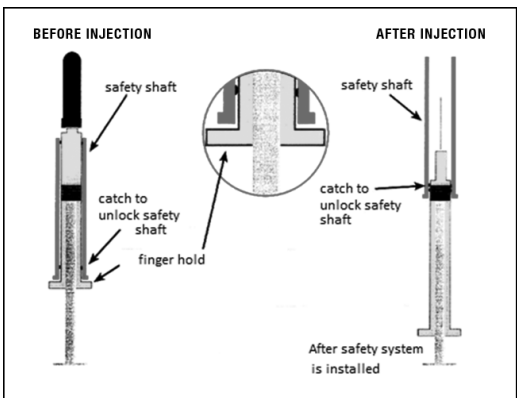
- 3) Remove the syringe from the injection site keeping your finger on the plunger rod. To minimize bruising, do not rub the injection site after completion of the injection.



- 4) 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.

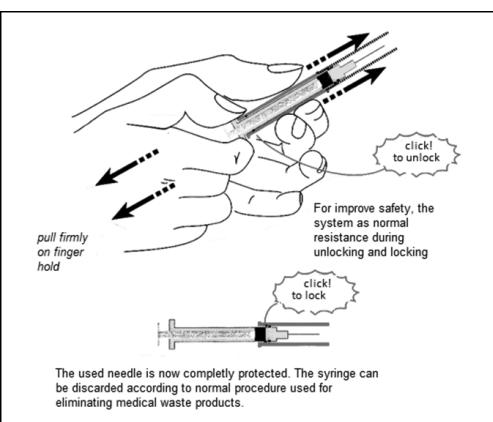


This blister contains a prefilled syringe of HEPAXANE with a safety device system to protect the needle after the injection

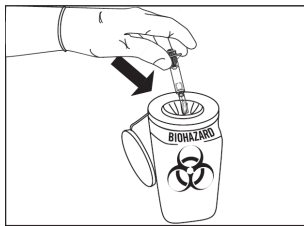


Installing safety system on HEPAXANE syringe after injection

Hold syringe securely in one hand by the shaft and pull firmly with other hand on the finger hold to unlock shaft and slide it until you hear a clicking sound for locking it in place.



- 5) Immediately dispose of the syringe in the appropriate container.



Changing of anticoagulant treatment

- Changing from HEPAXANE to blood thinners called vitamin-K antagonists (e.g. warfarin)
Your doctor will request you perform blood tests called INR and tell you when to stop HEPAXANE accordingly.
- Changing from blood thinners called vitamin-K antagonists (e.g. warfarin) to HEPAXANE
Stop taking the vitamin-K antagonist. Your doctor will request you perform blood tests called INR and tell you when to start HEPAXANE accordingly.
- Changing from HEPAXANE to treatment with direct oral anticoagulant
Stop taking HEPAXANE. Start taking the direct oral anticoagulant 0-2 hours before the time you would have had the next injection, then continue as normal.
- Changing from treatment with direct oral anticoagulant to HEPAXANE
Stop taking direct oral anticoagulant. Do not start treatment with HEPAXANE (and associated names) until 12 hours after the final dose of direct oral anticoagulant.

Use in children and adolescents

The safety and efficacy of HEPAXANE (and associated names) has not been evaluated in children or adolescents.

If you use more HEPAXANE than you should

If you think that you have used too much or too little HEPAXANE, tell your doctor, nurse or pharmacist immediately, even if you have no signs of a problem. If a child accidentally injects or swallows HEPAXANE, take them to a hospital casualty department straight away.

If you forget to use HEPAXANE

If you forget to give yourself a dose, have it as soon as you remember. Do not give yourself a double dose on the same day to make up for a forgotten dose. Keeping a diary will help to make sure you do not miss a dose.

If you stop using HEPAXANE

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse. It is important for you to keep having HEPAXANE injections until your doctor decides to stop them. If you stop, you could get a blood clot which can be very dangerous.

4. Possible side effects

Like other similar medicines, HEPAXANE may cause bleeding which may potentially be life-threatening. In some cases the bleeding may not be obvious.

If you experience any bleeding event that does not stop by itself or if you experience signs of excessive bleeding (exceptional weakness, tiredness, paleness, dizziness, headache or unexplained swelling), consult your doctor immediately.

Your doctor may decide to keep you under closer observation or change your medicine.

Stop using HEPAXANE and talk to a doctor or nurse at once if you get any signs of a severe allergic reaction (such as difficulty breathing, swelling of the lips, mouth, throat or eyes).

You should tell your doctor straight away

- If you have any sign of blockage of a blood vessel by a blood clot such as:
 - cramping pain, redness, warmth, or swelling in one of your legs – these are symptoms of deep vein thrombosis
 - breathlessness, chest pain, fainting or coughing up blood – these are symptoms of a pulmonary embolism
- If you have a painful rash of dark red spots under the skin which do not go away when you put pressure on them.

Your doctor may request you perform a blood test to check your platelet count.

Overall list of possible side effects:

Very common (may affect more than 1 in 10 people)

- Bleeding
- Increases in liver enzymes
- Common** (may affect up to 1 in 10 people)
- You bruise more easily than usual. This could be because of a blood problem with low platelet counts.
- Pink patches on your skin. These are more likely to appear in the area you have been injected with HEPAXANE.
- Skin rash (hives, urticaria).
- Itchy red skin.
- Bruising or pain at the injection site.
- Decreased red blood cell count.
- High platelet counts in the blood.
- Headache.

Uncommon (may affect up to 1 in 100 people)

- Sudden severe headache. This could be a sign of bleeding in the brain.
- A feeling of tenderness and swelling in your stomach. You may have bleeding in your stomach.
- Large red irregularly shaped skin lesions with or without blisters.
- Skin irritation (local irritation).
- You notice yellowing of your skin or eyes and your urine becomes darker in colour. This could be a liver problem.
- Rare** (may affect up to 1 in 1000 people)
- Severe allergic reaction. The signs may include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- Increased potassium in your blood. This is more likely to happen in people with kidney problems or diabetes. Your doctor will be able to check this by carrying out a blood test.
- An increase in the number of eosinophils in your blood. Your doctor will be able to check this by carrying out a blood test.
- Hair loss.
- Osteoporosis (a condition where your bones are more likely to break) after long term use.
- Tingling, numbness and muscular weakness (particularly in the lower part of your body) when you have had a spinal puncture or a spinal anaesthetic.
- Lost of control over your bladder or bowel (so you cannot control when you go to the toilet).
- Hard mass or lump at the injection site.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V". By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store HEPAXANE

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after Exp.The expiry date refers to the last day of that month.

Do not use this medicine if you notice any visible change in the appearance of the solution. Do not freeze.

HEPAXANE pre-filled syringes are for single dose use only. Discard any unused medicine. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

6. Contents of the pack and other information

What HEPAXANE contains

- Each pre-filled syringe contains enoxaparin sodium 2,000 IU anti-Xa activity (equivalent to 20mg) in 0.2ml water for injections
- Each pre-filled syringe contains enoxaparin sodium 4,000 IU anti-Xa activity (equivalent to 40mg) in 0.4ml water for injections
- Each pre-filled syringe contains enoxaparin sodium 6,000 IU anti-Xa activity (equivalent to 60mg) in 0.6ml water for injections
- Each pre-filled syringe contains enoxaparin sodium 8,000 IU anti-Xa activity (equivalent to 80mg) in 0.8ml water for injections
- Each pre-filled syringe contains enoxaparin sodium 10,000 IU anti-Xa activity (equivalent to 100mg) in 1ml water for injections
- The other ingredient is water for injections

What HEPAXANE looks like and contents of the pack

HEPAXANE is a clear, colourless to pale yellow solution for injection in a Type I glass pre-filled syringe fitted with an injection needle, needle shield and an automatic safety device, it is supplied in packs of 2, 6 and 10 syringes. The pre-filled syringes for 6,000 IU (60 mg)/0.6 ml, 8,000 IU (80 mg)/0.8 ml, 10,000 IU (100 mg)/1 ml, are graduated.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Chemi S.p.A (Italfarmaco Gourp)
Via dei Lavoratori, 54
20092 Cinisello Balsamo (MI)
ITALY

Licencee

Versalya Pharma S.L (Italfarmaco Gourp)
C/San Rafael, 3 – 28108
Alcobendas Madrid.
Spain

Manufacturer

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20126 Milan.
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