

Package leaflet: Information for the user

Arovi 12,000 IU (120 mg)/0.8 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, 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Arovi is and what it is used for

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

Arovi works in two ways.

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

Arovi can be used to:

- Treat blood clots that are in your blood.
- Stop blood clots from 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 Arovi

Do not use Arovi

- 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 Arovi to treat blood clots in your body and going to receive spinal or epidural anaesthesia or lumbar puncture within 24 hours.

Warnings and precautions

Arovi 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 Arovi 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 Arovi 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)
- 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 Arovi

Tell your doctor or pharmacist if you are taking or might 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 known 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 you doctor that you are using Arovi. See “Do not use Arovi”. Also, tell your doctor if you have any problem with your spine or if you ever had spinal surgery.

Pregnancy and breastfeeding

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 breast-feeding or plan to breast-feed, you should ask your doctor for advice before taking this medicine.

Driving and using machines

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

It is advised that the trade name and batch number of the product you are using are recorded by your healthcare professional.

3. How to use Arovi

Always use this medicine exactly as your doctor 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 Arovi. This is because it needs to be given as an injection.
 - When you go home, you may need to continue to use Arovi and give it yourself (see instructions below on how to do this).
 - Arovi is usually given by injection underneath the skin (subcutaneous).
 - Arovi can be given by injection into your vein (intravenous) after certain types of heart attack or operation.
 - Arovi can be added to the tube leaving the body (arterial line) at the start of the dialysis session.
- Do not inject Arovi into a muscle.

How much will be given to you

- Your doctor will decide how much Arovi 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 Arovi.

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/mg (1 mg) for every kilogram of your weight twice a day.
- Your doctor will decide how long you should receive Arovi.

2. Stopping blood clots forming in your blood in the following situations:

❖ 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 Arovi 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 (40 mg) of Arovi each day.
- Your doctor will decide how long you should receive Arovi.

❖ After you have had a heart attack

Arovi can be used for two different types of heart attack called STEMI (ST segment elevation myocardial infarction) or Non STEMI (NSTEMI). The amount of Arovi given to you will depend on your age and the kind of heart attack you have had.

NSTEMI type of heart attack:

- The usual dose is 100 IU (1 mg) 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 Arovi.

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

- An initial dose of 3,000 IU (30 mg) of Arovi will be given as injection into your vein.
- At the same time you will also be given Arovi as an injection underneath your skin (subcutaneous injection). The usual dose is 100 IU (1 mg) 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 Arovi.

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

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

For patients have an operation called percutaneous coronary intervention (PCI):

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

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

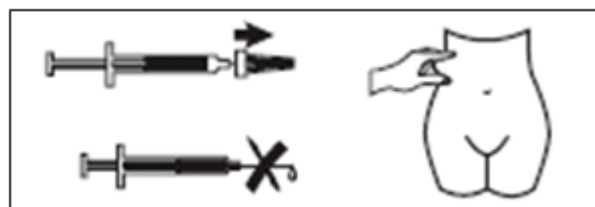
- The usual dose is 100 IU (1 mg) for every kilogram of your weight.
- Arovi is added to the tube leaving the body (arterial line) at the start of the dialysis session. This amount is usually enough for a 4-hour session. However, your doctor may give you a futher dose of 50 IU to 100 IU (0.5 to 1 mg)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

Instructions for use of the syringe

If you are able to give Arovi 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.

You should follow these steps:

- Wash your hands well and sit or lie in a comfortable position.
- Choose an area of the waist, at least 5 centimetres away from your belly button and from existing scars or bruises and clean the skin carefully.
- Use different places for the injection on different days, for example, first on the left hand side, next time on the right.
- Pull the needle cap off the syringe.
- To keep the needle sterile, make sure it doesn't touch anything.
- This pre-filled syringe is now ready for use.
- Before injecting, do not push the plunger to get rid of any air bubbles, because you might lose the medicine



- Hold the syringe in one hand and with your other hand, using your forefinger and thumb, gently pinch the area of skin which you've cleaned and make a skin fold.
- Insert the full length of the needle into the folded skin, straight in at a 90° angle.
- Press down on the plunger, making sure you hold the skin fold in position throughout the injection.



- Remove the needle by pulling it straight out and let go of the skin fold.
- Don't rub the skin where you put the needle in. This will help to avoid bruises.
- Don't try to put the needle cap back on the syringe. Just drop it (needle first) into a sharps bin, close the container lid tightly and place it out of reach of children.
- If you get the impression that the dose is either too strong (for example, you are experiencing unexpected bleeding) or too weak (for example, the dose doesn't seem to be working), talk to your doctor or pharmacist.

To avoid bruising, do not rub the injection site after you have injected yourself.

Changing of anticoagulant treatment

- *Changing from Arovi 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 Arovi accordingly.
- *Changing from blood thinners called vitamin-K antagonists (e.g. warfarin) to Arovi*
Stop taking the vitamin-K antagonist. Your doctor will request you perform blood tests called INR and tell you when to start Arovi accordingly.
- *Changing from Arovi to treatment with direct oral anticoagulant*
Stop taking Arovi. 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 Arovi*
Stop taking direct oral anticoagulant. Do not start treatment with Arovi until 12 hours after the final dose of direct oral anticoagulant.

Use in children and adolescents

The safety and efficacy of Arovi has not been evaluated in children or adolescents.

If you use more Arovi than you should

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

If you forget to use Arovi

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 Arovi

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 Arovi 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 (medicines to reduce blood clotting), Arovi 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 Arovi 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 Arovi.
- 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 1,000 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 or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Arovi

Store below 25°C. Do not freeze.

Arovi pre-filled syringes are single dose containers – discard any unused product.

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 label. The expiry date refers to the last day of that month.

Do not use this medicine if you notice the syringe is damaged or the product is not clear.

Medicines should not be disposed 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 Arovi contains

- The active substance is enoxaparin sodium.

Each pre-filled syringe contains enoxaparin sodium 12,000 IU anti-Xa activity (equivalent to 120 mg) in 0.8 mL water for injections.

- The other ingredient is water for injections.

What Arovi looks like and contents of the pack

Arovi is a clear, colourless to pale yellow solution for injection in a Type I glass pre-filled syringe fitted with an injection needle and with or without an automatic safety device. It is supplied as follows:

Arovi 12,000 IU (120 mg)/0.8mL solution for injection in a 1 mL graduated pre-filled syringe.
Packs of 10 and 30 syringes.

Not all pack sizes may be marketed.

In some package sizes, the prefilled syringe may be combined to a safety device system.

For syringes with safety device system the needle must be oriented away from the user and anyone else who is present. The safety system is activated by pressing firmly on the plunger rod. The protective sleeve will automatically cover the needle and will produce an audible click which confirms the activation of the device.

Immediately, the syringe must be discarded by throwing it into the nearest sharps bin (the needle in). The container lid must be closed tightly and the container placed out of the reach of children.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Laboratorios Farmacéuticos ROVI, S.A.
Julián Camarillo, 35
28037 - Madrid Spain

Manufacturer
ROVI CONTRACT MANUFACTURING, S.L.
Julián Camarillo, 35
28037 - Madrid Spain

This medicinal product is authorised in the Member States of the EEA under the following names:

Enoxaparin Becat: Germany

Enoxaparine Becat: Belgium

Enoxaparina Rovi: Spain

Losmina: Poland

Arovi: United Kingdom

This leaflet was last revised in February 2018.

Other sources of information

Detailed information on this medicine is available on the website of MHRA (<https://www.gov.uk>)