Package Leaflet: Information for the patient

Heparin sodium 5,000 I.U. / mL Solution for injection / infusion

Heparin sodium

Read all of this leaflet carefully before you are given 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 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 nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Heparin sodium 5,000 I.U. / mL is and what it is used for

The name of this medicine is Heparin sodium 5,000 I.U. / mL Solution for injection/infusion (referred to as 'Heparin sodium 5,000 I.U. / mL' in this leaflet).
Heparin sodium 5,000 I.U. / mL belongs to a group of medicines called anticoagulants. Heparin prevents blood clotting.

Heparin sodium 5,000 I.U. / mL is used to treat and prevent:
- Blood clots in leg veins (deep vein thrombosis)
- Blood clots in the lung (pulmonary embolism) as well as for:
- The treatment of chest pains resulting from disease of the heart arteries (unstable angina pectoris)
- The treatment of severe blockages affecting arteries in the legs (acute peripheral arterial occlusion)
- The prevention of blood clots in the heart following a heart attack (mural thrombosis)

It is also used during heart and lung operations and during kidney dialysis.

2. What you need to know before you are given Heparin sodium 5,000 I.U. / mL

You should not be given Heparin sodium 5,000 I.U. / mL if you:

- are allergic to heparin or any of the other ingredients of this medicine (listed in section 6)
- bleed or bruise easily
- have had severe skin problems resulting from previous heparin treatment
- are about to have surgery of the brain, spine or eye, a lumbar puncture or local anaesthetic nerve block or some other procedure where bleeding could be a problem.

- drink large amounts of alcohol
- are currently bleeding from anywhere in the body, (apart from your normal periods which do not stop you being given heparin injection)
- have haemophilia (a genetic disorder which may cause you to bleed excessively) or any other bleeding problem
- bruise easily (fragile capillaries) or have lots of purple spots that look like bruises (purpura)
- have very high blood pressure
- are suffering from tuberculosis (TB)

Warnings and precautions
Talk to your doctor or nurse before receiving Heparin sodium 5,000 I.U. / mL. Particularly careful medical supervision is required if you:

- are over 60 years of age
- have any condition which makes you likely to bleed more easily. If you are unsure, ask your doctor or nurse
- are diabetic
- have high levels or potassium in your blood or are taking a medicine that may increase the potassium level in your blood
- have kidney or liver disease. Your doctor may decide that a lower dose is necessary
- suffer from allergies or have previously had an allergic reaction to heparin.

Your doctor will check your blood if you receive treatment for longer than five days and may do other blood tests if you have major surgery.

Other medicines and Heparin sodium 5,000 I.U. / mL
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Some medicines may affect the way heparin injection works. Taking some medicines at the same time as heparin may mean you may be likely to bleed more.

In particular, tell your doctor if you are taking any of the following:

- Aspirin or other non-steroidal anti-inflammatory drugs (e.g diclofenac or ibuprofen)
- Medicines which may interfere with the proper clotting of the blood (e.g. dipyridamole, epoprostenol, clopidogrel or streptokinase)
- Medicines that may increase the potassium level in your blood
- Glyceryl trinitrate (for heart disease)

If you need one of the above medicines your doctor may decide to alter the dose of heparin injection or the other medication. If you have any doubts about whether this medicine should be administered then discuss things more fully with your doctor or nurse before Heparin sodium 5,000 I.U. / mL is given.

Tobacco smoke can also interfere with the working of heparin injection. You should inform your doctor if you smoke.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before receiving this medicine.

If you are being given heparin injection bleeding may be a problem during pregnancy or after delivery. Particular caution is required at the time of delivery and heparin should be stopped at the onset of labour, due to the risk of bleeding.

Your bones may get thinner if you receive heparin for a long time during pregnancy.

If you are pregnant and are going to have an epidural anaesthetic, you should stop having your medicine. Ask your doctor for advice.

Breast-feeding
Heparin is not excreted in breast milk.

Driving and using machines
Heparin sodium 5,000 I.U. / mL has not been reported to affect ability to drive or operate machines.

Heparin sodium contains sodium

1 mL ampoule: This medicinal product contains less than 1 mmol sodium (23 mg) per mL, that is to say essentially "sodium free" (maximum about 3.76 mg sodium per 1 mL ampoule).

5 mL ampoule: This medicinal product contains less than 1 mmol sodium (23 mg) per 5 mL, that is to say essentially "sodium free" (maximum about 18.80 mg sodium per 5 mL ampoule).

This should be taken into consideration in patients on a controlled sodium diet.

3. How Heparin sodium 5,000 I.U. / mL is given

Your doctor or nurse will inject your dose of heparin into a vein either all at once or over a longer period of time (usually via a drip). Alternatively, they may inject your heparin underneath your skin.

The amount injected all at once into a vein should not be greater than 15 mL.

You may need to have blood tests if you are receiving higher doses of heparin to check on the effects of your heparin treatment.

You may require a lower dose if you have kidney or liver disease.

To prevent blood clots in leg veins (deep vein thrombosis) and blood clots in the lung (pulmonary embolism):

Adults
The usual dose of heparin injection in adults is 5,000 units injected under the skin 2 hours before your operation, followed by

- 5,000 units injected under the skin every 8 – 12 hours, for 7 – 10 days or until you are fully able to move about.
- During pregnancy: 5,000 – 10,000 units every 12 hours under the skin.

Elderly
Lower doses may be used in the elderly. You may need to have blood tests if you are elderly, to check on the effects of your heparin treatment.

Children
No specific doses are recommended.

To treat blood clots in leg veins (deep vein thrombosis) and blood clots in the lung (pulmonary embolism):

Adults
The usual dose in adults is 5,000 units injected into a vein. This is followed by:
- 1,000 – 2,000 units / hour injected slowly into a vein or
- 10,000 – 20,000 units 12 hourly injected under the skin or
- 5,000 – 10,000 units 4 hourly injected all at once into a vein.

Elderly
Lower doses may be used in the elderly

Small adults and children
Small adults and children will be given 50 units / kg bodyweight injected into a vein followed by:
- 15 – 25 units / kg bodyweight/hour injected slowly into a vein or
- 250 units / kg bodyweight 12 hourly injected under the skin or
- 100 units / kg bodyweight 4 hourly injected all at once into a vein

To treat chest pains (unstable angina pectoris) and severe blood clots in the arteries (acute peripheral arterial occlusion):

Adults
The usual dose in adults is 5,000 units injected into a vein. This is followed by:
- 1,000 – 2,000 units / hour injected slowly into a vein or
- 5,000 – 10,000 units 4 hourly injected all at once into a vein.

Elderly
Lower doses maybe used in the elderly

Small adults and children
Small adults and children will be given 50 units / kg body weight injected into a vein followed by:
- 15 – 25 units / kg bodyweight / hour injected slowly into a vein or
- 100 units / kg body weight 4 hourly injected all at once into a vein

You will have blood tests every day to check the effects of your heparin.

To prevent a blood clot in the heart following a heart attack:

Adults
The usual dose for adults is 12,500 units 12 hourly injected under the skin for at least 10 days.

Elderly
A lower dose may be needed.

During Heart and Lung Surgery (Adults)
Initially you will be given 300 units / kg body weight. This will be changed according to the results of your blood tests.

During kidney dialysis (Adults)
Initially you will be given 1,000 – 5,000 units. This will be changed according to the results of your blood tests.

If you think you have been given too much Heparin sodium 5,000 I.U. / mL

Your doctor will decide which dose is best for you.

Too much heparin can cause bleeding. Slight bleeding can be stopped by stopping your heparin

treatment. However, if you have more severe bleeding you may need blood tests and an injection of a medicine called protamine sulphate.

If you think too much medicine has been given to you, contact your doctor or nurse.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, tell your doctor or pharmacist.

Important side effects to look out for (frequency not stated)**:**

Severe allergic reactions
Heparin can cause a severe allergic reaction with wheezing, difficulty breathing, a blue tinge to the lips, fever, chills, swelling of the eyes and lips and shock.

If you think you are having a severe allergic reaction you must stop receiving heparin and tell your doctor or nurse immediately.

Bleeding and Bruising
Signs that you are bleeding more easily include:
- unusual bruising or purple spots on your skin
- unusual bleeding from your gums
- unusual nose bleeds
- blood in your urine (which may cause this to go dark)
- black, tarry-looking stools
- bleeding that will not stop from any operation site or other injury. This is most likely to occur within the first few days of treatment but may occur later too. The risk of bleeding is increased in the elderly (particularly elderly women).

If you are concerned about unusual bleeding you must tell your doctor or nurse immediately as you may need to stop your heparin treatment.

Other side effects (frequency not stated) **include:**
- red lumps or red, itchy patches like eczema often develop 3 – 21 days after the start of heparin treatment, where injections have been given under the skin
- sloughing of skin may occur around the injection site.
- persistent erection of the penis
- abnormal results for blood tests that report on how the liver is working
- high level of blood fats after stopping heparin
- high or low blood potassium. If affected you may feel tired and weak.

If heparin injection is given over many months then the following may occur:
- loss of hair
- thinning of the bones (osteoporosis)

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 at: Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Heparin sodium 5,000 I.U. / mL

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

Your doctor or nurse will usually be responsible for storing and preparing injection before use and for checking that the ampoules have not passed their expiry date stated on the carton and the label. This medicine must not be used after the expiry date which is stated on the carton and the label. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Heparin sodium 5,000 I.U. / mL should not be given if it shows signs of deterioration such as discolouration.

Shelf-life after first opening and dilution:
Chemical and physical in-use stability after dilution in glucose 5% and in 0.9% sodium chloride solution has been demonstrated for 48 hours below 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Heparin sodium 5,000 I.U. / mL contains
- The active substance is heparin sodium.

Each ampoule with 1 mL Heparin sodium 5,000 I.U. / mL Solution for injection / infusion contains 5,000 I.U. of heparin sodium.
Each ampoule with 5 mL Heparin sodium 5,000 I.U. / mL Solution for injection / infusion contains 25,000 I.U. of heparin sodium.
- The other ingredients are sodium hydroxide or hydrochloric acid and water for injections.

Each ampoule with 1 mL Heparin sodium 5,000 I.U. / mL Solution for injection / infusion contains 3.76 mg (0.164 mmol) of sodium.
Each ampoule with 5 mL Heparin sodium 5,000 I.U. / mL Solution for injection / infusion contains 18.80 mg (0.817 mmol) of sodium.

What Heparin sodium 5,000 I.U. / mL looks like and contents of the pack
Heparin sodium 5,000 I.U. / mL Solution for injection / infusion is packed in clear glass ampoules. Packs of 5, 10, 50 ampoules of 1 mL or 5 mL solution for injection / infusion are available.

Heparin sodium 5,000 I.U. / mL Solution for injection / infusion is packed in plastic ampoules, overwrapped with or without a protective pouch. Packs of 5, 10 and 50 ampoules of 5 mL solution for injection / infusion are available.

Not all packs sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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The following information is intended for healthcare professionals only:

Posology and Method of administration
Method of administration
By continuous intravenous infusion in 5% glucose or 0.9% sodium chloride or by intermittent intravenous injection, or by subcutaneous injection.

The intravenous injection volume of heparin injection should not exceed 15 mL. As the effects of heparin are short-lived, administration by intravenous infusion or subcutaneous injection is preferable to intermittent intravenous injections.

Posology
Prophylaxis of deep vein thrombosis and pulmonary embolism:

Adults:
2 hours pre-operatively: 5,000 units subcutaneously
followed by: 5,000 units subcutaneously every 8 – 12 hours, for 7 – 10 days or until the patient is fully ambulant.
No laboratory monitoring should be necessary during low dose heparin prophylaxis. If monitoring is considered desirable, anti-Xa assays should be used as the activated partial thromboplastin time (APTT) is not significantly prolonged.

During pregnancy: 5,000 – 10,000 units every 12 hours, subcutaneously, adjusted according to APTT or anti-Xa assay

Elderly:
Dosage reduction and monitoring of APTT may be advisable.

Paediatric population: No dosage recommendations.

Treatment of deep vein thrombosis and pulmonary embolism:
Adults:
Loading dose: 5,000 units intravenously (10,000 units may be required in severe pulmonary embolism)
Maintenance: 1,000 – 2,000 units / hour by intravenous infusion,

	or 10,000 – 20,000 units 12 hourly subcutaneously, or 5,000 – 10,000 units 4-hourly by intravenous injection.

Elderly:
Dosage reduction may be advisable.

Children and small adults:

Loading dose:	50 units / kg intravenously
Maintenance:	15 – 25 units / kg / hour by intravenous infusion, or 250 units / kg 12 hourly subcutaneously, or 100 units / kg 4-hourly by intravenous injection.

Treatment of unstable angina pectoris and acute peripheral arterial occlusion:
Adults:

Loading dose:	5,000 units intravenously
Maintenance:	1,000 – 2,000 units/hour by intravenous infusion, or 5,000 – 10,000 units 4-hourly by intravenous injection.

Elderly:
Dosage reduction may be advisable.

Children and small adults:

Loading dose:	50 units / kg intravenously
Maintenance:	15 – 25 units / kg / hour by intravenous infusion, or 100 units / kg 4-hourly by intravenous injection.

Daily laboratory monitoring (ideally at the same time each day, starting 4 – 6 hours after initiation of treatment) is essential during full-dose heparin treatment, with adjustment of dosage to maintain an APTT value 1.5 – 2.5 x midpoint of normal range or control value.

Prophylaxis of mural thrombosis following myocardial infarction:
Adults:
12,500 units 12 hourly subcutaneously for at least 10 days.

Elderly:
Dosage reduction may be advisable

In extracorporeal circulation and haemodialysis:
Adults:
Cardiopulmonary bypass:
Initially 300 units / kg intravenously, adjusted thereafter to maintain the activated clotting time (ACT) in the range 400 – 500 seconds.

Haemodialysis and haemofiltration:
Initially 1,000 – 5,000 units,
Maintenance: 1,000 – 2,000 units/hour, adjusted to maintain clotting time > 40 minutes.

Heparin resistance
Patients with altered heparin responsiveness or heparin resistance may require disproportionately higher doses of heparin to achieve the desired effect. Also refer to section 4.4, Special warnings and precautions for use.

Special precautions for disposal and other handling
For single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section *"Special precautions for storage"*.

Special precautions for storage
This medicinal product does not require any special storage conditions.

Shelf-life after first opening and dilution
Chemical and physical in-use stability after dilution in glucose 5% and in 0.9% sodium chloride solution has been demonstrated for 48 hours below 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Overdose
Bleeding is the main sign of overdose with heparin.

As heparin is eliminated quickly, a discontinuation of treatment is sufficient in case of minor haemorrhages. In case of severe haemorrhages heparin may be neutralised with protamine sulphate injected slowly intravenously. One mg of protamine sulphate neutralises approximately 100 IU of heparin. Nevertheless, the required protamine sulphate dose varies according to the time of heparin administration and the dose administered.

It is important to avoid overdosage of protamine sulphate because protamine itself has anticoagulant properties. A single dose of protamine sulphate should never exceed 50 mg. Intravenous injection of protamine may cause a sudden fall in blood pressure, bradycardia, dyspnoea and transitory flushing, but these may be avoided or diminished by slow and careful administration.