Package leaflet: Information for the user

HEPARIN SODIUM 5,000 I.U./ml solution for injection or concentrate for solution for infusion
Contains Preservative

Read all of this leaflet carefully before you start taking 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, please 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 pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

The name of your medicine is heparin sodium 5,000 I.U./ml solution for injection or concentrate for solution for infusion. In the rest of this leaflet it is called heparin injection.

What is in this leaflet

1. What Heparin Injection is and what it is used for

Heparin belongs to a group of drugs that are called anticoagulants.
These help to stop blood clotting. Heparin injection 5,000 I.U./ml is used in conditions where blood vessels may become blocked by blood clots. It is therefore 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 Injection

This medicine should not be injected into your muscles.

This medicine should not be used after major trauma.

Heparin injection should not be given if you:
• are allergic to heparin or any of the other ingredients of this medicine (listed in section 6)
• drink large amounts of alcohol

• are currently bleeding from anywhere in the body, (apart from your normal period which does not stop you being given heparin injection)
• have haemophilia (a genetic disorder which may cause you to bleed excessively) or any other bleeding problem
• have or have ever had thrombocytopenia (a serious blood disorder which prevents blood from clotting properly)
• 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)
• 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
• have recently had an operation
• suffer from severe liver problems which can lead to bleeding into the oesophagus (gullet)
• have bleeding into the brain.
• are about to be treated for pain and inflammation with intravenous diclofenac

Important: If you are having an epidural or spinal anaesthetic

You must remind your doctor that you are having heparin before you receive any anaesthetic.

After you have the anaesthetic your doctor or nurse will make regular checks. This is to check if you are getting any major bleeding or bruising around your spine. This may cause paralysis that could be permanent. Any signs this may be happening to you include tingling, weakness or numbness in your lower legs or body, back pain or problems in going to the toilet. This happens very rarely.

After you have the anaesthetic your doctor will tell you when you can take your medicine again.

Warnings and precautions

Heparin injection must not be given to premature or newborn babies.

Talk to your doctor before heparin injection is given if you:
• are over 60 years of age
• have any condition which makes you likely to bleed more easily (for example a stomach ulcer, hiatus hernia, inflammation of the heart, problems in the back of your eye, haemorrhoids (piles), a stroke, cancer or threatened miscarriage). If you are unsure, ask your doctor or nurse.
• suffer from diabetes
• suffer from excess acid or high levels of potassium in your blood or are taking a medicine that may increase the potassium level in your blood (e.g. amiloride, triamterene, eplerenone or spironolactone). If any of these apply you may need to have a blood test before the start of your heparin treatment. If you are unsure, ask your doctor or nurse
• 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 low molecular weight (LMW) heparin. A small test dose of heparin sodium injection may be given first.
• if you are taking another medicine that may affect your blood clotting. For a list of these medicines see the section ‘‘Other medicines and Heparin Injection’’.

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.

Your doctor may take a blood test up to several weeks after the end of your heparin treatment. This is so the doctor can check the level of the clotting cells (platelets) in your blood.

Your doctor will take particular care if:
• the patient is an infant or child under three years old
• you have an epidural or an anaesthetic given into the spine. After an epidural or an anaesthetic is given into the spine, your doctor or nurse will make regular checks for signs of tingling, weakness or numbness in your lower legs or body, back pain or problems in going to the toilet. You should alert your doctor or nurse if you experience any of these.

Other medicines and Heparin Injection

Tell your doctor if you are taking, have recently taken or might take any other medicines, including those medicines obtained without a prescription, as 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. ketorolac, diclofenac or ibuprofen)
• dextran solutions (used to treat shock)
• medicines which may interfere with the proper clotting of the blood (e.g. dipyridamole, epoprostenol, clopidogrel or streptokinase)
• cephalosporins, used to treat infections
• ACE inhibitors (e.g. captopril, enalapril, lisinopril, ramipril), angiotensin II antagonists (e.g. losartan or valsartan) or a renin inhibitor drug called aliskiren, used for treating high blood pressure or heart problems
• medicines that may increase the potassium level in your blood (e.g. amiloride, triamterene, eplerenone or spironolactone)
• glyceryl trinitrate given into a vein (for coronary heart disease)
• aminoglycoside antibiotics (e.g. gentamicin, amikacin, neomycin or tobramycin)
• probenecid, used in the treatment of gout

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 it is given.

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

The presence of heparin in the blood can affect the results of some blood tests such as thyroid tests and the levels of calcium or some antibiotics (e.g. gentamicin) in the blood.

Important information about the ingredients

Benzyl alcohol

This medicine contains 10 mg/ml benzyl alcohol. Benzyl alcohol may cause allergic reactions.

Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children.

Do not give to your newborn baby (up to 4 weeks old), unless recommended by your doctor.

Do not use for more than a week in young children (less than 3 years old), unless advised by your doctor or pharmacist.

Large amounts of benzyl alcohol can build up in pregnant or breastfeeding women. This may cause side effects (called ‘‘metabolic acidosis’’). This side effect can also be seen in people with liver or kidney disease.

Methyl parahydroxybenzoate

The methyl parahydroxybenzoate in heparin injection may cause allergic reactions (possibly delayed) and exceptionally bronchospasm.

Pregnancy, breast-feeding and fertility
You should let your doctor or nurse know before you are given heparin injection if you are pregnant, wish to become pregnant or have a history of, or known risk to miscarriage.

If you are being given heparin injection bleeding may be a problem during pregnancy or after delivery. 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.

Ask your doctor or nurse for advice if you wish to breast-feed.

Driving and using machines
Heparin injection has not been reported to affect ability to drive or operate machines.

3. How Heparin Injection should be 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 or if you are pregnant to check on the effects of your heparin treatment.

Heparin injection must not be given to premature or newborn babies.

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.

Pregnancy

During pregnancy the dosage is 5,000-10,000 units injected under the skin every 12 hours. The dose may be adjusted according to your blood tests.

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 body weight injected into a vein followed by:

• 15-25 units/kg body weight/hour injected slowly into a vein

or

• 250 units/kg body weight 12 hourly injected under the skin

or

• 100 units/kg body weight 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 may be 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 body weight/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 injection
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 sulfate. If you think too much medicine has been given to you contact your doctor or nurse.

4. Possible side effects

Like all medicines, heparin injection can cause side effects, although not everybody gets them. These are most likely to occur when treatment is first started. You should inform your doctor or nurse immediately if you feel unwell.

Important side effects to look out for:

• Severe allergic reactions

• allergic reactions including an itchy skin rash, eye irritation, runny nose, wheezing, rapid breathing, a blue tinge to the lips, fever, chills, swelling of the eyes and lips, and shock.

Allergic reactions may be due to the ingredients in your heparin rather than the heparin itself. This occurs particularly in infants or children up to three years old.

If you think you are having a severe allergic reaction (see symptoms above) you must tell your doctor or nurse immediately.

• Bleeding and Bruising

Heparin injection can reduce the number of cells that help your blood clot (thrombocytopenia) and so can cause bleeding and bruising. 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).

Thrombocytopenia may result in the formation of dangerous blood clots causing chest pains, shortness of breath, coughing, feeling faint, dizziness or loss of consciousness. If thrombocytopenia develops, Heparin treatment should be stopped immediately.

Thrombocytopenia can occur up to several weeks after the end of your heparin treatment. As such, your doctor may take a blood test in that time. This is so the doctor can check the level of the clotting cells (platelets) in your blood.

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.

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

• signs of developing paralysis **(After having an epidural or spinal anaesthetic)**

Signs of developing paralysis include:
- tingling, weakness or numbness in your legs or lower body
- back pain
- incontinence of urine or incontinence from back passage or other problem in those areas

You must get urgent medical help if you have any of these symptoms following an epidural or spinal anaesthetic.

Other side effects include:
Common: may affect up to 1 in 10 people
• 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

Rare: may affect up to 1 in 1,000 people
• raised levels of potassium in the blood, particularly in patients with kidney failure or diabetes. If affected you may feel tired and weak.
• irritation or sloughing of skin which may occur around the injection site.

Not known; frequency cannot be estimated from the available data
• loss of hair (alopecia) if heparin sodium injection is given over many months
• weakening of the bones (osteoporosis) if heparin sodium injection is given over many months
• fractures of the spine and ribs if heparin is given over many months
• persistent erection of the penis (priapism)
• abnormal liver tests
• the amount of a hormone called aldosterone may be lower than normal. Your doctor can explain this more.

• high lipid levels on stopping heparin

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 below.

HPRA Pharmacovigilance
Website: www.hpra.ie

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

5. How to store Heparin Injection

Keep this medicine out of the sight and reach of children.
Your doctor or nurse will usually be responsible for storing and preparing heparin injection before use and for checking that the vials have not passed their expiry date stated on the carton and the label.
Do not use this medicine after the expiry date which is stated on the carton and the label. The expiry date refers to the last day of that month.

Heparin injection should not be given if it shows signs of deterioration such as discolouration.
Do not store above 25°C. Store in the original packaging in order to protect the product from light.
After opening, heparin vials may be kept for 28 days at 25°C, after which they should be discarded.

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 injection contains
The active substance is heparin sodium.

1 ml of solution of heparin sodium injection 5,000 I.U./ml contains 5,000 international units of the active ingredient. It is available in 5 ml multidose vials containing 25,000 I.U. in 5 ml of solution.

The other ingredients include benzyl alcohol (10 mg/ml), methyl parahydroxybenzoate (E218), water for injections, hydrochloric acid and sodium hydroxide.

What heparin injection looks like and contents of the pack
Heparin injection is a colourless or straw-coloured liquid.
Each carton contains 10 glass vials.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
Pinewood Laboratories Ltd., Ballymacarbry, Clonmel, Co. Tipperary, Ireland

Manufacturer: CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

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Information for Health Care Professionals

Heparin sodium 5,000 I.U./ml solution for injection or concentrate for solution for infusion

Qualitative and Quantitative Composition

Heparin sodium 5,000 I.U./ml - Heparin sodium 5,000 I.U./ml (25,000 I.U. in 5 ml)
For the full list of excipients, see section 6.1.

Posology and method of administration

Route 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.

Recommended dosage
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.

Children:
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.

List of excipients

Benzyl alcohol
Methyl parahydroxybenzoate (E218)
Water for injections
Sodium hydroxide solution
Hydrochloric acid

Incompatibilities

Heparin is incompatible with many injectable preparations e.g. some antibiotics, opioid analgesics and antihistamines.

The following drugs are incompatible with heparin;

Alteplase, amikacin sulfate, amiodarone hydrochloride, ampicillin sodium, aprotinin, benzylpenicillin potassium or sodium, cefalotin sodium, chlorpromazine hydrochloride, ciprofloxacin lactate, cisatracurium besilate, cytarabine, dacarbazine, daunorubicin hydrochloride, diazepam, doxorubicin hydrochloride, droperidol, erythromycin lactobionate, gentamicin sulfate, haloperidol lactate, hyaluronidase, hydrocortisone sodium succinate, kanamycin sulfate, labetolol hydrochloride, levofloxacin, methicillin sodium, methotrimeprazine, netilmicin sulfate, nicardipine hydrochloride, oxytetracycline hydrochloride, pethidine hydrochloride, polymyxin B sulfate, promethazine hydrochloride, streptomycin sulfate, tobramycin sulfate, trifluprazine hydrochloride, vancomycin hydrochloride, vinblastine sulfate and vinorelbine tartrate.

Dobutamine hydrochloride and heparin should not be mixed or infused through the same intravenous line, as this causes precipitation.

Heparin and reteplase are incompatible when combined in solution.

If reteplase and heparin are to be given through the same line this, together with any Y-lines, must be thoroughly flushed with a 0.9% saline or a 5% glucose solution prior to and following the reteplase injection.

Shelf life

3 years

Chemical and physical in use stability has been demonstrated for 28 days at 25°C.

From a microbiological point of view, once opened, the product may be stored for a maximum of 28 days at 25°C. Other in use storage times and conditions are the responsibility of the user.

Special precautions for storage
Do not store above 25°C.
Store in the original package.

Special precautions for disposal
Each multidose vial should be restricted to use in a single patient.

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