SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL ampoule: Each ampoule with 1 mL solution for injection / infusion contains 5000 I.U. of sodium heparin (from porcine intestinal mucosa).

5 mL ampoule: Each ampoule with 5 mL solution for injection / infusion contains 25000 I.U. of sodium heparin (from porcine intestinal mucosa).

Excipient with known effect:

Each mL of heparin in ampoule contains maximum about 3.76 mg (0.164 mmol) sodium.

Each ampoule of 5 mL contains maximum about 18.80 mg (0.817 mmol) sodium

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection / infusion

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Prophylaxis of deep vein thrombosis and pulmonary embolism.
- Treatment of deep vein thrombosis and pulmonary embolism, unstable angina pectoris and acute peripheral arterial occlusion.
- Prophylaxis of mural thrombosis following myocardial infarction.
- In extracorporeal circulation and haemodialysis.

4.2 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.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Current (or history of) heparin-induced thrombocytopenia.

Generalised or local haemorrhagic tendency.

An epidural anaesthesia during birth in pregnant women treated with heparin is contraindicated.

Regional anaesthesia in elective surgical procedures is contra-indicated because the use of heparin may be very rarely associated with epidural or spinal haematoma resulting in prolonged or permanent paralysis.

Patients who consume large amounts of alcohol, who are sensitive to the drug, who are actively bleeding or who have haemophilia or other bleeding disorders, severe liver disease (including oesophageal varices), purpura, severe hypertension, active tuberculosis or increased capillary permeability.

4.4 Special warnings and precautions for use

Heparin should be used with caution in patients with hypersensitivity to low molecular weight heparin.

Care should be taken when heparin is administered to patients with increased risk of bleeding complications, hypertension, renal or hepatic insufficiency. In patients with advanced renal or hepatic disease, a reduction in dosage may be necessary. The risk of bleeding is increased with severe renal impairment and in the elderly (particularly elderly women).

Heparin can suppress adrenal secretion of aldosterone leading to hyperkalaemia, particularly in patients such as those with diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, a raised plasma potassium or taking potassium sparing drugs. The risk of hyperkalaemia appears to increase with duration of therapy but is usually reversible. Plasma potassium should be measured in patients at risk before starting heparin therapy and monitored regularly thereafter particularly if treatment is prolonged beyond about 7 days.

Drugs affecting platelet function or the coagulation system should in general not be given concomitantly with heparin (see Section 4.5).

In patients undergoing peri-dural or spinal anaesthesia or spinal puncture, the prophylactic use of heparin may be very rarely associated with epidural or spinal haematoma resulting in prolonged or permanent paralysis. The risk is increased by the use of a peri-dural or spinal catheter for anaesthesia, by the concomitant use of drugs affecting haemostasis such as non-steroidal anti-inflammatory drugs, platelet inhibitors or anticoagulants and by traumatic or repeated puncture. In decision making on the interval between the last administration of heparin at prophylactic doses and the placement or removal of a peri-dural or spinal catheter, the product characteristics and the patient profile should be taken into account. Subsequent dose should not take place before at least four hours have elapsed. Re-administration should be delayed until the surgical procedure is completed.

Should a physician decide to administer anti-coagulation in the context of peridural or spinal anaesthesia, extreme vigilance and frequent monitoring must be exercised to detect any signs and symptoms of neurologic impairment, such as back pain, sensory and motor deficits and bowel or bladder dysfunction. Patients should be instructed to inform immediately a nurse or a clinician if they experience any of these.

Heparin should not be administered by intramuscular injection due to the risk of haematoma.

Due to increased bleeding risk, care should be taken when giving concomitant intramuscular injections, lumbar puncture and similar procedures.

As there is a risk of antibody-mediated heparin-induced thrombocytopenia, platelet counts should be measured in patients receiving heparin treatment for longer than 5 days and the treatment should be stopped immediately in those who develop thrombocytopenia.

Heparin induced thrombocytopenia and heparin induced thrombocytopenia with thrombosis can occur up to several weeks after discontinuation of heparin therapy. Patients presenting with thrombocytopenia or thrombosis after discontinuation of heparin should be evaluated for heparin induced thrombocytopenia and heparin induced thrombocytopenia with thrombosis.

<u>Sodium content:</u>

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.

4.5 Interaction with other medicinal products and other forms of interaction

Heparin may prolong the one stage prothrombin time. Accordingly, when Heparin is given with dicoumarol or warfarin sodium, a period of at least 5 hours after the last intravenous dose of heparin should elapse before blood is drawn, if a valid prothrombin time is to be obtained.

The anticoagulant effect of heparin may be enhanced by concomitant medication with other drugs affecting platelet function or the coagulation system, e.g. platelet aggregation inhibitors, thrombolytic agents, salicylates, non-steroidal anti-inflammatory drugs, vitamin K antagonists, dextrans, activated protein C. Where such combination cannot be avoided, careful clinical and biological monitoring is required.

Combined use with ACE inhibitors or angiotensin II antagonists may increase the risk of hyperkalaemia.

Tobacco smoke: Nicotine may partially counteract the anticoagulant effect of heparin. Increased heparin dosage may be required in smokers.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Heparin is not contraindicated in pregnancy. Heparin does not cross the placental barrier. The decision to use heparin in pregnancy should be taken after evaluation of the risk/benefit in any particular circumstances.

Osteoporosis has been reported with prolonged heparin treatment during pregnancy.

Particular caution is required at the time of delivery. Due to the risk of uteroplacental haemorrhage, heparin treatment should be stopped at the onset of labour.

The use of heparin in women with abortus imminens is contraindicated (see Section 4.3).

If epidural anaesthesia is envisaged, heparin treatment should be suspended whenever possible.

Breast-feeding

Heparin is not excreted in breast milk.

Fertility

There are no clinical studies with heparin regarding fertility.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

The following adverse reactions have been observed and reported during treatment with Heparin Sodium with the following frequencies: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse Drug Reactions

System Organ Class (SOC)	MedDRA Preferred Term	Frequency
Vascular disorders	Haemorrhage	Not known
	Epistaxis	Not known
	Contusion	Not known
Blood and lymphatic system disorders	Thrombocytopenia	Not known
Renal and urinary disorders	Haematuria	Not known
Endocrine disorders	Adrenal insufficiency	Not known
	Hypoaldosteronism	Not known
Skin and subcutaneous tissue	Alopecia	Not known

System Organ Class (SOC)	MedDRA Preferred Term	Frequency
	Skin necrosis	Not known
Musculoskeletal, connective tissue and bone disorders	Osteoporosis	Not known
Immune system disorders	Hypersensitivity	Not known
	Rebound hyperlipidaemia	Not known
Metabolism and nutrition disorders	Hyperkalaemia Hypokalaemia	Not known
Reproductive system and breast disorders	Priapism	Not known
General disorders and administration site conditions	Injection site reaction	Not known
Investigations	Alanine aminotransferase increased; Aspartate aminotransferase increased	Not known

Hypersensitivity reactions to heparin are rare. They include urticaria, conjunctivitis, rhinitis, asthma, cyanosis, tachypnoea, feeling of oppression, fever, chills, angioneurotic oedema and anaphylactic shock.

Erythematous nodules, or infiltrated and sometimes eczema-like plaques, at the site of subcutaneous injections are common, occurring 3 – 21 days after starting heparin treatment.

Haemorrhage:

Haemorrhage is the chief complication that may result from heparin therapy. An overly prolonged clotting time or minor bleeding during therapy can usually be controlled by withdrawing the drug. It should be appreciated that gastrointestinal or urinary tract bleeding during anticoagulant therapy may indicate the presence of an underlying occult lesion. Bleeding can occur at any site but certain specific haemorrhage complications may be difficult to detect.

Adrenal haemorrhage, with resultant acute adrenal insufficiency, has occurred during anticoagulant therapy. Therefore, such treatment should be discontinued in patients who develop signs and symptoms of acute adrenal haemorrhage and insufficiency. Initiation of corrective therapy should not depend on laboratory confirmation of the diagnosis, since any delay in an acute situation may result in the patient's death.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions 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.

4.9 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antithrombotic agents, ATC code: B01AB01

Heparin prevents the coagulation of blood *in-vivo* and *in-vitro*. It potentiates the inhibition of several activated coagulation factors, including thrombin and factor X.

5.2 Pharmacokinetic properties

Absorption

Heparin is not absorbed from the gastrointestinal tract. Heparin is administered by injection.

Distribution

Heparin binds extensively to plasma proteins.

Elimination

Heparin and its metabolites are excreted in the urine.

The half-life of heparin depends on the dose administered, the route of administration and is subject to wide inter- and intra-individual variation.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide or hydrochloric acid (for pH adjustment)

Water for injections.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 4.2 and 6.3.

6.3 Shelf life

36 months

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.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

For storage conditions after first opening and after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Type I, clear glass ampoules .

Packs of 5, 10 and 50 ampoules of 1 mL solution for injection / infusion.

Packs of 5, 10 and 50 ampoules of 5 mL solution for injection / infusion.

Polypropylene ampoules, overwrapped with or without a protective pouch.

Packs of 5, 10 and 50 ampoules of 5 mL solution for injection / infusion.

Not all packs sizes may be marketed.

6.6 Special precautions for disposal

For single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

DEMO PHARMA UK LIMITED

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1 Dover Place,

Ashford,

Kent

TN23 1FB,

England

8 MARKETING AUTHORISATION NUMBER(S)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

06/08/2025

10 DATE OF REVISION OF THE TEXT

06/08/2025