SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Proprietary name: HEPANEP
International Non-proprietary Name (INN): Heparin Sodium Injection USP 5000 IU/ml (5ml)
Each ml contains:
Heparin Sodium USP : 5000 IU
Benzyl Alcohol BP : 0.95 %w/v
Water for Injections BP : Q.S.

2. Qualitative and Quantitative Composition

Each ml contains Heparin Sodium USP 5000 IU, Benzyl Alcohol BP 0.95 %w/v, and Water for Injections BP Q.S. For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Liquid Injection

4. Clinical Particulars

4.1 Therapeutic indications

Heparin Sodium Injection is an anticoagulant indicated for

- Prophylaxis and treatment of venous thrombosis and pulmonary embolism
- Prevention of postoperative deep venous thrombosis and pulmonary embolism in patients undergoing
- major abdominothoracic surgery or who, for other reasons, are at risk of developing thromboembolic
- disease
- Atrial fibrillation with embolization
- Treatmentof acute and chronic consumptive coagulopathies (disseminated intravascular coagulation)
- Prevention of clotting in arterial and cardiac surgery
- Prophylaxis and treatment of peripheral arterial embolism
- Use as an anticoagulant in blood transfusions, extracorporeal circulation, and dialysis procedures

4.2 Posology and method of administration

Administer heparin sodium injection by intermittent intravenous injection, intravenous
infusion, or deep subcutaneous (intrafat, i.e., above the iliac crest or abdominal fat layer) injection. Do not administer heparin sodium injection by intramuscular injection because of the risk of hematoma at the injection site.

Laboratory Monitoring for Efficacy and Safety

Adjust the dosage of heparin sodium injection according to the patient's coagulation test results. Dosage is considered adequate when the activated partial thromboplastin time (aPTT) is 1.5 to 2 times normal or when the whole blood clotting time is elevated approximately 2.5 to 3 times the control value. When initiating treatment with heparin sodium injection by continuous intravenous infusion, determine the coagulation status (aPTT, INR, platelet count) at baseline and continue to follow aPTT approximately every 4 hours and then at appropriate intervals thereafter. When the drug is administered intermittently by intravenous injection, perform coagulation tests before each injection during the initiation of treatment and at appropriate intervals thereafter. After deep subcutaneous (intrafat) injections, tests for adequacy of dosage are best performed on samples drawn 4 to 6 hours after the injection.

Periodic platelet counts and hematocrits are recommended during the entire course of heparin therapy, regardless of the route of administration.

Therapeutic Anticoagulant Effect with Full-Dose Heparin

The dosing recommendations in TABLE 1 are based on clinical experience. Although
dosages must be adjusted for the individual patient according to the results of suitable
laboratory tests, the following dosage schedules may be used as guidelines:

Table 1: Recommended Adult Full-Dose Heparin Regimens for Therapeutic Anticoagulant Effect

METHOD OF ADMINISTRATION	FREQUENCY	RECOMMENDED DOSE [based on 150 lb (68 kg) patient]
Deep Subcutaneous (Intrafat) Injection A different site should be used for each injection to prevent the development of massive hematoma	Initial Dose	5,000 units by intravenous injection, followed by 10,000 to 20,000 units of a concentrated solution, subcutaneously
	Every 8 hours or Every 12 hours	8,000 to 10,000 units of a concentrated solution 15,000 to 20,000 units of a concentrated solution
Intermittent Intravenous Injection	Initial dose	10,000 units, either undiluted or in 50 to 100 mL of 0.9% Sodium Chloride Injection, BP
	Every 4 to 6 hours	5,000 to 10,000 units, either undiluted or in 50 to 100 mL of 0.9% Sodium Chloride Injection, BP
Intravenous Infusion	Initial dose	5,000 units by intravenous injection
	Continuous	20,000 to 40,000 units/24 hours in 1,000 mL of 0.9% Sodium Chloride Injection, BP(or in any compatible solution) for infusion

Pediatric Use
Do not use this product in neonates and infants. Use preservative-free heparin sodium injection in neonates and infants.
There are no adequate and well controlled studies on heparin use in pediatric patients.
Pediatric dosing recommendations are based on clinical experience. In general, the following dosage schedule may be used as a guideline in pediatric patients:

Initial Dose

75 to 100 units/kg (IV bolus over 10 minutes)
Infants: 25 to 30 units/kg/hour
Infants < 2 months have the highest requirements (average 28 units/kg/hour)

Maintenance Dose

Children > 1 year of age: 18 to 20 units/kg/hour
Older children may require less heparin, similar to weight adjusted adult dosage

Monitoring

Adjust heparin to maintain APTT of 60 to 85 seconds, assuming this reflects an anti-Factor Xa level of 0.35 to 0.70

Cardiovascular Surgery
Patients undergoing total body perfusion for open-heart surgery should receive an initial dose of not less than 150 units of heparin sodium per kilogram of body weight.
Frequently, a dose of 300 units per kilogram is used for procedures estimated to last less than 60 minutes, or 400 units per kilogram for those estimated to last longer than 60 minutes.

Low-Dose Prophylaxis of Postoperative Thromboembolism
The most widely used dosage has been 5,000 units 2 hours before surgery and 5,000 units every 8 to 12 hours thereafter for 7 days or until the patient is fully ambulatory, whichever is longer. Administer the heparin by deep subcutaneous (intrafat, i.e., above the iliac crest or abdominal fat layer, arm, or thigh) injection with a fine (25 to 26-gauge) needle to minimize tissue trauma.

Blood Transfusion
Add 450 to 600 USP units of heparin sodium per 100 mL of whole blood to prevent coagulation. Usually, 7,500 USP units of heparin sodium are added to 100 mL of 0.9%

Sodium Chloride Injection, BP(or 75,000 USP units per 1,000 mL of 0.9% Sodium Chloride Injection, BP) and mixed; from this sterile solution, 6 to 8 mL are added per 100 mL of whole blood.

Converting to Warfarin
To ensure continuous anticoagulation when converting from heparin sodium injection to warfarin, continue full heparin therapy for several days until the INR (prothrombin time) has reached a stable therapeutic range. Heparin therapy may then be discontinued without tapering.

Converting to Oral Anticoagulants other than Warfarin
For patients currently receiving intravenous heparin, stop intravenous infusion of heparin sodium immediately after administering the first dose of oral anticoagulant; or for

intermittent intravenous administration of heparin sodium, start oral anticoagulant 0 to 2 hours before the time that the next dose of heparin was to have been administered.

Extracorporeal Dialysis
Follow equipment manufacturers' operating directions carefully. A dose of 25 to 30 units/kg followed by an infusion rate of 1,500 to 2,000 units/hour is suggested based on pharmacodynamic data if specific manufacturers' recommendations are not available.

DOSAGE FORMS AND STRENGTHS
Heparin Sodium Injection, USP is available as:
Heparin Sodium Injection: 5,000 USP units per mL *preserved with benzyl alcohol* clear solution in 1 mL vial and 10 mL multiple-dose vials

4.3 Contraindications

The use of heparin sodium is contraindicated in patients with the following conditions:

History of heparin-induced thrombocytopenia and heparin-induced thrombocytopenia and thrombos is Known hypersensitivity to heparin or pork products (e.g., anaphylactoid reactions)

In whom suitable blood coagulation tests, e.g., the whole blood clotting time, partial thromboplastin time, etc., cannot be performed at appropriate intervals (this contraindication refers to full-dose heparin; there is usually no need to monitor coagulation parameters in patients receiving low-dose heparin)

An uncontrolled active bleeding state, except when this is due to disseminated intravascular coagulation

4.4 Special warnings and precautions for use

Fatal Medication Errors
Do not use heparin sodium as a “catheter lock flush” product. Heparin sodium is supplied in vials containing various strengths of heparin, including vials that contain a highly concentrated solution of 10,000 units in 1 mL. Fatal hemorrhages have occurred in pediatric patients due to medication errors in which 1 mL heparin sodium vials were confused with 1 mL “catheter lock flush” vials. Carefully examine all heparin sodium vials to confirm the correct vial choice prior to administration of the drug.

Hemorrhage
Avoid using heparin in the presence of major bleeding, except when the benefits of heparin therapy outweigh the potential risks.
Hemorrhage can occur at virtually any site in patients receiving heparin. Fatal hemorrhages have occurred. Adrenal hemorrhage (with resultant acute adrenal insufficiency), ovarian hemorrhage, and retroperitoneal hemorrhage have occurred during anticoagulant therapy with heparin.

A higher incidence of bleeding has been reported in patients, particularly women, over 60 years of age. An unexplained fall in hematocrit, fall in blood pressure or any other unexplained symptom should lead to serious consideration of a hemorrhagic event.
Use heparin sodium with caution in disease states in which there is increased risk of hemorrhage, including:
Cardiovascular - Subacute bacterial endocarditis, severe hypertension.

Surgical - During and immediately following (a) spinal tap or spinal anesthesia or (b) major surgery, especially involving the brain, spinal cord, or eye.
Hematologic - Conditions associated with increased bleeding tendencies, such as hemophilia, thrombocytopenia and some vascular purpuras.
Patients with hereditary antithrombin III deficiency receiving concurrent antithrombin III therapy -The anticoagulant effect of heparin is enhanced by concurrent treatment with antithrombin III (human) in patients with hereditary antithrombin III deficiency.
To reduce the risk of bleeding, reduce the heparin dose during concomitant treatment with antithrombin III (human).
Gastrointestinal - Ulcerative lesions and continuous tube drainage of the stomach or small intestine.
Other - Menstruation, liver disease with impaired hemostasis.

Heparin-Induced Thrombocytopenia and Heparin-Induced Thrombocytopenia and Thrombosis

Heparin-induced thrombocytopenia (HIT) is a serious antibody-mediated reaction. HIT occurs in patients treated with heparin and is due to the development of antibodies to a platelet Factor 4-heparin complex that induce in vivo platelet aggregation. HIT may progress to the development of venous and arterial thromboses, a condition referred to as heparin-induced thrombocytopenia with thrombosis (HITT). Thrombotic events may also be the initial presentation for HITT. These serious thromboembolic events include deep vein thrombosis, pulmonary embolism, cerebral vein thrombosis, limb ischemia, stroke, myocardial infarction, mesenteric thrombosis, renal arterial thrombosis, skin necrosis, gangrene of the extremities that may lead to amputation, and possibly death.
If the platelet count falls below 100,000/mm3 or if recurrent thrombosis develops, promptly discontinue heparin, evaluate for HIT and HITT, and, if necessary, administer an alternative anticoagulant. HIT or HITT can occur up to several weeks after the discontinuation of heparin therapy.
Patients presenting with thrombocytopenia or thrombosis after discontinuation of heparin sodium should be evaluated for HIT or HITT.

Risk of Serious Adverse Reactions in Infants Due to Benzyl Alcohol Preservative

Serious and fatal adverse reactions including “gasping syndrome” can occur in neonates and infants treated with benzyl alcohol-preserved drugs, including heparin sodium multiple-dose vials. The “gasping syndrome” is characterized by central nervous system depression, metabolic acidosis, and gasping respirations.
When prescribing heparin sodium multiple-dose vials in infants consider the combined daily metabolic load of benzyl alcohol from all sources including heparin sodium multipledose vials (contains 10.42 mg of benzyl alcohol per mL) and other drugs containing benzyl alcohol. The minimum amount of benzyl alcohol at which toxicity may occur is not known.

Thrombocytopenia
Thrombocytopenia in patients receiving heparin has been reported at frequencies up to 30%. It can occur 2 to 20 days (average 5 to 9) following the onset of heparin therapy.
Obtain platelet counts before and periodically during heparin therapy. Monitor thrombocytopenia of any degree closely. If the count falls below 100,000/mm 3 or if recurrent thrombosis develops, promptly discontinue heparin, evaluate for HIT and HITT, and, if necessary, administer an alternative anticoagulant.

Coagulation Testing and Monitoring
When using a full dose heparin regimen, adjust the heparin dose based on frequent blood coagulation tests. If the coagulation test is unduly prolonged or if hemorrhage
occurs, discontinue heparin promptly. Periodic platelet counts and hematocrits are
recommended during the entire course of heparin therapy, regardless of the route of administration.

Heparin Resistance
Resistance to heparin is frequently encountered in fever, thrombosis, thrombophlebitis,
infections with thrombosing tendencies, myocardial infarction, cancer, in postsurgical
patients, and patients with antithrombin III deficiency. Close monitoring of coagulation tests is recommended in these cases. Adjustment of heparin doses based on anti-Factor Xa levels may be warranted.

Hypersensitivity
Patients with documented hypersensitivity to heparin should be given the drug only in clearly life-threatening situations.
Because heparin sodium is derived from animal tissue, it should be used with caution in patients with a history of allergy.

4.5 Interaction with other medicinal products and other forms of interaction

Oral Anticoagulants
Heparin sodium may prolong the one-stage prothrombin time. Therefore, when heparin sodium is given with dicumarol or warfarin sodium, a period of at least 5 hours after the last intravenous dose or 24 hours after the last subcutaneous dose should elapse before blood is drawn, if a valid prothrombin time is to be obtained.

Platelet Inhibitors
Drugs such as NSAIDS (including salicylic acid, ibuprofen, indomethacin, and celecoxib), dextran, phenylbutazone, thienopyridines, dipyridamole, hydroxychloroquine, glycoprotein IIb/IIIa antagonists (including abciximab, eptifibatide, and tirofiban), and others that interfere with platelet-aggregation reactions (the main hemostaticdefense of heparinized patients) may induce bleeding and should be used with caution in patients receiving heparin sodium. To
reduce the risk of bleeding, a reduction in the dose of antiplatelet agent

or heparin is recommended.

Other Interactions

Digitalis, tetracyclines, nicotine or antihistamines may partially counteract the anticoagulant action of heparin sodium. Intravenous nitroglycerin administered to heparinized patients may result in a decrease of the partial thromboplastin time with subsequent rebound effect upon discontinuation of nitroglycerin. Careful monitoring of partial thromboplastin time and adjustment of heparin dosage are recommended during coadministration of heparin and intravenous nitroglycerin.

Antithrombin III (human) – The anticoagulant effect of heparin is enhanced by concurrent treatment with antithrombin III (human) in patients with hereditary antithrombin III deficiency. To reduce the risk of bleeding, a reduced dosage of heparin is recommended during treatment with antithrombin III (human).

4.6 Pregnancy and lactation

Pregnancy

Risk Summary

There are no available data on heparin sodium use in pregnant women to inform a drug associated risk of major birth defects and miscarriage. In published reports, heparin exposure during pregnancy did not show evidence of an increased risk of adverse maternal or fetal outcomes in humans. No teratogenicity, but early embryo-fetal death was observed in animal reproduction studies with administration of heparin sodium to pregnant rats and rabbits during organogenesis at doses approximately 10 times the maximum recommended human dose (MRHD) of 45,000 units/ day.

Consider the benefits and risks of heparin sodium for the mother and possible risks to the fetus when prescribing heparin sodium to a pregnant woman.

If available, preservative-free heparin sodium is recommended when heparin therapy is needed during pregnancy. There are no known adverse outcomes associated with fetal exposure to the preservative benzyl alcohol through maternal drug administration; however, the preservative benzyl alcohol can cause serious adverse events and death when administered intravenously to neonates and infant .

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Human Data

The maternal and fetal outcomes associated with uses of heparin via various dosing numerous studies. These studies generally reported normal deliveries with no maternal or fetal bleeding and no other complications.

Animal Data

In a published study conducted in rats and rabbits, pregnant animals received heparin intravenously during organogenesis at a dose of 10,000 units/kg/day, approximately 10 times the maximum human daily dose based on body weight. The number of early resorptions increased in both species. There was no evidence of teratogenic effects.

Lactation
Risk Summary
If available, preservative-free heparin sodium is recommended when

heparin therapy is

needed during lactation. Benzyl alcohol present in maternal serum is likely to cross into

human milk and may be orally absorbed by a nursing infant. There is no information
regarding the presence of heparin sodium in human milk, the effects on the breastfed infant, or the effects on milk production. Due to its large molecular weight, heparin is not likely to
be excreted in human milk, and any heparin in milk would not be orally absorbed by a
nursing infant. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for heparin sodium and any potential adverse effects on the breastfed infant from heparin sodium or from the underlying maternal condition.

4.7 Effects on ability to drive and use machines

Heparin Sodium has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following clinically significant adverse reactions are described elsewhere in the labeling:

Hemorrhage
Heparin-Induced Thrombocytopenia and
Heparin-Induced Thrombocytopenia and Thrombosis
Risk of Serious Adverse Reactions in Infants Due to Benzyl Alcohol Preservative
Thrombocytopenia
Heparin Resistance Hypersensitivity

Post marketing Experience

The following adverse reactions have been identified during post approval use of heparin sodium. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Hemorrhage is the chief complication that may result from heparin therapy. 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 hemorrhagic complications may be difficult to detect:
Adrenal hemorrhage, with resultant acute adrenal insufficiency, has occurred with heparin therapy, including fatal cases.
Ovarian (corpus luteum) hemorrhage developed in a number of women of reproductive age receiving short- or long-term heparin therapy.
Retroperitoneal hemorrhage.

HIT and HITT, including delayed onset cases.
Local Irritation – Local irritation, erythema, mild pain, hematoma or ulceration may follow deep subcutaneous (intrafat) injection of heparin sodium. Because these complications are much more common after intramuscular use, the intramuscular route is not recommended.
Histamine-like reactions – Such reactions have been observed at the site of injections. Necrosis of the skin has been reported at the site of subcutaneous injection of heparin, occasionally requiring skin grafting.
Hypersensitivity – Generalized hypersensitivity reactions have been reported, with chills,
fever and urticaria as the most usual manifestations, and asthma, rhinitis, lacrimation,headache, nausea and vomiting, and anaphylactoid reactions, including shock, occurring less frequently. Itching and burning, especially on the plantar side of the feet, may occur.
Elevations of aminotransferases – Significant elevations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels have occurred in
patients who have received heparin.
Miscellaneous – Osteoporosis following long-term administration of high doses of heparin, cutaneous necrosis after systemic administration, suppression of aldosterone synthesis, delayed transient alopecia, priapism, and rebound hyperlipemia on discontinuation of heparin sodium have also been reported.

Reporting of Undesirable effects
Healthcare professionals are requested to report any suspected adverse reactions to the
Pharmacy and Poisons Board (PPB) via https://pv.pharmacyboardkenya.org

4.9 Overdose

Bleeding is the chief sign of heparin overdosage. Neutralization of Heparin Effect
When clinical circumstances (bleeding) require reversal of the heparin effect, protamine
sulfate (1% solution) by slow infusion will neutralize heparin sodium. No more than 50 mg should be administered, very slowly, in any 10-minute period. Each mg of protamine sulfate neutralizes approximately 100 USP heparin units. The amount of protamine required decreases over time as heparin is metabolized. Although the metabolism of heparin is complex, it may, for the purpose of choosing a protamine dose, be assumed to have a half-life of about 1/2 hour after intravenous injection.
Because fatal reactions often resembling anaphylaxis have been reported with protamine, it should be given only when resuscitation techniques and treatment of anaphylactoid shock are readily available.
For additional information consult the labeling of Protamine Sulfate Injection.

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Mechanism of Action
Heparin interacts with the naturally occurring plasma protein, Antithrombin III, to induce a conformational change, which markedly enhances the serine protease activity of Antithrombin III, thereby inhibiting the activated coagulation factors involved in the clotting sequence, particularly Xa and IIa. Small amounts of

heparin inhibit Factor Xa, and larger amounts inhibit thrombin (Factor IIa). Heparin also prevents the formation of a stable fibrin clot by inhibiting the activation of the fibrin stabilizing factor. Heparin does not have fibrinolytic activity; therefore, it will not lyse existing clots.

5.2 Pharmacokinetic properties

Various times (activated clotting time, activated partial thromboplastin time, prothrombin
time, whole blood clotting time) are prolonged by full therapeutic doses of heparin; in most cases, they are not measurably affected by low doses of heparin. The bleeding time is usually unaffected by heparin.

Absorption
Heparin is not absorbed through the gastrointestinal tract and therefore administered via parenteral route. Peak plasma concentration and the onset of action are achieved immediately after intravenous administration.

Distribution
Heparin is highly bound to antithrombin, fibrinogens, globulins, serum proteases and
lipoproteins. The volume of distribution is 0.07 L/kg.

Elimination
Metabolism
Heparin does not undergo enzymatic degradation.
Excretion
Heparin is mainly cleared from the circulation by liver and reticuloendothelial cells mediated
uptake into extravascular space. Heparin undergoes biphasic clearance, a) rapid saturable
clearance (zero order process due to binding to proteins, endothelial cells and macrophage) and b) slower first order elimination. The plasma half-life is dose dependent and it ranges from 0.5 to 2 h.

5.3 Preclinical safety data
There are no pre-clinical data of relevance to the prescriber which are already included in other additional to those

6. Pharmaceutical Particulars

6.1 List of excipients

Heparin Sodium
Sodium Chloride
Benzyl Alcohol
Water for Injection

6.2 Incompatibilities
NA

6.3 Shelf life
24 Months

USP BP BP
BP

6.4 Special precaution for storage
Store at below 25°C. Protect from heat, light and moisture. KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container
1×5 ml, Clear glass vial USP Type-1.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Marketing Authorization Holder and Manufacturing Site Addresses

Marketing Authorization Holder
LAVITA PHARMA PRIVATE LIMITED
Ahmedabad Gujarat, India

Manufacturing Site Addresses
CTD12602

8. Marketing Authorization Number

16/11/2025

9. Date of First Registration

16/11/2025