For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

℞ Heparin Sodium Injection IP 25000 IU/5ml

HABISTOP®

COMPOSITION
Each ml contains:
Heparin Sodium IP..... 5000 IU
(Derived from porcine
intestinal mucosa)
Benzyl Alcohol IP..... 0.95% W/V
Water for Injections IP..... q.s.

PHARMACEUTICAL FORM
Solution for injection

THERAPEUTIC INDICATIONS
Prophylaxis and treatment of Venous thrombosis
Prevention of postoperative Deep Vein Thrombosis (DVT)
Prophylaxis and treatment of Pulmonary Embolism (PE)
Atrial fibrillation with embolization
Diagnosis and treatment of acute and chronic Consumptive Coagulopathies
Prevention of clotting in arterial and cardiac surgery
Prophylaxis and treatment of Peripheral Arterial Embolism
As an anticoagulant in several procedures and laboratory purposes.

POSOLOGY AND METHOD OF ADMINISTRATION
Heparin Sodium I.P. injection is administered by intravenous or deep subcutaneous routes. Dose must be adjusted for the individual patient according to the results of suitable laboratory tests.
Adult dosing: Deep Subcutaneous injection: 8,000 to 10,000 units every 8 hours or 15,000 to 20,000 units every 12 hours.
Intermittent IV: 5,000 to 10,000 units every 4 to 6 hours.
IV infusion: Initial dose 5,000 units; continuous 20,000 to 40,000 units/24 hours.

CONTRAINDICATIONS
Hypersensitivity to the active substance or to any of the excipients.
Must not be given to premature babies or neonates (contains benzyl alcohol).
Heparin should not be administered by intramuscular injection or after major trauma.
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.
Patients with present or previous thrombocytopenia. The rare occurrence of skin necrosis in patients receiving Heparin contra-indicates the further use of Heparin either by subcutaneous or intravenous routes because of the risk of thrombocytopenia. Because of the special hazard of post-operative haemorrhage Heparin is contra-indicated during surgery of the brain, spinal cord and eye, in procedures at sites where there is a risk of bleeding, in patients that have had recent surgery, and in patients undergoing lumbar puncture or regional anaesthetic block.
The relative risks and benefits of Heparin should be carefully assessed in patients with a bleeding tendency or those patients with an actual or potential bleeding site e.g. hiatus hernia, peptic ulcer, neoplasm, bacterial endocarditis, retinopathy, bleeding haemorrhoids, suspected intracranial haemorrhage, cerebral thrombosis or threatened abortion.
In patients receiving Heparin for treatment rather than prophylaxis, locoregional anaesthesia in elective surgical procedures is contraindicated because use of Heparin may be very rarely associated with epidural or spinal haematoma resulting in prolonged or permanent paralysis. If such a procedure is planned the Heparin should be stopped and the procedure should be delayed until the aPTT has returned to normal. Epidural anaesthesia use during birth in pregnant women treated with Heparin is contraindicated.
Menstruation is not a contra-indication.
Concomitant use of intravenous diclofenac with Heparin (including low dose Heparin) is contraindicated.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
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 (HIT) and Heparin induced thrombocytopenia with thrombosis (HITT) 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 HIT or HITT.
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).
Although Heparin hypersensitivity is rare, it is advisable to give a trial dose of 1,000 I.U. in patients with a history of allergy. Caution should be exercised in patients with known hypersensitivity to low molecular weight heparin.
In most patients, the recommended low-dose regimen produces no alteration in clotting time. However, patients show an individual response to Heparin, and it is therefore essential that the effect of therapy on coagulation time should be monitored in patients undergoing major surgery.
Caution is recommended in patients receiving Heparin prophylactically and undergoing spinal or epidural anaesthesia or spinal puncture (risk of spinal or epidural haematoma resulting in prolonged or permanent paralysis). The risk is increased by the use of a peridural or spinal catheter for anaesthesia, by the concomitant use of drugs affecting haemostasis such as non-steroidal anti-inflammatory drugs (NSAIDs), 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 peridural 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 anticoagulation 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 a nurse or clinician immediately if they experience any of these.
Heparin can suppress adrenal secretion of aldosterone leading to hyperkalemia, 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 hyperkalemia 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 in all patients treated for more than 7 days.
Heparin resistance
There is considerable variation in individual anticoagulant responses to Heparin.
Heparin resistance, defined as an inadequate response to Heparin at a standard dose for achieving a therapeutic goal occurs in approximately 5 to 30% of patients.
Factors predisposing to the development of Heparin resistance include:
• Antithrombin III activity less than 60% of normal (antithrombin III-dependent Heparin resistance):
Reduced antithrombin III activity may be hereditary or more commonly, acquired (secondary to preoperative Heparin therapy in the main, chronic liver disease, nephrotic syndrome, cardiopulmonary bypass, low grade disseminated intravascular coagulation or drug induced, e.g. by aprotinin, oestrogen or possibly nitroglycerin)
• Patients with normal or supranormal antithrombin III levels (antithrombin III-independent Heparin resistance)

- Thromboembolic disorders
- Increased Heparin clearance

• Elevated levels of Heparin binding proteins, factor VIII, von Willebrand factor, fibrinogen, platelet factor 4 or histidine-rich glycoprotein

- Active infection (sepsis or endocarditis)
- Preoperative intra-aortic balloon counterpulsation
- Thrombocytopenia
- Thrombocytosis
- Advanced age
- Plasma albumin concentration ≤ 35g/dl
- Relative hypovolaemia

Heparin resistance is also often encountered in acutely ill patients, in patients with malignancy and during pregnancy or the post-partum period.
Drugs affecting platelet function or the coagulation system should in general not be given concomitantly with Heparin.

Heparin Injection contains Benzyl alcohol and Methyl parahydroxybenzoate
Benzyl alcohol
This medicine contains 10mg/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.
Large amounts of benzyl alcohol can build up in pregnant or breast feeding women which 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.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
Analgesics: Drugs that interfere with platelet aggregation e.g. aspirin and other NSAIDs should be used with care. Increased risk of haemorrhage with;
- Ketorolac
- Intravenous diclofenac.

Avoid concomitant use of either ketorolac or intravenous diclofenac, even with low-dose Heparin.
Anticoagulants, platelet inhibitors, etc: Increased risk of bleeding with oral anticoagulants, epoprostenol, clopidogrel, ticlopidine, streptokinase, dipyridamole, dextran solutions, abciximab, eptifibatide or any other drug which may interfere with coagulation.
Cephalosporins: Some cephalosporins, e.g. cefaclor, cefixime and ceftriaxone, can affect the coagulation process and may therefore increase the risk of haemorrhage when used concurrently with Heparin.
ACE inhibitors, angiotensin-II receptor antagonists or the renin inhibitor aliskiren: Hyperkalaemia may occur with concomitant use.
Nitrates: Reduced activity of Heparin has been reported with simultaneous intravenous glyceryl trinitrate infusion.
Probenecid: May increase the anticoagulant effects of Heparin.
Tobacco smoke: Nicotine may partially counteract the anticoagulant effect of Heparin. Increased Heparin dosage may be required in smokers.
Interference with diagnostic tests may be associated with pseudo-hypocalcaemia (in haemodialysis patients), artefactual increases in total thyroxine and triiodothyronine, simulated metabolic acidosis and inhibition of the chromogenic lysate assay for endotoxin. Heparin may interfere with the determination of aminoglycosides by immunoassays.

FERTILITY, PREGNANCY AND LACTATION
Heparin is not contraindicated in pregnancy. Heparin does not cross the placenta or appear in breast milk. 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.
If epidural anaesthesia is envisaged, Heparin treatment should be suspended whenever possible.
Use in women with threatened abortion is contraindicated.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
None stated.

UNDESIRABLE EFFECTS
Blood disorders:
Haemorrhage.
Thrombocytopenia has been observed occasionally. It has been reported that thrombocytopenia occurs more frequently with bovine-derived Heparin than porcine-derived Heparin. Two types of Heparin-induced thrombocytopenia have been defined. Type I is frequent, mild (usually >50 x 10^9/L) and transient, occurring within 1-5 days of Heparin administration. Type II is less frequent but often associated with severe thrombocytopenia (usually <50 x 10^9/L). It is immune-mediated and occurs after a week or more (earlier in patients previously exposed to Heparin). It is associated with the production of a platelet-aggregating antibody and thromboembolic complications, due to platelet-rich thrombi (the 'white clot syndrome'), which may precede the onset of thrombocytopenia. Pulmonary embolism has been reported as thromboembolic complications of Heparin-induced thrombocytopenia. Heparin should be discontinued immediately in patients who develop thrombocytopenia.
Heparin-induced thrombocytopenia (HIT) and Heparin-induced thrombocytopenia and thrombosis (HITT) can occur up to several weeks after the discontinuation of Heparin therapy. Patients presenting with thrombocytopenia or thrombosis after discontinuation of Heparin should be evaluated for HIT and HITT.

Endocrine disorders:
Adrenal insufficiency secondary to adrenal haemorrhage has been associated with Heparin (rarely). Heparin products can cause hypoaldosteronism which may result in an increase in plasma potassium. Rarely, clinically significant hyperkalemia may occur particularly in patients with chronic renal failure and diabetes mellitus.

Hepatic disorders:
Increased serum transaminase values may occur but usually resolve on discontinuation of Heparin.

Immune system disorders:
Hypersensitivity reactions to Heparin are rare. They include urticaria, conjunctivitis, rhinitis, asthma, cyanosis, tachypnoea, feeling of oppression, fever, chills, angioneurotic oedema and anaphylactic shock.
In some instances the precipitating agent will prove to be the preservative rather than the Heparin itself.

Metabolic disorders:
Heparin administration is associated with release of lipoprotein lipase into the plasma; rebound hyperlipidaemia may follow Heparin withdrawal.

Muscle and tissue disorders:
There is some evidence that prolonged dosing with Heparin (i.e. over many months) may cause osteoporosis and fractures in the vertebra and ribs. Significant bone demineralisation has been reported in women taking more than 10,000 I.U. per day of Heparin for three months or longer.

Reproductive and breast disorders:
Priapism has been reported.

Skin and subcutaneous tissue disorders:
Local irritation and skin necrosis may occur but are rare. There is some evidence that prolonged dosing with Heparin (i.e. over many months) may cause alopecia.

Pruritus
Rash (including erythematous and maculopapular)

Vascular disorders:
Haematoma. Very rare cases of epidural and spinal haematoma have been reported in patients receiving Heparin for prophylaxis undergoing spinal or epidural anaesthesia or spinal puncture.

Reporting of suspected adverse reactions-
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Kindly report any suspected adverse reactions to pharmavigil@jbpharma.com

OVERDOSE
A potential hazard of Heparin therapy is haemorrhage, but this is usually due to overdosage and the risk is minimised by strict laboratory control. Slight haemorrhage can usually be treated by withdrawing the drug. If bleeding is more severe, clotting time and platelet count should be determined. Prolonged clotting time will indicate the presence of an excessive anticoagulant effect requiring neutralisation by intravenous protamine sulfate, at a dosage of 1 mg for every 100 I.U. of Heparin to be neutralised. The bolus dose of protamine sulfate should be given slowly over about 10 minutes and not exceed 50 mg. If more than 15 minutes have elapsed since the injection of Heparin, lower doses of protamine will be necessary.

PHARMACOLOGICAL PROPERTIES
PHARMACODYNAMIC PROPERTIES
Heparin is an anticoagulant and acts by inhibiting thrombin and by potentiating the naturally occurring inhibitors of activated Factor X (Xa).

PHARMACOKINETIC PROPERTIES
As Heparin is not absorbed from the gastrointestinal tract and sublingual sites, it is administered by injection.
After injection, Heparin extensively binds to plasma proteins.
Heparin is metabolised in the liver and the inactive metabolic products are excreted in the urine.
The half life of Heparin is dependent on the dose.

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

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, meticillin sodium, methotrimeprazine, netilmicin sulfate, nicardipine hydrochloride, oxytetracycline hydrochloride, pethidine hydrochloride, polymyxin B sulfate, promethazine hydrochloride, streptomycin sulfate, tobramycin sulfate, trifluprom azine 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.

PACKAGING INFORMATION
Vial of 5ml

STORAGE & HANDLING INSTRUCTION
Store below 30°C. Do not freeze.
Keep out of reach of children.

Marketed by & ® Regd. Trade Mark of:
J. B. CHEMICALS & PHARMACEUTICALS LTD.
Neelam Centre, 'B' Wing, Hind Cycle Road, Worli, Mumbai - 400 030, India.

Note: This prescribing information is applicable for India Market only

DATE OF REVISION:
August 2024.