For use only by a registered physician, hospital, or laboratory.

Heparin Sodium Injection USP 5000 IU/mL

For deep subcutaneous or intravenous use only

Composition: Each mL contains:
Heparin Sodium USP ..... 5,000 IU
(Mucosa-derived)
Benzyl Alcohol USP ..... 0.0095 mL
(As a preservative)
Water for Injection USP ..... q.s.

Heparin Sodium Injection USP is a heterogeneous group of straight-chain anionic mucopolysaccharides, known as glycosaminoglycans, possessing anticoagulant properties.
Heparin Sodium Injection USP is a sterile solution of heparin sodium. Heparin Sodium Injection USP must be administered intravenously or by deep subcutaneous injection and is not intended for intramuscular use.

MECHANISM OF ACTION: Heparin Sodium Injection USP inhibits reactions that lead to blood coagulation and the formation of fibrin clots, both in vitro and in vivo. In the normal coagulation cascade, heparin acts at multiple sites. Heparin Sodium Injection USP, in combination with Antithrombin III, inactivates activated Factor X, thereby inhibiting thrombosis. Heparin Sodium Injection USP inhibits the conversion of prothrombin to thrombin.
This inactivation prevents the conversion of fibrinogen to fibrin and, consequently, prevents the formation of a stable fibrin clot. Bleeding time is generally unaffected by heparin sodium. In most cases, clotting time is prolonged by full therapeutic doses of Heparin Sodium Injection USP.

PHARMACODYNAMICS/KINETICS: Heparin Sodium Injection USP is not absorbed from the gastrointestinal tract. The onset of anticoagulation is immediate with intravenous use and occurs within 20–30 minutes with subcutaneous use. Peak plasma levels of Heparin Sodium Injection USP are reached two to four hours after subcutaneous administration, although considerable individual variation is possible. Biotransformation occurs in the liver and the reticuloendothelial system. Heparin Sodium Injection USP has no fibrinolytic activity; therefore, it will not lyse existing clots. Heparin Sodium Injection USP does not cross the placental barrier and is not distributed into human milk. The mean half-life is 1.5 hours. Elimination occurs via renal excretion, primarily as metabolites, with small amounts excreted unchanged in the urine.

CONTRAINDICATIONS:
Heparin should not be used in patients with hypersensitivity to Heparin Sodium Injection USP or any of its components, severe thrombocytopenia, subacute bacterial endocarditis, suspected intracranial hemorrhage, or uncontrollable bleeding (unless secondary to disseminated intravascular coagulation). Furthermore, heparin should not be used in patients for whom suitable blood coagulation tests—e.g., whole blood clotting time, partial thromboplastin time, etc.—cannot be performed at appropriate intervals.

DOSAGE AND ADMINISTRATION:
Visually inspect for particulate matter and discoloration prior to administration. Slight discoloration does not alter potency.
Heparin Sodium Injection USP is not effective when administered orally and must be administered via intermittent intravenous injection, intravenous infusion, or deep subcutaneous injection (into fat, i.e., above the iliac crest or the abdominal fat layer). The intramuscular route of administration should be avoided due to the frequent occurrence of hematoma at the injection site.
The dosage of Heparin Sodium Injection USP must be adjusted according to the patient's coagulation test results. When Heparin Sodium Injection USP is administered by continuous intravenous infusion, clotting time should be determined approximately every four hours following the initial IV injection. The dosage is considered adequate when the activated partial thromboplastin time (aPTT) is 1.5 to 2 times normal or when the blood clotting time is approximately 2.5 to 3 times the control value. Following deep subcutaneous (intrafat) injections, testing for dosage adequacy is best performed on samples collected four to six hours after administration. Therapeutic anticoagulant effect with full-dose Heparin Sodium Injection, USP: Although the dosage should be adjusted for the individual patient based on appropriate laboratory test results, the following dosage regimens may be used as guidelines:

METHOD OF ADMINISTRATION	FREQUENCY	RECOMMONDED DOSE*
Deep subcutaneous injections (into the fat)	Initial dose	5,000 Units by IR injection followed by 10,000 to 20,000 Units of a concentrated solution, subcutaneously
A different site must be used for each injection to prevent the development of a massive hematoma.	Every 8 hours	8 horas 8.000 a 10.000 Unidades de uma solução concentrada
	or	
	Every 12 hours	15,000 to 20,000 units of a concentrated solution
Intermittent intravenous injection	Initial dose	10,000 units, undiluted or in 50 to 100 mL of 0.9% sodium chloride injection
	Every 4 to 6 hours	6 hours: 5,000 to 10,000 units, undiluted or in 50 to 100 mL of 0.9% sodium chloride injection
Continuous intravenous infusion	Initial dose	5,000 Units per IV injection
	Continuous	20,000 to 40,000 units/24 hours in 1000 mL of 0.9% sodium chloride injection (or in any infusion solution)

* Based on a (68 kg) patient.

Pediatric use: The following dosage regimen is generally recommended:
Initial dosage: 50 units/kg (IV infusion)
Maintenance dosage: 100 units/kg (IV infusion) every four hours or 20,000 units/24 hours by continuous infusion.
Cardiovascular surgery: Patients undergoing total body perfusion for open-heart surgery should receive an initial dose of 150 units of Heparin Sodium Injection USP per kilogram of body weight for procedures lasting less than 60 minutes, or 400 units per kilogram for those with an estimated duration of more than 60 minutes.
Low-dose prophylaxis of postoperative thromboembolism: The most commonly used dosage is 5,000 units two hours before surgery and 5,000 units every 8 to 12 hours thereafter for seven days or until the patient is fully ambulatory, whichever is longer.
Extracorporeal dialysis: Carefully follow the equipment manufacturer's operating instructions.
Blood transfusion: Addition of 400 to 600 USP units per 100 mL of whole blood is generally employed to prevent clotting. Typically, 7,500 USP units of Heparin Sodium Injection USP are added to 100 mL of 0.9% Sodium Chloride Injection USP (or 75,000 USP units/1,000 mL of 0.9% Sodium Chloride Injection USP) and mixed. From this sterile solution, 6 to 8 mL are added per 100 mL of whole blood.

ADVERSE REACTIONS
Hemorrhage: Hemorrhage is the principal complication that may result from therapy with Heparin Sodium Injection USP. Discontinuation of the drug can usually control an excessively prolonged clotting time or minor bleeding during therapy. Adrenal hemorrhage, ovarian hemorrhage (corpus luteum), and retroperitoneal hemorrhage are also known to occur.
Local Reaction: Local irritation, erythema, mild pain, and ulceration of the hematoma may occur following deep subcutaneous (intrafat) injection of Heparin Sodium Injection USP; however, these complications are much more common following intramuscular use, and such use is not recommended.
Hypersensitivity: Generalized hypersensitivity reactions have been reported, with chills, fever, and urticaria being the most common manifestations; asthma, rhinitis, lacrimation, headache, nausea, vomiting, and anaphylactoid reactions (including shock) occur more rarely.

WARNINGS:
Hemorrhage can occur at virtually any site in patients receiving heparin sodium. Heparin Sodium Injection USP should be used with extreme caution in conditions where there is an increased risk of hemorrhage. Risk factors for hemorrhage include peptic ulcer, IM injection, increased capillary permeability, menstruation, severe renal, hepatic, or biliary disease, subacute bacterial endocarditis, hypertension, hemophilia, thrombocytopenia, and certain vascular purpuras. Use with caution in patients with shock or severe hypotension. Concomitant use of NSAIDs may also increase the risk of hemorrhage.
Thrombocytopenia: Occurrence has been reported in patients receiving heparin sodium. Mild thrombocytopenia (count above 100,000/mm³) may remain stable or reverse even if heparin is continued. However, thrombocytopenia of any degree should be closely monitored. If the count falls below 100,000/mm³ or if recurrent thrombosis occurs, therapy with Heparin Sodium Injection USP must be discontinued.

PRECAUTIONS:
General: It has been reported that patients receiving Heparin Sodium Injection USP may develop new thrombus formation in association with thrombocytopenia resulting from heparin-induced irreversible platelet aggregation—the so-called "white clot syndrome." The process can lead to thromboembolic complications such as skin necrosis, gangrene of the extremities (which may lead to amputation), myocardial infarction, pulmonary embolism, stroke, and possibly death. Administration of Heparin Sodium Injection USP must be immediately discontinued if a patient develops new thrombosis in association with thrombocytopenia.
Increased risk in older women: A higher incidence of bleeding has been reported in women over 60 years of age.
Laboratory Tests: Periodic platelet counts, hematocrit, and tests for occult blood in the stool are recommended throughout the course of therapy with Heparin Sodium Injection USP, regardless of the route of administration.

Pregnancy:
Teratogenic effects: Pregnancy Category C. Animal reproduction studies have not been conducted with heparin sodium. It is also not known whether Heparin Sodium Injection USP can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Heparin Sodium Injection USP should be administered to pregnant women only if clearly needed.
Nursing mothers: Heparin is not excreted in human milk.

Overdosage:
Bleeding is the principal sign of overdosage. Major bleeding episodes may be neutralized by the administration of protamine sulfate.

Storage: Store below 30ºC. Protect from light and freezing.

Keep all medicines out of the reach of children.

Presentation: 1 x 5 mL vial packed in a box with a package leaflet.

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