PORT CAP. The membrane of the infusion port is sterile, and disinfection before initial use is not necessary if proper aseptic handling technique is followed.

To Prepare for Administration:
1. Immediately before connecting the infusion set, firmly grasp the BLUE infusion port cap with the arrow pointing away from the bag between index finger and thumb. Gently break off the port cap. The membrane of the infusion port is sterile, and disinfection before initial use is not necessary if proper aseptic handling technique is followed.
2. Place the bag on a clean, flat surface. Starting in the bottom corner, peel the overwrap open slowly and remove the bag.
3. Check the bag for leaks by squeezing firmly. If leaks are found, discard the bag.

Dosage Forms and Strengths:
- Heparin Sodium in 0.45% Sodium Chloride Injection:
  - Injection: 50 USP units/mL in 0.45% Sodium Chloride clear solution (25,000 USP units per 500 mL) in single-dose freeflex® bag
  - Injection: 100 USP units/mL in 0.45% Sodium Chloride clear solution (25,000 USP units per 250 mL) in single-dose freeflex® bag

Heparin Sodium in 5% Dextrose Injection:
- Injection: 40 USP units/mL in 5% Dextrose clear solution (20,000 USP units per 500 mL) in single-dose freeflex® bag
- Injection: 50 USP units/mL in 5% Dextrose clear solution (25,000 USP units per 500 mL) in single-dose freeflex® bag
- Injection: 100 USP units/mL in 5% Dextrose clear solution (25,000 USP units per 250 mL) in single-dose freeflex® bag

Recommended Adult Dosages:
- Therapeutic Anticoagulant Effect with Full-Dose Heparin® (2.3):
  - Intravenous Infusion
    - Initial Dose: 10,000 units
      - Every 4 to 6 hours
    - Continuous Infusion
      - Initial Dose: 5,000 units by intravenous injection

Contraindications:
- History of Heparin-Induced Thrombocytopenia (HIT) and Heparin-Induced Thrombocytopenia and Thrombosis (HITT) (4)
- Known hypersensitivity to heparin or pork products (4)
- In whom suitable blood coagulation tests cannot be performed at appropriate intervals (4)

Warnings and Precautions:
- Fatal Medication Errors: Confirm choice of correct strength prior to administration. (5.1)
- Hemorrhage: Fatal cases have occurred. Use caution in conditions with increased risk of hemorrhage. (5.2)
- HIT and HITT: Monitor for signs and symptoms and discontinue if indicative of HIT and HITT. (5.3)
- Blood Coagulation Tests: Use these tests for full-dose heparin. Monitor platelet count and hematocrit in all patients receiving heparin. (5.5)

Adverse Reactions:
Most common adverse reactions are hemorrhage, HIT and HITT, hypersensitivity reactions, and elevations of amniotransferase levels. (6.1)

Drug Interactions:
Drugs that interfere with coagulation, platelet aggregation or drugs that counteract coagulation may induce bleeding. (7)

See 17 for Patient Counseling Information.

2.4 Pediatric Use
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 dosage schedule may be used as a guideline in pediatric patients:
- Initial Dose: 75 to 100 units/kg (intravenous bolus over 10 minutes)
- Maintenance Dose: Infants: 25 to 30 units/kg/hour; Infants <2 months have the highest requirements (average 28 units/kg/hour)
- 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 40 to 65 seconds, assuming this reflects an anti-Factor Xa level of 0.35 to 0.70.

2.5 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. A frequency 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.

2.6 Converting to Warfarin
To ensure continuous anticoagulation when converting from Heparin to warfarin, continue full heparin therapy for several days and then slowly taper the warfarin dose. (7.1)

2.7 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. (7.2)

2.8 Extracorporeal Dialysis
Follow equipment manufacturer's operating instructions carefully. A dose of 25 to 30 units/kg/hour is suggested based on pharmacodynamic data if specific manufacturers' recommendations are not available.

3. DOSE FORMS AND STRENGTHS
Heparin Sodium in 0.45% Sodium Chloride Injection is available as:
- Injection: 50 USP units/mL in 0.45% Sodium Chloride clear solution (25,000 USP units per 500 mL) in single-dose freeflex® bag
- Injection: 100 USP units/mL in 0.45% Sodium Chloride clear solution (25,000 USP units per 250 mL) in single-dose freeflex® bag

Heparin Sodium in 5% Dextrose Injection is available as:
- Injection: 40 USP units/mL in 5% Dextrose clear solution (20,000 USP units per 500 mL) in single-dose freeflex® bag
- Injection: 50 USP units/mL in 5% Dextrose clear solution (25,000 USP units per 500 mL) in single-dose freeflex® bag
- Injection: 100 USP units/mL in 5% Dextrose clear solution (25,000 USP units per 250 mL) in single-dose freeflex® bag

4. CONTRAINDICATIONS
The use of Heparin Sodium in 0.45% Sodium Chloride Injection or Heparin Sodium in 5% Dextrose Injection is contraindicated in the following patients with the conditions specified:
- History of Heparin-Induced Thrombocytopenia (HIT) and Heparin-Induced Thrombocytopenia and Thrombosis (HITT) (see Warnings and Precautions (5.3))
- Known hypersensitivity to heparin or pork products (e.g., anaphylactic reactions) [see Adverse Reactions (6.1)]
- 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) [see Warnings and Precautions (5.5)]
- An uncontrolled bleeding state [see Warnings and Precautions (5.2)], except when this is due to disseminated intravascular coagulation.

5.5 Fatal Medication Errors
Do not use this product as a “catcher lock flush” product. Heparin is supplied in various strengths. Fatal hemorrhages have occurred due to medication errors. Carefully examine all heparin solutions to confirm the correct solution prior to administration of the drug.

5.2 Hemorrhage
Avoid using heparin in the presence of major bleeding, except when the benefits of heparin therapy outweigh the potential risks.

Hemorrhage, including fatal events, has occurred in patients receiving Heparin Sodium. Hemorrhage can occur at virtually any site in patients receiving heparin. Adrenal hemorrhage (with resultant acute adrenal insufficiency), ovarian hemorrhage, and retropertitoneal hemorrhage have occurred during anticoagulant therapy with heparin [see Adverse Reactions (6.1)]. A higher incidence of bleeding has been reported in patients, particularly women, over 60 years of age [see Clinical Pharmacology (12.3)]. An unexplained fall in hematocrit or fall in blood pressure 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:
- Cardiogenic — In bacteremic endocarditis, severe hypertrophy.
- 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 vasculare 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, use heparin sodium in combination with antithrombin III (human)
- Gastrointestinal — Ulcerative lesions and continuous tube drainage of the stomach or small intestine.
- Other — Menorrhagia, liver disease with impaired hemostasis.
5.3 Heparin-Induced Thrombocytopenia (HIT) and Heparin-Induced Thrombocytopenia and Thrombosis (HITT)

HIT is a serious antibody-mediated reaction resulting from irreversible aggregation of platelets. 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 known as HIT with thrombosis (HITT). HIT and HITT may also be the initial presentation for HIT. These serious thrombotic events include deep vein thrombosis, pulmonary embolism, cerebrovascular events, limb ischemia, strike, myocardial infarction, thrombosis on a prosthetic valve, recurrent stroke, renal arterial thrombosis, skin necrosis, gangrene of the extremities that lead to amputation, and possibly death. Monitor thrombocytopenia of any degree closely. If the platelet count falls below 100,000/mm³ without a history of heparin-free days, promptly discontinue heparin, evaluate for HIT and HITT, and, if necessary, administer an alternative anticoagulant.[see Warnings and Precautions (5.3)]

5.4 Thrombocytopenia

Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of up to 30%. It can occur 2 to 20 days (average 5 to 9) after 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/mm³ or if thrombocytopenia develops, promptly discontinue heparin, evaluate for HIT and, if necessary, administer an alternative anticoagulant.[see Warnings and Precautions (5.3)]

5.5 Coagulation Testing and Monitoring

When using a full dose heparin regimen, adjust the heparin dose based on frequent coagulation tests. If the coagulation test is unduly prolonged or if hemorrhage occurs, heparin sodium should be discontinued promptly.[see Overdosage (10)]. Periodic platelet counts, hematocrits are recommended during the entire course of heparin therapy.[see Dosage and Administration (2.3)]

5.6 Heparin Resistance

Increased resistance to heparin is frequently encountered in fever, thrombosis, thromboembolisms, infections with thrombosing tendencies, myocardial infarction, cancer, in postpartum 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.

5.7 Hypersensitivity

Patients with documented hypersensitivity to heparin should be given the drug only in clearly life-threatening situations.[see Adverse Reactions (5.1)]. Because heparin sodium is derived from animal tissue, monitor for signs and symptoms of hypersensitivity in patients with a history of allergy to heparin.

5.8 Heparin Sodium in 5% Dextrose Injection

This product contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic shock when administered to individuals with a history of sulfite sensitivity.[see Warnings and Precautions (5.3)].

5.9 Heparin Sodium in 0.45% Sodium Chloride Injection and Heparin Sodium in 5% Dextrose Injection

Heparin sodium, sodium metabisulfite, and water for injection are ingredients of these products. The concentration of sodium metabisulfite is 250 parts per million (250 ppm) in each 100 mL of heparin sodium. It is included to prevent bacterial contamination of the heparin solution. It will be destroyed during the heating step of the solution preparation process.

5.10 Heparin Sodium in 5% Dextrose Injection

Heparin Sodium in 5% Dextrose Injection is sterile.

5.11 Other Interactions

Heparin sodium may prolong the one-stage prothrombin time. Therefore, when heparin sodium is given with warfarin sodium, the patient's prothrombin time is likely to be prolonged. Heparin sodium is a potent antithrombotic agent that competes with warfarin sodium for plasma anticoagulant protein C. Heparin sodium may also interfere with the anticoagulant action of warfarin sodium. Heparin sodium has been reported to produce a prolongation of the INR, the prothrombin time, the activated partial thromboplastin time, and the thrombin time. Heparin sodium also prolongs the activated partial thromboplastin time and the partial thromboplastin time. These effects can increase the risk for bleeding and should be considered when heparin sodium is administered to patients receiving warfarin sodium. Heparin sodium may reduce the effectiveness of oral anticoagulants when given together for more than 2 days.

5.12 Lactation

Heparin Sodium is distributed into human milk. The amount of heparin in breast milk is not known. It is unknown whether this drug is absorbed by a nursing infant. The developmental and health benefits of breastfeeding should be considered when a decision is made to discontinue breastfeeding or when nursing women receive this drug.[see Use in Specific Populations (8.3)].

5.13 Other Interactions

Heparin sodium may prolong the partial thromboplastin time and the thrombin time with subsequent rebound effect upon discontinuation of nitroglycerin. Careful monitoring of partial thromboplastin time and adjustments of heparin dosage are recommended during concomitant administration of heparin and intravenous nitroglycerin.

7.2 Platelet Inhibitors

Drugs such as NSAIDs (including salicylic acid, ibuprofen, indomethacin, and celecoxib), dextran, phenylbutazone, thienopyridines, dipyrone, dipyridamole, cyclo-oxygenase inhibitors (including aspirin, ibuprofen, and tolfenamic acid), and others that interfere with platelet-aggregation reactions (the main hemostatic defense of the body) may inhibit heparin sodium's antithrombotic effect. Use of these drugs may result in a decrease in the dose of aspirin, clopidogrel, or other platelet-aggregation inhibitors that should be used with caution in patients receiving heparin sodium. To reduce the risk of bleeding, a reduction in the dose of aspirin or other antiplatelet agent is recommended.

7.3 Other Interactions

Digitalis, tetracyclines, nicotine, antihistamines, or intravenous nitroglycerin may partially counteract the anticoagulant action of heparin sodium.

Heparin Sodium in 5% Dextrose Injection, Intravenous nitroglycerin administered to heparinized patients may result in a decrease in 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 concomitant administration of heparin and intravenous nitroglycerin.

Heparin Sodium in 5% Dextrose Injection, Intravenous nitroglycerin administered to heparinized patients may result in a decrease in 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 concomitant administration of heparin and intravenous nitroglycerin.