Heparin Sodium Injection, USP (porcine), preservative free, is available as follows:

- Each mL of the 1,000 units per mL preparation contains: 1,000 USP Heparin units (porcine); 9 mg sodium chloride; Water for Injection q.s. Made isotonic with sodium chloride. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (5.0 to 7.5).

- Each mL of the 5,000 units per 0.5 mL preparation contains: 5,000 USP Heparin units (porcine); Water for Injection q.s. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (5.0 to 7.5).

Heparin Sodium Injection, USP (porcine), preserved with benzyl alcohol, is available as follows:

- Each mL of the 5,000 units per mL preparation contains: 5,000 USP Heparin units (porcine); 6 mg sodium chloride; 15 mg benzyl alcohol (as a preservative); Water for Injection q.s. Made isotonic with sodium chloride. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (5.0 to 7.5).

- Each mL of the 10,000 units per mL preparation contains: 10,000 USP Heparin units (porcine); 5 mg sodium chloride; 10.42 mg benzyl alcohol (as a preservative); Water for Injection q.s. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (5.0 to 7.5).

Heparin Sodium Injection, USP (porcine), preserved with paraben, is available as follows:

- Each mL of the 1,000 units per mL preparation contains: 1,000 USP Heparin units (porcine); 9 mg sodium chloride; 1.5 mg methylparaben; 0.15 mg propylparaben; Water for Injection q.s. Made isotonic with sodium chloride. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (5.0 to 7.5).

- Each mL of the 5,000 units per mL preparation contains: 5,000 USP Heparin units (porcine); 5 mg sodium chloride; 1.5 mg methylparaben; 0.15 mg propylparaben; Water for Injection q.s. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (5.0 to 7.5).

Heparin Sodium Injection vials have been designed for use in the following circumstances: Hemorrhage occurs, heparin sodium should be promptly discontinued (see WARNINGS). Heparin-induced thrombocytopenia and heparin-induced thrombocytopenia and thrombosis (HITT) can occur up to several weeks after the discontinuation of heparin sodium therapy. Use preservative-free HEPARIN SODIUM INJECTION in neonates and infants. Treating preservative-free heparin sodium injection vials to confirm the correct vial choice prior to administration of the drug. Benzyl Alcohol Toxicity. Occasionally, benzyl alcohol toxicity has been observed in neonates and infants receiving benzyl alcohol-containing heparin solutions. Hypersensitivity. Patients with documented hypersensitivity to heparin should be given the drug only in clearly indicated situations. Thrombocytopenia and Thrombosis (HITT). Hemorrhage can occur at virtually any site in the body. In the gastrointestinal tract, heparin may be indicated in these patients (see INDICATIONS AND ADMINISTRATION).
life-threatening situations (see ADVERSE REACTIONS, Hypersensitivity). Hemorrhage

Hemorrhage can occur at virtually any site in patients receiving heparin. An unexplained fall in the patient’s blood pressure or any unexplained symptom should lead to severe consideration of a hemorrhagic event. Heparin therapy should be used with extreme caution in diseases in which there is increased danger of hemorrhage. Some of the common sites of increased danger of hemorrhage exist are:

Cardiovascular—Subacute bacterial endocarditis, severe hypertension.

Surgical—During and immediately following (causing 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 problems.

Gastrointestinal—Ulcerative lesions and continuous tube drainage of the stomach or small intestine.

Other—Menstruation, liver disease with impaired hemostasis.

Coagulation Testing

When heparin sodium is administered in therapeutics, coagulation studies, especially partial thromboplastin time (PTT), should be followed by frequent blood coagulation tests. If the coagulation test is unduly prolonged or if hemorrhage does occur, heparin therapy should be promptly discontinued (see OVERDOSE).

Thrombocytopenia

Thrombocytopenia has been reported to occur in up to 30% of patients receiving heparin with a reported incidence of up to 30%. Platelet counts should be obtained at baseline and periodically during treatment. Mild thrombocytopenia (count greater than 100,000/mm³) may remain stable or reverse even if heparin is continued. However, thrombocytopenia of any degree should be monitored closely. If the count falls below 100,000/mm³ or if recurrent thrombocytopenia occurs, Heparin-induced Thrombocytopenia and Thrombosis (HIT) should be suspected and, if necessary, an alternative anticoagulant administered.

Heparin-induced Thrombocytopenia (HIT) and Heparin-induced Thrombocytopenia and Thrombosis (HITT)

Heparin-induced Thrombocytopenia (HIT) is a serious antibody-mediated reaction resulting from an immune response and is a condition referred to as Heparin-induced Thrombocytopenia and Thrombosis (HITT). Thrombotic events include: deep vein thrombosis, pulmonary embolus, stroke, myocardial infarction, mesenteric thrombosis, renal arterial thrombosis, and skin necrosis. If the extremities that may lead to amputation, and possibly death. Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/mm³ or if recurrent thrombosis develops, the heparin product should be promptly discontinued and alternative anticoagulants considered, if patients require continued anticoagulation.

Delayed Onset of HIT and HITT

Heparin-induced Thrombocytopenia and Heparin-induced Thrombocytopenia and Thrombosis 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.

PRECAUTIONS:

General

Thrombocytopenia, Heparin-induced Thrombocytopenia and Thrombosis (HITT) and Heparin-induced Thrombocytopenia and Thrombosis (HITT) See WARNINGS.

Heparin Resistance—Increased resistance to heparin is frequently encountered in liver, thrombosis, thrombophlebitis, infections with thrombogenic tendencies, myocardial infarction, cancer and in postoperative patients.

Increased Risk to Older Patients, Especially Women

A higher incidence of bleeding has been reported in patients, particularly women, over 60 years of age.

Laboratory Tests

Periodic platelet counts, hematocrits, and tests for occult blood in stool are recommended during the entire course of heparin therapy, regardless of the route of administration (see DOSAGE AND ADMINISTRATION).

Drug Interactions

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

Platelet Inhibitors—Drugs such as acetylsalicylic acid, dextran, phenylbutazone, ibuprofen, indomethacin, dipyridamole, hydroxychloroquine and others that interfere with platelet-aggregation reactions (the main hemostatic defense of heparinized patients) should be used with caution in patients receiving heparin sodium.

Other Interactions—Digitalis, tetracyclines, nico-
tine or antihistamines may partially counteract the anticoagulant action of heparin sodium. Intravenous nitroglycerin administered to heparinized patients may lead to a decrease of the partial thromboplastin time with subsequent rebound effect upon discontinuation of nitro-glycerin. Calcium chloride and intravenous thromboplastin time and adjustment of heparin dosage are recommended during coadministration of heparin and intravenous nitroglycerin.

Drug/Laboratory Tests Interactions

Heparin is strongly acidic because of its content of sulfate units, and/or sodium hydroxide may have been added for pH adjustment (5.0 to 7.5).

Each mL of the 5,000 units per mL preparation contains: 5,000 USP Heparin units (porcine); 0.1% sodium chloride, 0.01% benzyl alcohol, is available as a sterile solution.

Each mL of the 10,000 units per mL preparation contains: 10,000 USP Heparin units (porcine); 0.2% sodium chloride, 0.01% benzyl alcohol, is available as a sterile solution.

Each mL of the 20,000 units per mL preparation contains: 20,000 USP Heparin units (porcine); 0.4% sodium chloride, 0.01% benzyl alcohol, is available as a sterile solution.

Heparin Sodium Injection, USP (porcine), each mL of the 10,000 units per mL preparation contains: 10,000 USP Heparin units (porcine); 0.4% sodium chloride, 0.01% benzyl alcohol, is available as a sterile solution.

Heparin Sodium Injection, USP (porcine), each mL of the 20,000 units per mL preparation contains: 20,000 USP Heparin units (porcine); 0.4% sodium chloride, 0.01% benzyl alcohol, is available as a sterile solution.

Each mL of the 1,000 units per mL preparation contains: 1,000 USP Heparin units (porcine); 0.01% sodium chloride, 0.01% benzyl alcohol, is available as a sterile solution.

Each mL of the 5,000 units per mL preparation contains: 5,000 USP Heparin units (porcine); 0.1% sodium chloride, 0.01% benzyl alcohol, is available as a sterile solution.

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 more rarely. Itching and burning, especially on the plantar side of the feet, may occur (see WARNINGs and PRECAUTIONs).

Certain episodes of painful, ischemic and cyanosed limbs have in the past been attributed to allergic vasospastic reactions. Whether these are in fact identical to the thrombocytopenia-associated complications, remains to be determined.

**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.

Significant elevations of aminotransferase (SGOT [S-AST] and SGPT [S-ALT]) levels have occurred in a high percentage of patients (and healthy subjects) who have received heparin.

**OVERDOSE:**

**Symptoms**

Bleeding is the chief sign of heparin overdosage. Nosebleeds, blood in urine or tarry stools may be noted as the first sign of bleeding. Easy bruising or petechial formations may precede frank bleeding.

**Treatment**

Neutralization of Heparin Effect—When clinical circumstances (bleeding) require reversal of heparinization, 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.

Administration of protamine sulfate can cause severe hypotensive and anaphylactoid reactions. Because fatal reactions often resembling anaphylaxis have been reported, the drug 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, USP products.

**DOSEAGE AND ADMINISTRATION:**

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Confirm the choice of the correct Heparin Sodium Injection vial prior to administration of the drug to a patient (see WARNINGs, Fatality Medication Errors). The 1 mL vial must not be confused with a “catheter lock flush” vial or other 1 mL vial of inappropriate strength. Confirm that you have selected the correct medication and strength prior to administration of the drug.

When heparin is added to an infusion solution for continuous intravenous administration, the container should be inverted at least six times to ensure adequate mixing and prevent pooling of the heparin in the solution.

Heparin sodium is not effective by oral administration and should be given by intermittent intravenous injection, intravenous infusion, or deep subcutaneous (intrrafat, i.e., above the iliac crest or abdominal fat layer) injection. The intramuscular route of administration should be avoided because of the frequent occurrence of hematoma at the injection site.

The dosage of heparin sodium should be adjusted according to the patient’s coagulation test results. When heparin is given by continuous intravenous infusion, the coagulation time should be determined approximately every four hours in the early stages of treatment. When the drug is administered intermittently by intravenous injection, coagulation tests should be performed before each injection during the early stages of treatment and at appropriate intervals thereafter. 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. After deep subcutaneous (intrrafat) injections, tests for adequacy of dosage are best performed on samples drawn four to six hours after the injection.

Periodic platelet counts, hematocrits and tests for occult blood in stool are recommended during the entire course of heparin therapy, regardless of the route of administration.

**Converting to Oral Anticoagulants**

When an oral anticoagulant of the coumarin or similar type is to be begun in patients already receiving heparin sodium, baseline and subsequent tests of prothrombin activity must be determined at a time when heparin activity is too low to affect the prothrombin time. This is about five hours after the last IV bolus and 24 hours after the last subcutaneous dose. If continuous IV heparin infusion is used, prothrombin time can usually be measured at any time.

In converting from heparin to an oral anticoagulant, the dose of the oral anticoagulant should be the usual initial amount and thereafter prothrombin time should be determined at the usual intervals. To ensure continuous anticoagulation, it is advisable to continue full heparin therapy for several days after the prothrombin time has reached the therapeutic range. Heparin therapy may then be discontinued without tapering.

**Therapeutic Anticoagulant Effect with Full-Dose Heparin**

Although dosage must be adjusted for the individual patient according to the results of suitable laboratory tests, the following dosage schedules may be used as a guideline:

**METHOD OF ADMINISTRATION FREQUENCY RECOMMENDED DOSE (based on 150 lb (68 kg) patient)**

| Deep Subcutaneous (Intrrafat) Injection | Initial Dose | 1,000 units by IV injection, followed by 10,000 to 30,000 units of a concentrated solution, subcutaneously |
| A different dose should be used for each injection to prevent the development of massive hematoma | Every 6 hours or 12 hours | 15,000 to 20,000 units of a concentrated solution |
| Intravenous Injection | Initial Dose | 10,000 units, either undiluted or in 50 to 100 mL of 0.9% Sodium Chloride Injection, USP |
| Every 4 to 6 hours | | |
| Intravenous Infusion | Initial Dose | 1,000 units by IV injection |
| Continuous | | 20,000 to 40,000 units/24 hours in 1,000 mL of 0.9% Sodium Chloride Injection, USP (or in any compatible solution) for infusion |

**Pediatric Use**

Use preservative-free HEPARIN SODIUM INJECTION in neonates and infants (see WARNINGs, Benzyl Alcohol Toxicity and PRECAUTIONs, 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 following dosage schedule may be used as a guideline in pediatric patients:

**Initial Dose**

| Infant < 1 year of age | | 75 to 100 units/kg (IV bolus over 10 minutes) |
| 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.

**Geriatric Use**

Patients over 60 years of age may require lower doses of heparin.

**Surgery of the Heart and Blood Vessels**

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 of heparin sodium per kilogram of body weight 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

A number of well-controlled clinical trials have demonstrated that low-dose heparin prophylaxis, given just prior to and after surgery, will reduce the incidence of postoperative deep vein thrombosis in the legs (as measured by the 1+15 fibrinogen technique and venography) and of clinical pulmonary embolism. 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 seven days or until the patient is fully ambulatory, whichever is longer. The heparin is given by deep subcutaneous injection in the arm or abdomen with a fine needle (25 to 28 gauge) to minimize tissue trauma. A concentrated solution of heparin sodium is recommended. Such prophylaxis should be reserved for patients over the age of 40 who are undergoing major surgery. Patients with bleeding disorders and those having neurosurgery, spinal anesthesia, eye surgery or potentially sanguineous operations should be excluded, as well as patients receiving oral anticoagulants or platelet-active drugs (see WARNINGS). The value of such prophylaxis in hip surgery has not been established. The possibility of increased bleeding during surgery or postoperatively should be borne in mind. If such bleeding occurs, discontinuance of heparin and neutralization with protamine sulfate should be advisable. If clinical evidence of thrombembolism develops despite low-dose prophylaxis, full therapeutic doses of anticoagulants should be given unless contraindicated. All patients should be screened prior to heparinization to rule out bleeding disorders, and monitoring should be performed with appropriate coagulation tests just prior to surgery. Coagulation test values should be normal or only slightly elevated. There is usually no need for daily monitoring of the effect of low-dose heparin in patients with normal coagulation parameters.

Extracorporeal Dialysis

Follow equipment manufacturers' operating directions carefully.

Blood Transfusion

Addition of 400 to 800 USP units per 100 mL of whole blood is usually employed to prevent coagulation. Usually, 7,500 USP units of heparin sodium are added to 100 mL of 0.9% Sodium Chloride Injection, USP (or 75,000 USP units/100 mL of 0.9% Sodium Chloride Injection, USP) of blood; from this sterile solution, 6 to 8 mL are added per 100 mL of whole blood.

Laboratory Samples

Addition of 70 to 150 units of heparin sodium per 10 to 20 mL sample of whole blood is usually employed to prevent coagulation of the sample. Leukocyte counts should be performed on heparinized blood within two hours after addition of the heparin. Heparinized blood should not be used for isoagglutinin, complement, or erythrocyte fragility tests or platelet counts.

HOW SUPPLIED:

Heparin Sodium Injection, USP (porcine), preservative free, is available as follows:

<table>
<thead>
<tr>
<th>Product No.</th>
<th>NDC No.</th>
<th>Strength</th>
<th>Fill Volume</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>27602</td>
<td>63323-276-02</td>
<td>2,000 USP Heparin units per 2 mL</td>
<td>2 mL fill in a 3 mL vial, in packages of 25.</td>
<td></td>
</tr>
<tr>
<td>504302</td>
<td>63323-543-02</td>
<td>5,000 USP Heparin units per 0.5 mL</td>
<td>0.5 mL fill in a 3 mL vial, in packages of 25.</td>
<td></td>
</tr>
</tbody>
</table>

Use only if solution is clear and seal intact. Do not use if solution is discolored or contains a precipitate. Discard unused portion.

This container closure is not made from natural rubber latex.

Heparin Sodium Injection, USP (porcine) contains benzyl alcohol and is available as follows:

<table>
<thead>
<tr>
<th>Product No.</th>
<th>NDC No.</th>
<th>Strength</th>
<th>Fill Volume</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>4710</td>
<td>63323-047-10</td>
<td>50,000 USP Heparin units per 10 mL</td>
<td>10 mL fill in a 3 mL vial, in packages of 25.</td>
<td></td>
</tr>
<tr>
<td>504509</td>
<td>63323-459-09</td>
<td>40,000 USP Heparin units per 4 mL</td>
<td>4 mL fill in a 3 mL vial, in packages of 25.</td>
<td></td>
</tr>
</tbody>
</table>

Use only if solution is clear and seal intact. Do not use if solution is discolored or contains a precipitate. This container closure is not made from natural rubber latex.

Heparin Sodium Injection, USP (porcine) contains parabens and is available in multi-dose, flip-top vials, in packages of 25, as follows:

<table>
<thead>
<tr>
<th>Product No.</th>
<th>NDC No.</th>
<th>Strength</th>
<th>Fill Volume</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>504001*</td>
<td>63323-540-01</td>
<td>1,000 USP Heparin units per 1 mL</td>
<td>1 mL fill in a 3 mL vial.</td>
<td></td>
</tr>
<tr>
<td>504011</td>
<td>63323-540-11</td>
<td>10,000 USP Heparin units per 10 mL</td>
<td>10 mL fill in a 10 mL vial.</td>
<td></td>
</tr>
<tr>
<td>504031</td>
<td>63323-540-31</td>
<td>30,000 USP Heparin units per 30 mL</td>
<td>30 mL fill in a 30 mL vial.</td>
<td></td>
</tr>
<tr>
<td>502601**</td>
<td>63323-262-01</td>
<td>5,000 USP Heparin units per 1 mL</td>
<td>1 mL fill in a 3 mL vial.</td>
<td></td>
</tr>
<tr>
<td>502401</td>
<td>63323-542-01</td>
<td>10,000 USP Heparin units per 1 mL</td>
<td>1 mL fill in a 3 mL vial.</td>
<td></td>
</tr>
<tr>
<td>502407</td>
<td>63323-542-07</td>
<td>50,000 USP Heparin units per 5 mL</td>
<td>5 mL fill in a 6 mL vial.</td>
<td></td>
</tr>
<tr>
<td>915501**</td>
<td>63323-915-01</td>
<td>20,000 USP Heparin units per 1 mL</td>
<td>1 mL fill in a 3 mL vial.</td>
<td></td>
</tr>
</tbody>
</table>

*Packaged in a plastic or glass vial. **Packaged in a plastic vial.

Use only if solution is clear and seal intact. Do not use if solution is discolored or contains a precipitate. This container closure is not made from natural rubber latex.

STORAGE:

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

REFERENCES: