

HEPARIN SODIUM- heparin sodium injection, solution

Hospira, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HEPARIN SODIUM IN SODIUM CHLORIDE INJECTION safely and effectively. See full prescribing information for HEPARIN SODIUM IN SODIUM CHLORIDE INJECTION.

HEPARIN SODIUM IN SODIUM CHLORIDE INJECTION, for intravenous use
Initial U.S. Approval: 1939

RECENT MAJOR CHANGES

Warnings and Precautions, Heparin-Induced Thrombocytopenia and Heparin-Induced Thrombocytopenia with Thrombosis (5.2)	11/2024
Warnings and Precautions, Heparin Resistance (5.4)	11/2024
Warnings and Precautions, Hypersensitivity Reactions (5.5)	11/2024
Warnings and Precautions, Hyperkalemia (5.7)	7/2024
Warnings and Precautions, Elevations of Serum Aminotransferases (5.8)	11/2024

INDICATIONS AND USAGE

Heparin Sodium in Sodium Chloride Injection at a concentration of 2 units/mL is indicated as an anticoagulant to maintain catheter patency. (1)

DOSAGE AND ADMINISTRATION

Infuse through intravenous catheter at a rate of 6 units per hour. (2.2)

DOSAGE FORMS AND STRENGTHS

- Injection: 1,000 USP units in Sodium Chloride per 500 mL single-dose infusion bag (2 units per mL) (3)
- Injection: 2,000 USP units in Sodium Chloride per 1,000 mL single-dose infusion bag (2 units per mL) (3)

CONTRAINDICATIONS

Heparin Sodium in Sodium Chloride Injection is contraindicated in patients with the following conditions: (4)

- Uncontrollable active bleeding state, except when this is due to disseminated intravascular coagulation (5.1)
- History of heparin-induced thrombocytopenia (HIT) and heparin-induced thrombocytopenia with thrombosis (HITT) (5.2)
- Severe thrombocytopenia (5.2, 5.3)
- Known hypersensitivity to heparin or pork products (5.5, 6.1)

WARNINGS AND PRECAUTIONS

- Hemorrhage: Fatal hemorrhages have occurred. Monitor for signs of bleeding and manage promptly. (5.1)
- HIT and HITT: Monitor for signs and symptoms and discontinue if indicative of HIT or HITT. (5.2)
- Thrombocytopenia: Monitor platelet count during therapy; discontinue heparin if HIT or HITT is suspected. (5.3)
- Heparin Resistance: Increased resistance to heparin is frequently encountered in fever, thrombosis, thrombophlebitis, infections with thrombosing tendencies, myocardial infarction, cancer and in postsurgical patients. (5.4)
- Hypersensitivity Reactions: Use in patients with prior reactions only in life-threatening situations. (5.5)
- Increased Risk of Bleeding in Older Patients, Especially Women: A higher incidence of bleeding has been reported in patients, particularly women, over 60 years of age. (5.6)
- Hyperkalemia: Measure blood potassium in patients at risk of hyperkalemia before starting heparin therapy and periodically in all patients. (5.7)
- Elevations of Serum Aminotransferases: Interpret elevation of these enzymes with caution. (5.8)
- 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.

(5.9)

-----**ADVERSE REACTIONS**-----

Most common adverse reactions are: hemorrhage, thrombocytopenia, HIT and HITT, hypersensitivity reactions, heparin resistance, hyperkalemia, and elevations of aminotransferase levels. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----**DRUG INTERACTIONS**-----

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

-----**USE IN SPECIFIC POPULATIONS**-----

Geriatric Use: A higher incidence of bleeding has been reported in patients over 60 years of age, especially women. (5.6, 8.5)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2024

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Heparin Sodium in Sodium Chloride Injection at a concentration of 2 units/mL is indicated as an anticoagulant to maintain catheter patency.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

Do not administer unless solution is clear and seal is intact. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Warning: Do not use plastic containers in series connection. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed.

Do not use Heparin Sodium in Sodium Chloride Injection as a “catheter lock flush” product.

Do not admix with other drugs. Discard unused portion.

To Open

Tear outer wrap and remove solution container.

Preparation for Administration

(Use aseptic technique)

1. Close flow control clamp of administration set.
2. Remove cover from outlet port at bottom of container.
3. Insert piercing pin of administration set into port with a twisting motion until the set is firmly seated.

NOTE: When using a vented administration set, replace bacterial retentive air filter with piercing pin cover. Insert piercing pin with twisting motion until shoulder of air filter housing rests against the outlet port flange.

4. Suspend container from hanger.
5. Squeeze and release drip chamber to establish proper fluid level in chamber.
6. Attach venipuncture device to set.
7. Open clamp to expel air from set and venipuncture device. Close clamp.
8. Perform venipuncture.
9. Regulate rate of administration with flow control clamp.

2.2 Recommended Dosage for Maintenance of Catheter Patency

The recommended starting dose is 6 units per hour by intravenous infusion through an intravenous catheter to maintain catheter patency.

3 DOSAGE FORMS AND STRENGTHS

- Injection: 1,000 USP units per 500 mL (2 units per mL) clear solution in a single-dose infusion bag
- Injection: 2,000 USP units per 1,000 mL (2 units per mL) clear solution in a single-dose infusion bag

4 CONTRAINDICATIONS

The use of Heparin Sodium in Sodium Chloride Injection is contraindicated in patients with the following conditions:

- Uncontrollable active bleeding state, except when this is due to disseminated intravascular coagulation [*see Warnings and Precautions (5.1)*]
- History of heparin-induced thrombocytopenia (HIT) and heparin-induced thrombocytopenia with thrombosis (HITT) [*see Warnings and Precautions (5.2)*]
- Severe thrombocytopenia [*see Warnings and Precautions (5.2, 5.3)*]
- Known hypersensitivity to heparin or pork products (e.g., anaphylactoid reactions) [*see Warnings and Precautions (5.5), Adverse Reactions (6.1)*]

5 WARNINGS AND PRECAUTIONS

5.1 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. An unexplained fall in hematocrit or 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.
- Gastrointestinal — Ulcerative lesions and continuous tube drainage of the stomach or small intestine.
- 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).
- Other — Menstruation, liver disease with impaired hemostasis.

5.2 Heparin-Induced Thrombocytopenia and Heparin-Induced Thrombocytopenia with Thrombosis

Heparin-induced thrombocytopenia (HIT) is a serious immune-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, thrombus formation on a prosthetic cardiac valve, renal arterial thrombosis, skin necrosis, gangrene of the extremities that may lead to amputation, and possibly death.

Once HIT or HITT is diagnosed or strongly suspected, discontinue all heparin sources (including heparin flushes) and use an alternative anticoagulant.

Immune-mediated HIT is diagnosed based on clinical findings supplemented by laboratory tests confirming the presence of antibodies to heparin, or platelet activation induced by heparin. Obtain platelet counts at baseline and periodically during heparin administration. A drop in platelet count greater than 50% from baseline is considered indicative of HIT. Platelet counts begin to fall 5 to 10 days after exposure to heparin in heparin-naïve individuals and reach a threshold by days 7 to 14. In contrast, “rapid onset” HIT can occur very quickly (within 24 hours following heparin initiation), especially in patients with a recent exposure to heparin (i.e., previous 3 months).

Thrombosis development shortly after documenting thrombocytopenia is a characteristic finding in almost half of all patients with HIT.

If the platelet count falls below $100,000/\text{mm}^3$ 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.

5.3 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. If the count falls below $100,000/\text{mm}^3$ or if recurrent thrombosis develops, promptly discontinue heparin, evaluate for HIT and HITT, and, if necessary, administer an alternative anticoagulant [see

Warnings and Precautions (5.2)].

5.4 Heparin Resistance

Increased resistance to heparin is frequently encountered in fever, thrombosis, thrombophlebitis, infections with thrombosing tendencies, myocardial infarction, cancer, in postsurgical patients, and patients with antithrombin deficiency. Consider measurement of antithrombin levels if heparin resistance is suspected. Monitor coagulation tests frequently in such patients. It may be necessary to adjust the dose of heparin based on coagulation test monitoring, such as anti-Factor Xa levels and/or partial thromboplastin time.

5.5 Hypersensitivity Reactions

Hypersensitivity reactions with chills, fever, and urticaria as the most usual manifestations and also asthma, rhinitis, lacrimation, and anaphylactoid reactions have been reported. Patients with documented hypersensitivity to heparin should be given the drug only in clearly life-threatening situations. Because Heparin Sodium in Sodium Chloride Injection is derived from animal tissue, it should be used with caution in patients with a history of allergy to pork products.

5.6 Increased Risk of Bleeding in Older Patients, Especially Women

A higher incidence of bleeding has been reported in patients, particularly women, over 60 years of age [*see Use in Specific Populations (8.5)*].

5.7 Hyperkalemia

Heparin can suppress adrenal secretion of aldosterone leading to hyperkalemia, particularly in patients 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 upon discontinuation of heparin.

Measure blood potassium in patients at risk of hyperkalemia before starting heparin therapy and periodically in all patients treated for more than 5 days or earlier as deemed fit by the clinician.

5.8 Elevations of Serum Aminotransferases

Significant elevations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels have occurred in patients who have received heparin. Elevation of these enzymes in patients receiving heparin should be interpreted with caution. These elevations typically resolve upon heparin discontinuation.

5.9 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.

6 ADVERSE REACTIONS

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

- Hemorrhage [see *Warnings and Precautions (5.1)*]
- Heparin-Induced Thrombocytopenia and Heparin-Induced Thrombocytopenia with Thrombosis [see *Warnings and Precautions (5.2)*]
- Thrombocytopenia [see *Warnings and Precautions (5.3)*]
- Heparin Resistance [see *Warnings and Precautions (5.4)*]
- Hypersensitivity Reactions [see *Warnings and Precautions (5.5)*]
- Increased Risk of Bleeding in Older Patients, Especially Women [see *Warnings and Precautions (5.6)*]
- Hyperkalemia [see *Warnings and Precautions (5.7)*]
- Elevations of Serum Aminotransferases [see *Warnings and Precautions (5.8)*]

6.1 Postmarketing Experience

The following adverse reactions have been identified during postapproval 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 - Hemorrhage is the chief complication that may result from heparin therapy [see *Warnings and Precautions (5.1)*]. An overly prolonged clotting time or minor bleeding during therapy can usually be controlled by withdrawing the drug [see *Overdosage (10)*]. 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 during anticoagulant therapy, including fatal cases.
- Ovarian (corpus luteum) hemorrhage developed in a number of women of reproductive age receiving short- or long-term anticoagulant therapy.
- Retroperitoneal hemorrhage.

Vascular disorders - Contusion, vasospastic reactions (including episodes of painful, ischemic, and cyanosed limbs).

HIT and HITT, including delayed onset [see *Warnings and Precautions (5.2)*]

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 more rarely. Itching and burning, especially on the plantar site of the feet, may occur [see *Warnings and Precautions (5.5)*].

Musculoskeletal, connective tissue and bone disorders - Osteoporosis with long-term administration of heparin.

Metabolism and nutrition disorders - Hyperkalemia.

General disorders and administration site conditions - Erythema, mild pain, ulceration.

Elevations of serum aminotransferases- Significant elevations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels have occurred in patients who have received heparin.

Others - Cutaneous necrosis after systemic administration, delayed transient alopecia, priapism, and rebound hyperlipemia on discontinuation of heparin sodium have also been reported.

7 DRUG INTERACTIONS

7.1 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.

7.2 Platelet Inhibitors

Drugs such as NSAIDS (including acetylsalicylic acid, ibuprofen, indomethacin, and celecoxib), dextran, phenylbutazone, thienopyridines, dipyridamole, hydroxychloroquine, glycoprotein IIb/IIIa antagonists (including abciximab, eptifibatid, and tirofiban), and others that interfere with platelet-aggregation reactions (the main hemostatic defense 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 the antiplatelet agent or heparin is recommended.

7.3 Other Medications that May Interfere with Heparin

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).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Heparin Sodium in Sodium Chloride Injection 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 (see *Data*). Consider the benefits and risks of Heparin Sodium in Sodium Chloride Injection for the mother and possible risks to the fetus when prescribing Heparin Sodium in Sodium Chloride Injection.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

Data

Human Data

The maternal and fetal outcomes associated with uses of heparin via various dosing methods and administration routes during pregnancy have been investigated in 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 USP units/kg/day, approximately >50 times the human daily dose. The number of early resorptions increased in both species. There was no evidence of teratogenic effects.

8.2 Lactation

Risk Summary

There is no information regarding the presence of heparin in human milk, the effects on the breastfed child, or the effects on milk production. Due to its large molecular weight, heparin is not likely to be excreted in human milk.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Heparin Sodium in Sodium Chloride Injection and any potential adverse effects on the breastfed child from Heparin Sodium in Sodium Chloride Injection or from the underlying maternal condition [*see Use in Specific Populations (8.4)*].

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

A higher incidence of bleeding has been reported in patients over 60 years of age, especially women [*see Warnings and Precautions (5.6)*].

10 OVERDOSAGE

An overdose requires immediate medical attention and treatment.

Symptoms

Bleeding is the chief sign of heparin overdosage. Easy bruising, petechial formations, nosebleeds, blood in urine or tarry stools may be the first signs or symptoms of a heparin overdose. In the event of symptomatic heparin overdose, consider stopping heparin infusion.

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 30 minutes after intravenous injection.

Ideally, the dose required to neutralize the action of heparin should be guided by blood coagulation tests or calculated from a protamine neutralization test.

Because fatal reactions often resembling anaphylaxis have been reported, protamine sulfate should be given only when resuscitation techniques and treatment of anaphylactoid shock are readily available.

For additional information, consult the prescribing information for Protamine Sulfate Injection, USP.

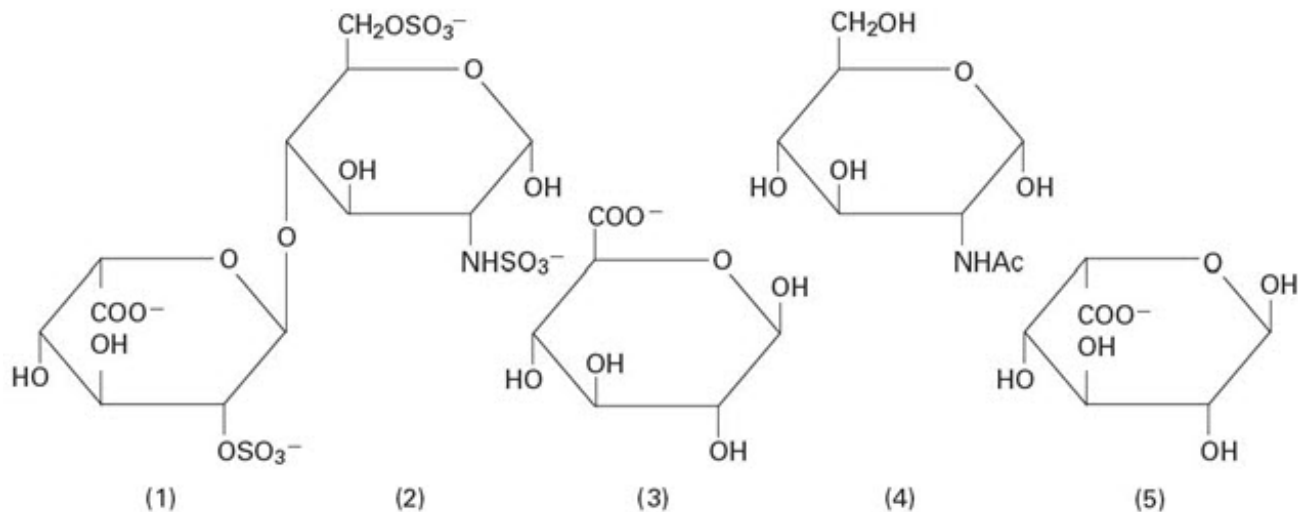
Blood or plasma transfusions may be necessary; these dilute but do not neutralize heparin.

11 DESCRIPTION

Intravenous solutions with heparin sodium (derived from porcine intestinal mucosa) are sterile, nonpyrogenic fluids for intravenous administration. Each 100 mL contains heparin sodium 200 USP units; sodium chloride, 0.9 g; citric acid, monohydrate, 40 mg and dibasic sodium phosphate, heptahydrate, 434 mg added as buffers. Each liter contains the following electrolytes: Sodium 186.4 mEq; phosphate (as $\text{HPO}_4^{=}$) 32.4 mEq, citrate 5.7 mEq and chloride 154 mEq. Osmolar concentration, 378 mOsmol/liter (calc.); pH 7.0 (5.0 – 7.5).

Heparin Sodium, USP is a heterogeneous group of straight-chain anionic mucopolysaccharides, called glycosaminoglycans having anticoagulant properties. Although others may be present, the main sugars occurring in heparin are: (1) α -L-iduronic acid 2-sulfate, (2) 2-deoxy-2-sulfamino- α -D-glucose-6-sulfate, (3) β -D-glucuronic acid, (4) 2-acetamido-2-deoxy- α -D-glucose, and (5) α -L-iduronic acid. These sugars are present in decreasing amounts, usually in the order (2) > (1) > (4) > (3) > (5), and are joined by glycosidic linkages, forming polymers of varying sizes. Heparin is strongly acidic because of its content of covalently linked sulfate and carboxylic acid groups. In heparin sodium, the acidic protons of the sulfate units are partially replaced by sodium ions. The potency is determined by a biological assay using a USP reference standard based on units of heparin activity per milligram.

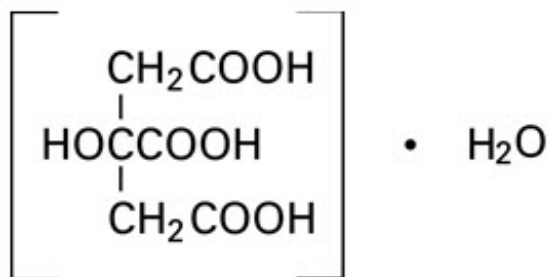
Structure of Heparin Sodium (representative subunits):



Sodium Chloride, USP is chemically designated NaCl, a white crystalline compound freely soluble in water.

Dibasic Sodium Phosphate, USP (heptahydrate), is chemically designated ($\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$), colorless or white granular salt freely soluble in water.

Citric Acid, USP, hydrous (monohydrate) is chemically designated $\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$, colorless, translucent crystals or white crystalline powder very soluble in water. It has the following structural formula:



Water for Injection, USP is chemically designated H_2O .

The flexible plastic container is fabricated from either polyvinylchloride or polyolefin plastic. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions inside the plastic container also can leach out certain of its chemical components in very small amounts before the expiration period is attained. However, the safety of the plastic has been confirmed by tests in animals according to USP biological standards for plastic containers.

12 CLINICAL PHARMACOLOGY

12.1 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 II, thereby inhibiting the activated coagulation factors involved in the closing 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.

12.2 Pharmacodynamics

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. Bleeding time is usually unaffected by heparin.

12.3 Pharmacokinetics

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 macrophages) and b) slower first order elimination. Low doses of heparin are cleared mostly by a saturable, rapid, zero-order process. Slower first order elimination usually occurs with very high doses of heparin and is dependent on renal function. The plasma half-life is dose-dependent and it ranges from 0.5 to 2 h.

Specific Populations

Geriatric Patients

Patients over 60 years of age, following similar doses of heparin, may have higher plasma levels of heparin and longer activated partial thromboplastin times (APTTs) compared with patients under 60 years of age [*see Use in Specific Populations (8.5)*].

Patients with Renal and Hepatic Impairment

The rate of clearance of unfractionated heparin may be decreased in patients with renal or hepatic impairment. Patients with renal or hepatic impairment, following similar doses of heparin may have higher plasma levels of heparin compared with patient with normal

renal and hepatic function [see *Warnings and Precautions (5.1)*].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies in animals have been performed to evaluate carcinogenic potential of heparin. Also, no reproduction studies in animals have been performed concerning mutagenesis or impairment of fertility.

16 HOW SUPPLIED/STORAGE AND HANDLING

Heparin Sodium in Sodium Chloride Injection is a clear solution and is available in single-dose containers as follows:

Unit of Sale	Concentration
NDC 0409-7620-03 Case of 18 Single-dose flexible plastic containers	1,000 USP Units/500 mL (2 USP Units/mL)
NDC 0409-1005-20 Case of 20 Single-dose flexible plastic containers	1,000 USP Units/500 mL (2 USP Units/mL)
NDC 0409-7620-59 Case of 12 Single-dose flexible plastic containers	2,000 USP Units/1,000 mL (2 USP Units/mL)
NDC 0409-2222-12 Case of 12 Single-dose flexible plastic containers	2,000 USP Units/1,000 mL (2 USP Units/mL)

Store at 20°C to 25°C (68°F to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.

17 PATIENT COUNSELING INFORMATION

Hemorrhage

Inform patients that it may take them longer than usual to stop bleeding, that they may bruise and/or bleed more easily when they are treated with heparin, and that they should report any unusual bleeding or bruising to their physician. Hemorrhage can occur at virtually any site in patients receiving heparin. Fatal hemorrhages have occurred [see *Warnings and Precautions (5.1)*].

Prior to Surgery

Advise patients to inform physicians and dentists that they are receiving heparin before any surgery is scheduled [see *Warnings and Precautions (5.1)*].

Heparin-Induced Thrombocytopenia

Inform patients of the risk of heparin-induced thrombocytopenia (HIT). HIT may

progress to the development of venous and arterial thromboses, a condition known as heparin-induced thrombocytopenia and thrombosis (HITT). HIT or HITT can occur up to several weeks after the discontinuation of heparin therapy [see *Warnings and Precautions (5.2)*].

Hypersensitivity

Inform patients that generalized hypersensitivity reactions have been reported. Necrosis of the skin has been reported at the site of subcutaneous injection of heparin [see *Warnings and Precautions (5.5)*, *Adverse Reactions (6.1)*].

Other Medications

Because of the risk of hemorrhage, advise patients to inform their physicians and dentists of all medications they are taking, including non-prescription medications, and before starting any new medication [see *Drug Interactions (7)*].

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

For medical information about Heparin Sodium in Sodium Chloride, please visit www.pfizermedinfo.com or call 1-800-438-1985.

Distributed by Hospira, Inc., Lake Forest, IL 60045

USA

LAB-0807-7.0

PRINCIPAL DISPLAY PANEL - 500 mL Bag - 7620

1,000 USP Units/500 mL
(2 USP Units/mL)

500 mL
NDC 0409-7620-13

HEPARIN SODIUM
1,000 USP Units/500 mL
(2 USP Units/mL)
in 0.9% Sodium Chloride Injection

EACH 100 mL CONTAINS HEPARIN SODIUM 200 USP UNITS (PORCINE INTESTINAL MUCOSA); SODIUM CHLORIDE 0.9 g; CITRIC ACID, MONOHYDRATE 40 mg AND DIBASIC SODIUM PHOSPHATE, HEPTAHYDRATE 434 mg ADDED AS BUFFERS. STERILE. NOT MADE WITH NATURAL RUBBER LATEX. USUAL DOSAGE: SEE INSERT

ADDITIVES SHOULD NOT BE MADE TO THIS SOLUTION.

SINGLE DOSE CONTAINER. DISCARD UNUSED PORTION. FOR INTRAVENOUS USE ONLY.

V
CONTAINS DEHP

Rx only

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14478901

IM-4470

1,000 USP Units/500 mL
(2 USP Units/mL)

NO COPY

MINIMUM CLEARANCE BETWEEN COLORS WHEN 2-COLOR PRINTING IS SPECIFIED. SEE NOTE #1

500 mL

NDC 0409-7620-13

HEPARIN SODIUM

1,000 USP Units/500 mL

(2 USP Units/mL)

in 0.9% Sodium Chloride Injection

EACH 100 mL CONTAINS HEPARIN SODIUM 200 USP UNITS (PORCINE INTESTINAL MUCOSA); SODIUM CHLORIDE 0.9 g; CITRIC ACID, MONOHYDRATE 40 mg AND DIBASIC SODIUM PHOSPHATE, HEPTAHYDRATE 434 mg ADDED AS BUFFERS. STERILE. NOT MADE WITH NATURAL RUBBER LATEX.

USUAL DOSAGE: SEE INSERT

ADDITIVES SHOULD NOT BE MADE TO THIS SOLUTION.

SINGLE DOSE CONTAINER. DISCARD UNUSED PORTION. FOR INTRAVENOUS USE ONLY.



Rx only

CONTAINS DEHP



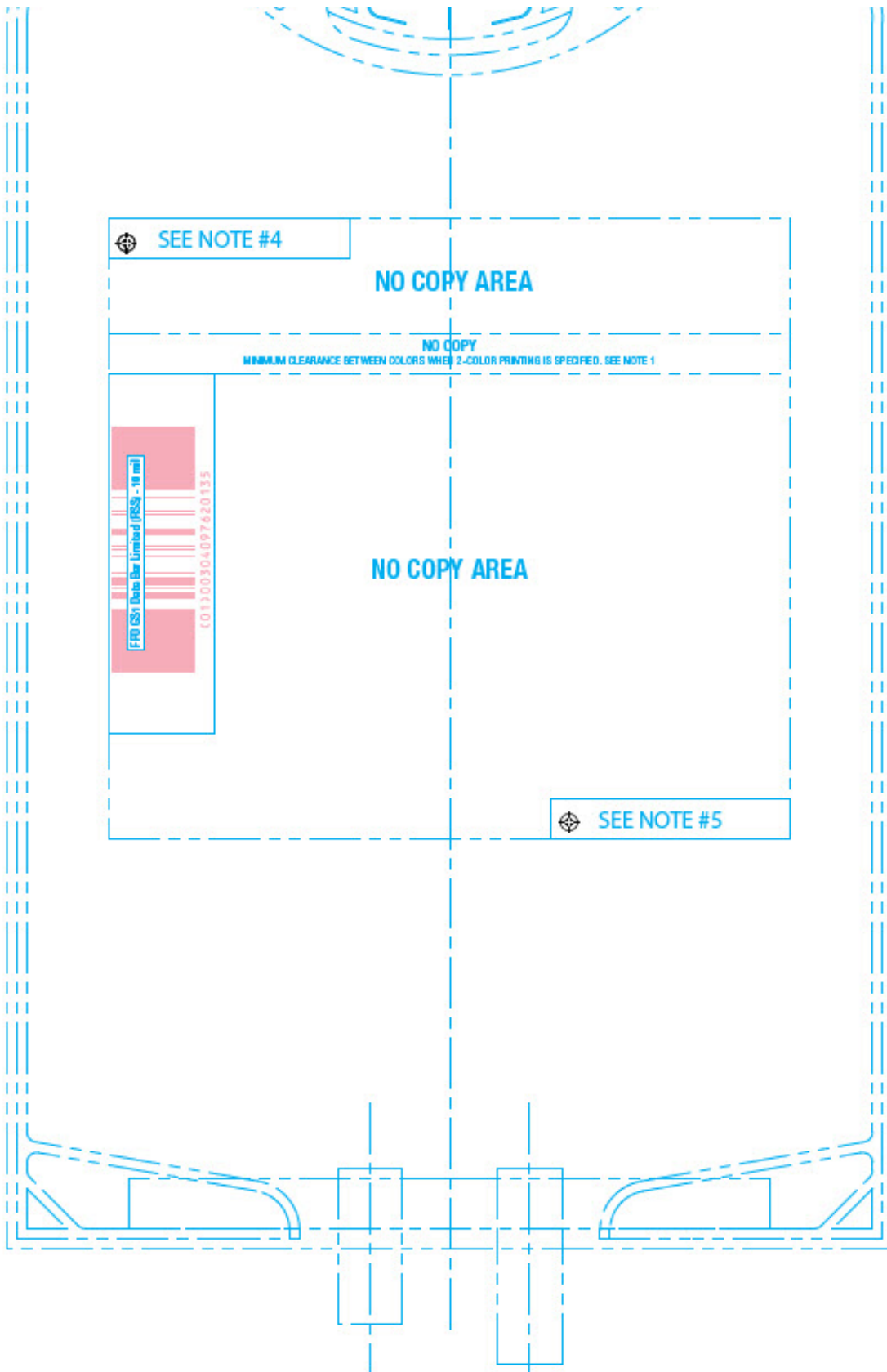
DISTRIBUTED BY
HOSPIRA, INC., LAKE FOREST, IL 60045 USA



14478901
IM-4470

NO COPY, NO INK

— 1
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— 2
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— 3
—
— 4



PRINCIPAL DISPLAY PANEL - 1,000 mL Bag - 7620

LOT NO.
EXP. DATE

2,000 USP Units /1,000 mL

(2 USP Units/mL)

1,000 mL

NDC 0409-7620-49

HEPARIN SODIUM

2,000 USP Units

per 1,000 mL

(2 USP Units/mL)

in 0.9% Sodium Chloride Injection

EACH 100 mL CONTAINS HEPARIN SODIUM
200 USP UNITS (PORCINE INTESTINAL
MUCOSA); SODIUM CHLORIDE 0.9 g; CITRIC
ACID, MONOHYDRATE 40 mg AND DIBASIC
SODIUM PHOSPHATE, HEPTAHYDRATE
434 mg ADDED AS BUFFERS. STERILE.
NOT MADE WITH NATURAL RUBBER LATEX.
USUAL DOSAGE: SEE INSERT

ADDITIVES SHOULD NOT BE MADE
TO THIS SOLUTION.

SINGLE DOSE CONTAINER. DISCARD UNUSED
PORTION. FOR INTRAVENOUS USE ONLY.

Rx only

3

V

CONTAINS DEHP

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IL 60045 USA

Hospira

14479101

IM-4471

LOT NO.

EXP. DATE

⊗	2,000 USP Units / 1,000 mL (2 USP Units/mL)
---	--

SEE NOTE #1

1,000 mL

NDC 0409-7620-49

— 1

HEPARIN SODIUM

— 2

2,000 USP Units
per 1,000 mL

— 3

(2 USP Units/mL)

in **0.9% Sodium Chloride Injection**

— 4

EACH 100 mL CONTAINS HEPARIN SODIUM
 200 USP UNITS (PORCINE INTESTINAL
 MUCOSA); SODIUM CHLORIDE 0.9 g; CITRIC
 ACID, MONOHYDRATE 40 mg AND DIBASIC
 SODIUM PHOSPHATE, HEPTAHYDRATE
 434 mg ADDED AS BUFFERS. STERILE.
 NOT MADE WITH NATURAL RUBBER LATEX.

— 5

USUAL DOSAGE: SEE INSERT

ADDITIVES SHOULD NOT BE MADE TO THIS SOLUTION.

— 6

SINGLE DOSE CONTAINER. DISCARD UNUSED
PORTION. FOR INTRAVENOUS USE ONLY.

— 7

Rx only



CONTAINS DEHP

— 8

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IL 60045 USA

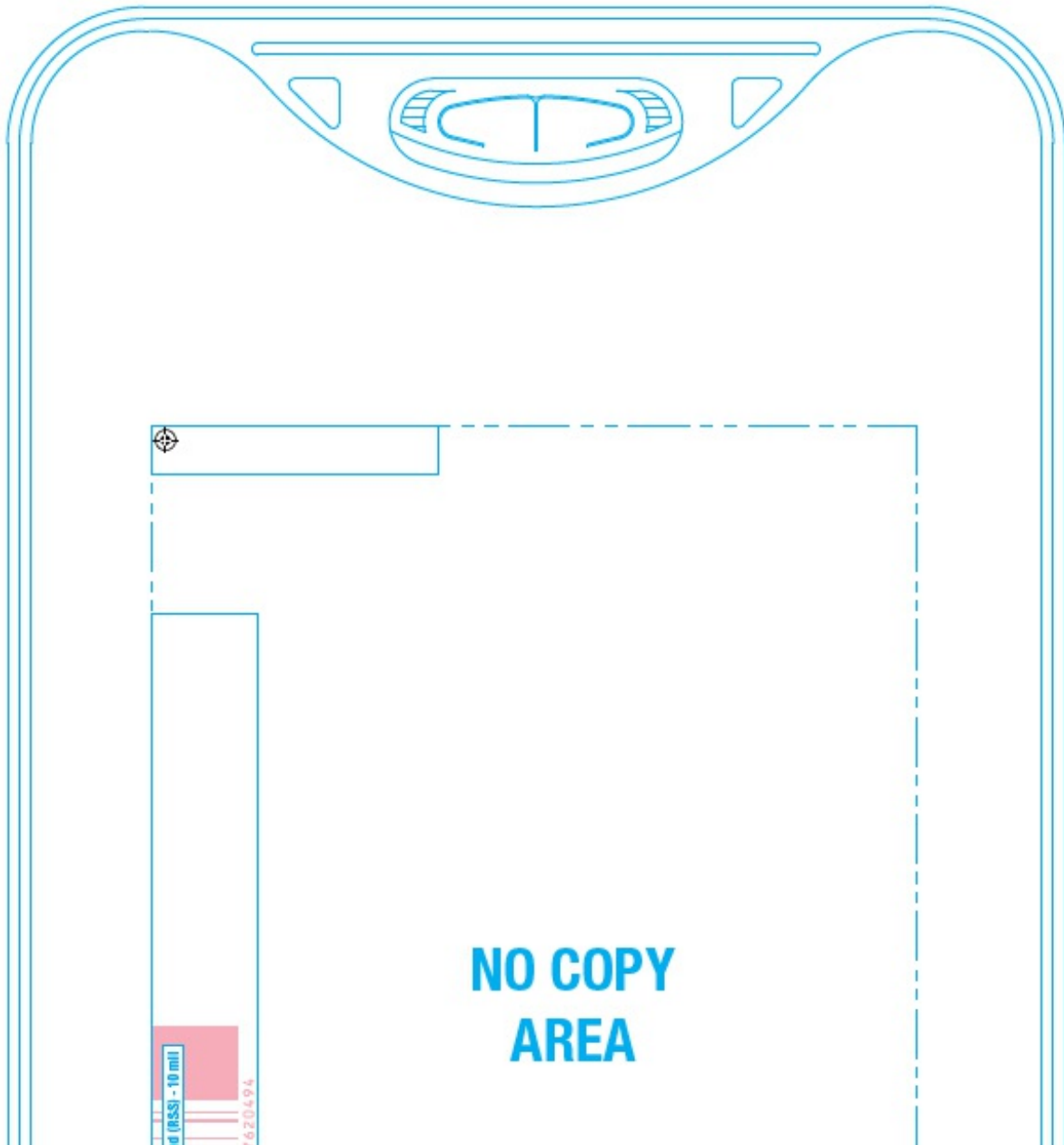
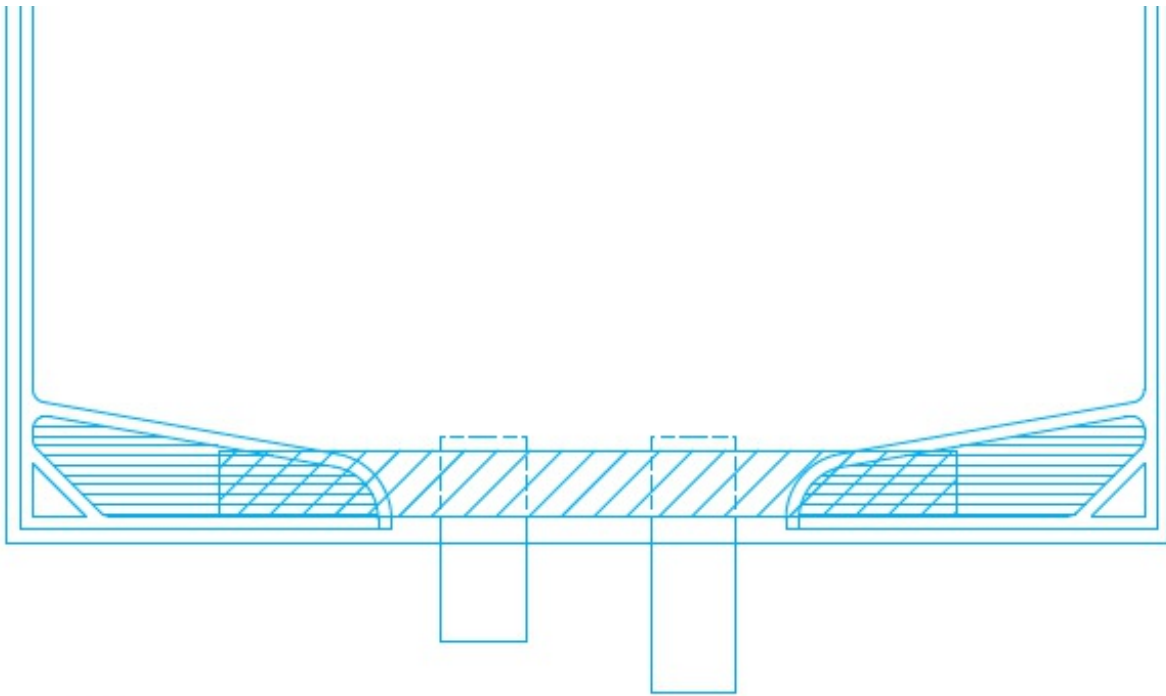


14479101
IM-4471



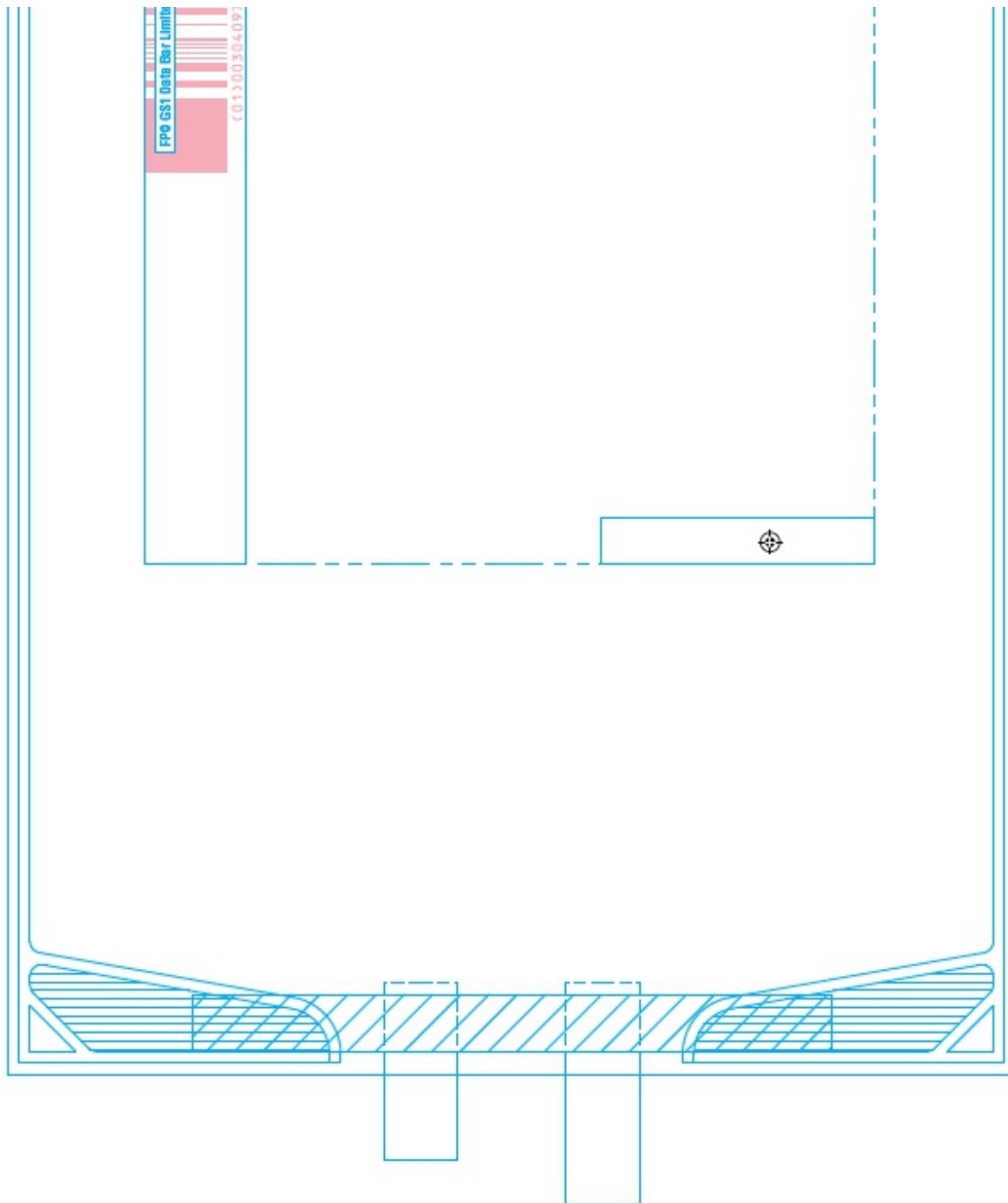
— 9

NO COPY, NO INK



**NO COPY
AREA**

10 ml
7670494



PRINCIPAL DISPLAY PANEL - Bag Overwrap

TO OPEN TEAR AT NOTCH

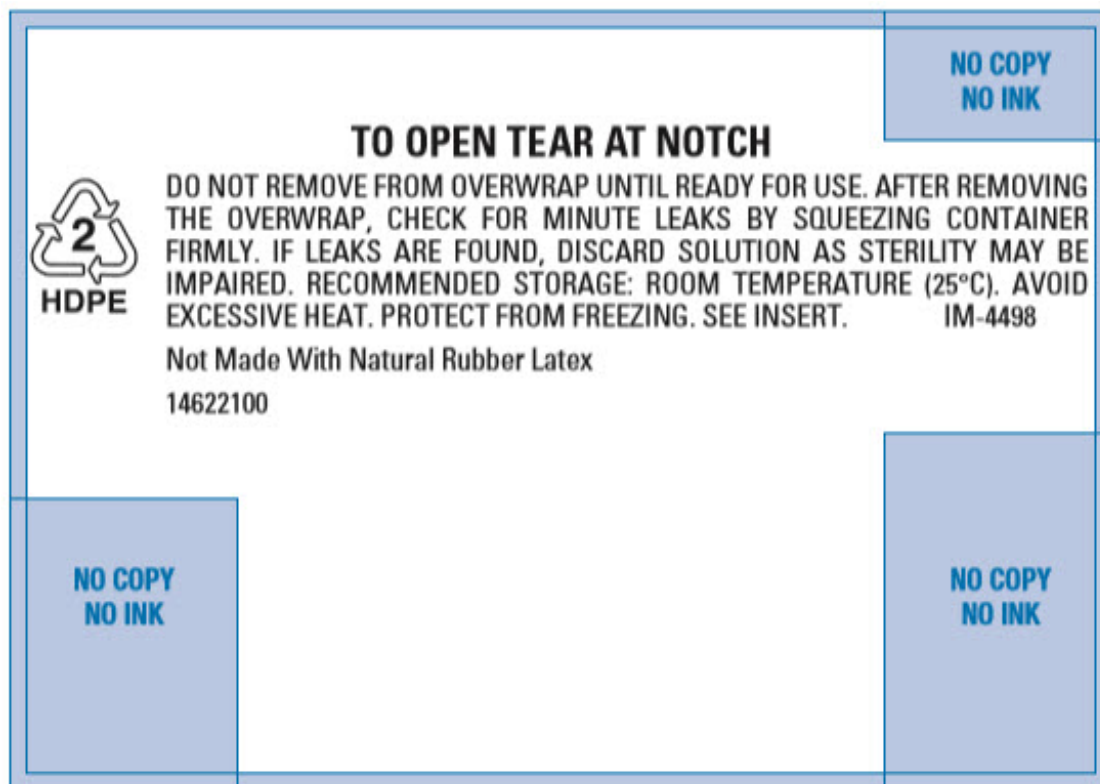
2
HDPE

DO NOT REMOVE FROM OVERWRAP UNTIL READY FOR USE. AFTER REMOVING THE OVERWRAP, CHECK FOR MINUTE LEAKS BY SQUEEZING CONTAINER FIRMLY. IF LEAKS ARE FOUND, DISCARD SOLUTION AS STERILITY MAY BE IMPAIRED. RECOMMENDED STORAGE: ROOM TEMPERATURE (25°C). AVOID EXCESSIVE HEAT. PROTECT FROM FREEZING. SEE INSERT.

IM-4498

Not Made With Natural Rubber Latex

14622100



PRINCIPAL DISPLAY PANEL - 500 mL Bag Label - 1005

500mL

NDC 0409-1005-01

Heparin Sodium

1,000 USP Units / 500 mL

(2 USP Units / mL)

in 0.9% Sodium Chloride Injection

Each 100 mL contains Heparin Sodium 200 USP Units (Porcine Intestinal Mucosa); Sodium Chloride 0.9 g; Citric acid, Monohydrate 40 mg and Dibasic Sodium Phosphate, Heptahydrate 434 mg added as buffers.

Sterile. Not made with natural rubber latex.

Recommended dosage: See prescribing information.

Additives should not be made to this solution.

Single dose container. Discard unused portion.

For Intravenous Use only. Inspect bag by squeezing firmly.

If leaks are found, discard. Store at 20°C to 25°C (68°F to 77°F).

[See USP Controlled Room Temperature.] Protect from freezing.

Do not remove from overwrap until ready for use.

Rx only

PP

Distributed by Hospira, Inc., Lake Forest, IL 60045 USA

Hospira

**1,000 USP Units/500 mL
(2 USP Units/mL)**

500 mL

NDC 0409-1005-01

Heparin Sodium
1,000 USP Units/500 mL
(2 USP Units/mL)
in 0.9% Sodium Chloride Injection

Each 100 mL contains Heparin Sodium 200 USP Units (Porcine Intestinal Mucosa); Sodium Chloride 0.9 g; Citric Acid, Monohydrate 40 mg and Dibasic Sodium Phosphate, Heptahydrate 434 mg added as buffers.
Sterile. Not made with natural rubber latex.
Recommended dosage: See prescribing information.

Additives should not be made to this solution.

Single dose container. Discard unused portion.
For Intravenous Use only. Check for minute leaks.
If leaks are found, discard. Store at 20°C to 25°C (68°F to 77°F).
[See USP Controlled Room Temperature.] Protect from freezing.
Do not remove from overwrap until ready for use.

Rx only



Distributed by Hospira, Inc., Lake Forest, IL 60045 USA



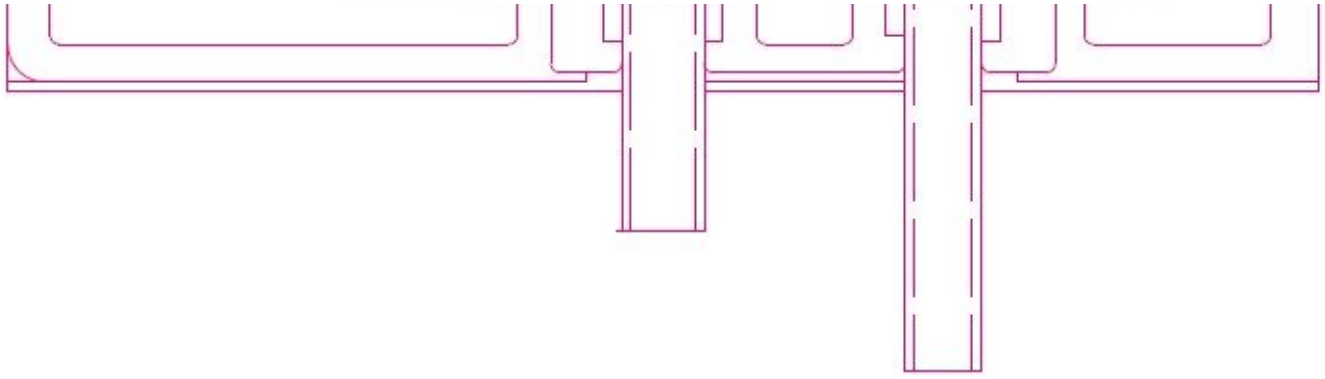
12133-04



(01)10304091005010

LOT: 12345678

EXP: YYYY-MMM



PRINCIPAL DISPLAY PANEL - 1000 mL Bag Label - 2222

2,000 USP Units / 1,000 mL
(2 USP Units / mL)

1,000mL
NDC 0409-2222-01

Heparin Sodium
2,000 USP Units / 1,000 mL
(2 USP Units / mL)
in 0.9% Sodium Chloride Injection

Each 100 mL contains Heparin Sodium 200 USP Units (Porcine Intestinal Mucosa); Sodium Chloride 0.9 g; Citric acid, Monohydrate 40 mg and Dibasic Sodium Phosphate, Heptahydrate 434 mg added as buffers.

Sterile. Not made with natural rubber latex.

Recommended dosage: See prescribing information.

Additives should not be made to this solution.

Single dose container. Discard unused portion.

For Intravenous Use only.

Check for minute leaks. If leaks are found, discard.

Store at 20°C to 25°C (68°F to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.

Do not remove from overwrap until ready for use.

Rx only

5
PP

Distributed by Hospira, Inc., Lake Forest, IL 60045 USA

Hospira

**2,000 USP Units/1,000 mL
(2 USP Units/mL)**

1,000 mL

NDC 0409-2222-01

Heparin Sodium

**2,000 USP Units/1,000 mL
(2 USP Units/mL)**

in 0.9% Sodium Chloride Injection

Each 100 mL contains Heparin Sodium 200 USP Units (Porcine Intestinal Mucosa); Sodium Chloride 0.9 g; Citric Acid, Monohydrate 40 mg and Dibasic Sodium Phosphate, Heptahydrate 434 mg added as buffers.

Sterile. Not made with natural rubber latex.

Recommended dosage: See prescribing information.

Additives should not be made to this solution.

Single dose container. Discard unused portion.

For Intravenous Use only.

Check for minute leaks. If leaks are found, discard.

Store at 20°C to 25°C (68°F to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.

Do not remove from overwrap until ready for use.

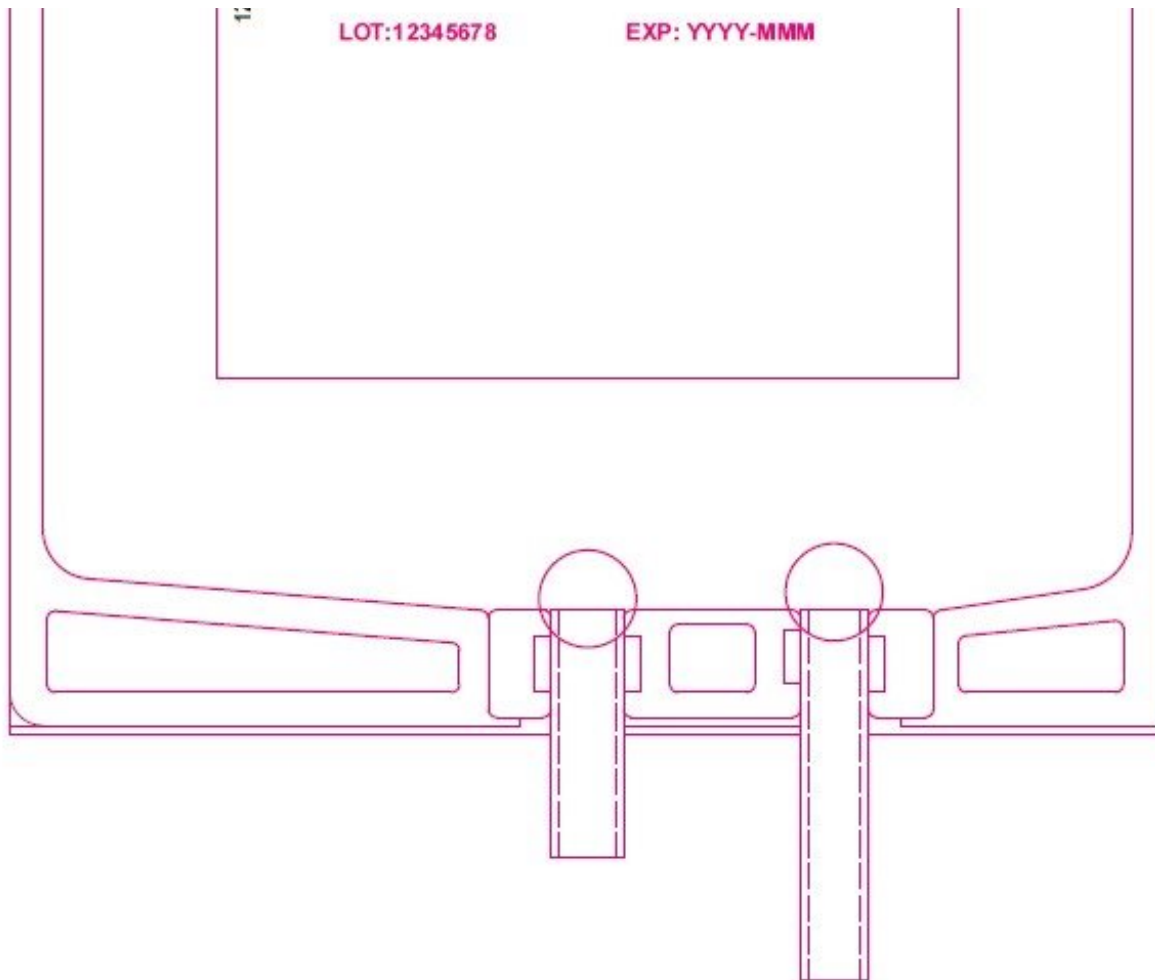
Rx only



Distributed by Hospira, Inc., Lake Forest, IL 60045 USA



(01)1030409222010



HEPARIN SODIUM

heparin sodium injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0409-7620
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HEPARIN SODIUM (UNII: ZZ45AB24CA) (HEPARIN - UNII:T2410KM04A)	HEPARIN	200 [USP'U] in 100 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.9 g in 100 mL
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	40 mg in 100 mL
SODIUM PHOSPHATE, DIBASIC, HEPTAHYDRATE (UNII: 70WT22SF4B)	434 mg in 100 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0409-7620-03	18 in 1 CASE	03/31/2005	
1		1 in 1 POUCH		
1	NDC:0409-7620-13	500 mL in 1 BAG; Type 0: Not a Combination Product		
2	NDC:0409-7620-59	12 in 1 CASE	03/31/2005	
2		1 in 1 POUCH		
2	NDC:0409-7620-49	1000 mL in 1 BAG; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA018916	03/31/2005	

HEPARIN SODIUM

heparin sodium injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0409-1005
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HEPARIN SODIUM (UNII: ZZ45AB24CA) (HEPARIN - UNII:T2410KM04A)	HEPARIN	200 [USP'U] in 100 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.9 g in 100 mL
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	40 mg in 100 mL
SODIUM PHOSPHATE, DIBASIC, HEPTAHYDRATE (UNII: 70WT22SF4B)	434 mg in 100 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0409-1005-20	20 in 1 CASE	02/27/2023	
1		1 in 1 POUCH		

1	NDC:0409-1005-01	500 mL in 1 BAG; Type 0: Not a Combination Product	
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Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA018916	02/27/2023	

HEPARIN SODIUM

heparin sodium injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0409-2222
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HEPARIN SODIUM (UNII: ZZ45AB24CA) (HEPARIN - UNII:T2410KM04A)	HEPARIN	200 [USP'U] in 100 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.9 g in 100 mL
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	40 mg in 100 mL
SODIUM PHOSPHATE, DIBASIC, HEPTAHYDRATE (UNII: 70WT22SF4B)	434 mg in 100 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0409-2222-12	12 in 1 CASE	02/27/2023	
1		1 in 1 POUCH		
1	NDC:0409-2222-01	1000 mL in 1 BAG; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA018916	02/27/2023	

Labeler - Hospira, Inc. (141588017)

Establishment

Name	Address	ID/FEI	Business Operations
Hospira, Inc.		030606222	ANALYSIS(0409-7620, 0409-1005, 0409-2222)

Establishment

Name	Address	ID/FEI	Business Operations
Hospira, Inc.		093132819	ANALYSIS(0409-7620) , MANUFACTURE(0409-7620) , PACK(0409-7620) , LABEL(0409-7620)

Establishment

Name	Address	ID/FEI	Business Operations
Hospira, Inc.		827731089	ANALYSIS(0409-7620, 0409-1005, 0409-2222)

Establishment

Name	Address	ID/FEI	Business Operations
Hospira Worldwide, LLC		963711309	ANALYSIS(0409-7620, 0409-1005, 0409-2222)

Revised: 11/2024

Hospira, Inc.