

Y36-003-003 LD-279-3

PRODUCT MONOGRAPH

CIV **HEPARIN SODIUM IN
0.9% SODIUM CHLORIDE INJECTION**

Solution, Heparin Sodium 1,000 units in 0.9% Sodium Chloride Injection

Prescribed

Therapeutic Classification: Heparin (Anticoagulant)

Manufactured by:

B | BRAUN

B. Braun Medical Inc.
824 Twelfth Avenue
Bethlehem, PA 18018-3524 USA

Date of Revision:
June 1, 2020

Distributed by:

B. Braun of Canada, Ltd.
2000 Ellesmere Road, Unit 16
Scarborough, Ontario M1H 2W4

Control #: 232621

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION.....	3
SUMMARY PRODUCT INFORMATION.....	3
INDICATIONS AND CLINICAL USE	3
CONTRAINDICATIONS	3
WARNINGS AND PRECAUTIONS	4
ADVERSE REACTIONS	7
DRUG INTERACTIONS.....	9
DOSAGE AND ADMINISTRATION.....	11
OVERDOSAGE.....	12
ACTION AND CLINICAL PHARMACOLOGY	13
STORAGE AND STABILITY	14
DOSAGE FORMS, COMPOSITION AND PACKAGING	14
PART II: SCIENTIFIC INFORMATION	16
PHARMACEUTICAL INFORMATION.....	16
PART III: CONSUMER INFORMATION.....	18

HEPARIN SODIUM IN 0.9% SODIUM CHLORIDE INJECTION

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
IV	Solution 1,000 units	Citric Acid Anhydrous USP Dibasic Sodium Phosphate Heptahydrate USP <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>

INDICATIONS AND CLINICAL USE

Heparin Sodium in 0.9% Sodium Chloride Injection is indicated as an anticoagulant to maintain catheter patency when delivered by continuous infusion only.

Geriatrics (> 60 years of age):

Evidence from clinical studies and experience suggests that use in the geriatric population is associated with a difference in safety or effectiveness and a brief discussion can be found in Warnings and Precautions and Dosage and Administration.

Pediatrics (< 16 years of age):

No data is available.

CONTRAINDICATIONS

Heparin Sodium in 0.9% Sodium Chloride Injection should not be used in patients:

- with severe thrombocytopenia
- 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)
- with an uncontrollable active bleeding state (see Warnings and Precautions), except when this is due to disseminated intravascular coagulation
- who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.
- when the administration solutions containing sodium or chloride could be clinically detrimental.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Fatal hemorrhages have occurred in infants and pediatric patients due to medication errors in which 1 mL Heparin Sodium Injection vials were confused with 1 mL “catheter lock flush” vials. Carefully examine all heparin products to ensure that the proper strength is selected for administration. See Warnings and Precautions, Hemorrhage.

General

Heparin is not intended for intramuscular use.

Do not use Heparin Sodium in 0.9% Sodium Chloride Injection as a “catheter lock flush” product. (“Catheter lock flush” describes a procedure where a small volume of a saline or heparin solution is injected into a cannula after placement of the cannula, drug administration or blood sampling, and then the catheter is capped. Heparin Sodium in 0.9% Sodium Chloride Injection is not suitable for this use. Use only products approved for catheter lock to perform catheter lock flush procedures.)

Hypersensitivity: Patients with documented hypersensitivity to heparin should be given the drug only in clearly life-threatening situations.

Hemorrhage: Hemorrhage can occur at virtually any site in patients receiving heparin. An unexplained fall in hematocrit, fall in blood pressure, or any other unexplained symptom should lead to serious consideration of a hemorrhagic event.

Heparin sodium should be used with extreme caution in disease states in which there is increased danger of hemorrhage. Some of the conditions in which increased danger of hemorrhage exists are:

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.

Other: Menstruation, liver disease with impaired hemostasis.

The administration of intravenous solutions can cause fluid and/or solute overload resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary edema. The risk of dilutional states is inversely proportional to the electrolyte concentration. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentration.

Excessive administration of potassium-free solutions may result in significant hypokalemia.

Extraordinary electrolyte losses such as may occur during protracted nasogastric suction, vomiting, diarrhea, or gastrointestinal fistula drainage may necessitate additional electrolyte supplementation.

Because dosages of this drug are titrated to response (see Dosage and Administration), **no additives should be made to Heparin Sodium in 0.9% Sodium Chloride Injection.**

Do not use plastic container in series connection.

If administration is controlled by a pumping device, care must be taken to discontinue pumping action before the container runs dry or air embolism may result.

These solutions are intended for intravenous administration using sterile equipment. It is recommended that any unused heparin solution and intravenous administration apparatus be replaced at least once every 24 hours.

Use only if solution is clear and container and seals are intact.

Carcinogenesis and Mutagenesis

Long term studies in animals to evaluate the carcinogenic potential, reproduction studies in animals to determine effects on fertility of males and females, and the studies to determine mutagenic potential have not been conducted with Heparin Sodium in 0.9% Sodium Chloride Injection.

Cardiovascular

Solution containing sodium ions should be used with great care, if at all, in patients with congestive heart failure and in clinical states in which there is sodium retention with edema.

Care should be exercised in administering solutions containing sodium to patients with cardiovascular insufficiency, with or without congestive heart failure, particularly if they are postoperative or elderly.

Hematologic

Thrombocytopenia: Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of up to 30%. Platelet counts should be obtained at baseline periodically during heparin administration. 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 thrombosis develops, the heparin product should be discontinued, 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 irreversible aggregation of platelets. HIT may progress to the development of venous and arterial thromboses, a condition referred to as Heparin-induced Thrombocytopenia and 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, thrombus formation on a prosthetic cardiac valve, mesenteric thrombosis, renal arterial thrombosis, skin necrosis, gangrene of the extremities that may lead to amputation, and possibly death.

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.

Renal

Solution containing sodium ions should be used with great care, if at all, in patients with severe renal insufficiency, and in clinical states in which there is sodium retention with edema. In patients with diminished renal function, administration of solutions containing sodium ions may result in sodium retention.

Sensitivity/Resistance

Increased resistance to heparin is frequently encountered in fever, thrombosis, thrombophlebitis, infections with thrombosing tendencies, myocardial infarction, cancer and in postsurgical patients.

Special Populations

Pregnant Women:

Animal reproduction studies have not been conducted with Heparin Sodium in 0.9% Sodium Chloride Injection. It is also not known whether Heparin Sodium in 0.9% Sodium Chloride Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Heparin Sodium in 0.9% Sodium Chloride Injection should be given to a pregnant woman only if clearly needed.

Nonteratogenic Effects: Heparin does not cross the placental barrier.

Nursing Women: Heparin is not excreted in human milk.

Neonates: Carefully examine all heparin drug product containers to confirm choice of the correct strength prior to administration of the drug. Pediatric patients, including neonates, have died as a result of medication errors in which Heparin Sodium Injection vials have been confused with “catheter lock flush” vials (see Warnings and Precautions).

Pediatrics (< 16 years of age): Fatal Medication Errors: Heparin is supplied in a wide range of strengths. Fatal hemorrhages have occurred in infants and pediatric patients due to medication errors in which 1 mL Heparin Sodium Injection vials were confused with 1 mL “catheter lock flush” vials. Carefully examine all heparin products to ensure that the proper strength is selected for administration.

Geriatrics (> 60 years of age): A higher incidence of bleeding has been reported in patients over 60 years of age, especially women. Clinical studies indicate that lower doses of heparin may be indicated in these patients (see Action and Clinical Pharmacology and Dosage and Administration).

Monitoring and Laboratory Tests

Coagulation Testing: When heparin sodium is administered in therapeutic amounts, its dosage

should be regulated by frequent blood coagulation tests. If the coagulation test is unduly prolonged or if hemorrhage occurs, heparin should be discontinued promptly (see Overdosage).

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).

Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance and electrolyte concentrations during prolonged parenteral therapy or whenever the condition of the patient warrants such evaluation.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

1. Hemorrhage.
Hemorrhage is the chief complication that may result from heparin therapy (see Warnings and Precautions). An overly prolonged clotting time or minor bleeding during therapy can usually be controlled by withdrawing the drug (see Overdosage). **It should be appreciated that 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:
 - a. Adrenal hemorrhage, with resultant acute adrenal insufficiency, has occurred during anticoagulant therapy. Therefore, such treatment should be discontinued in patients who develop signs and symptoms of acute adrenal hemorrhage and insufficiency. Initiation of corrective therapy should not depend on laboratory confirmation of the diagnosis, since any delay in an acute situation may result in the patient's death.
 - b. Ovarian (corpus luteum) hemorrhage developed in a number of women of reproductive age receiving short- or long-term anticoagulant therapy. This complication if unrecognized may be fatal.
 - c. Retroperitoneal hemorrhage.
2. Thrombocytopenia, Heparin-induced Thrombocytopenia (HIT), Heparin-induced Thrombocytopenia and Thrombosis (HITT) and Delayed Onset of HIT and HITT. (See Warnings and Precautions.)
3. Local Irritation.
Local irritation, erythema, mild pain, hematoma or ulceration may follow deep subcutaneous (intrafat) injection of heparin sodium. These complications are much more common after intramuscular use, and such use is not recommended.
4. 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.)

Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of up to 30%. While often mild and of no obvious clinical significance, such thrombocytopenia can be accompanied by severe thromboembolic complications such as skin necrosis, gangrene of the extremities that may lead to amputation, myocardial infarction, pulmonary embolism, stroke, and possibly death. (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.

5. 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 AST (SGOT) and ALT (SGPT) levels have occurred in a high percentage of patients (and healthy subjects) who have received heparin.

Reactions which may occur because of the solution or the technique of administration include febrile response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation, and hypervolemia.

Symptoms may result from an excess or deficit of one or more of the ions present in the solution; therefore, frequent monitoring of electrolyte levels is essential.

Hypernatremia may be associated with edema and exacerbation of congestive heart failure due to the retention of water, resulting in an expanded extracellular fluid volume.

If infused in large amounts, chloride ions may cause a loss of bicarbonate ions, resulting in an acidifying effect.

If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse drug reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Adverse reaction data from clinical trials is not available.

Post Market Adverse Drug Reactions:

Adverse reaction rates associated with the use of heparin sodium in clinical practice have recently been reviewed¹. Incidence rates in the following table are taken from this review.

Adverse Reaction	Incidence
Hemorrhage	Major bleeding: up to 7% Fatal bleeding: up to 2%
Thrombocytopenia Heparin Induced Thrombocytopenia (HIT) Heparin Induced Thrombocytopenia and Thrombosis (HITT) Delayed Onset HIT and HITT	HIT rate 1-3%
Miscellaneous: : osteoporosis	Osteopenia rate up to one-third of patients on long term therapy (osteopenia may lead to osteoporosis)

¹ Niccolai CS, Hicks RW, Oertel L, Francis JL; Heparin Consensus Group. Unfractionated heparin: focus on a high-alert drug. *Pharmacotherapy*. 2004 Aug;24(8 Pt 2):146S-155S.

DRUG INTERACTIONS

Overview

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.

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) may induce bleeding and should be used with caution in patients receiving heparin sodium.

Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Drug	Interaction
Oral Anticoagulants: when heparin sodium is given with dicumarol or warfarin sodium	Prolongation of one-stage prothrombin time; 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.
Platelet Inhibitors: Drugs such as acetylsalicylic acid, dextran, phenylbutazone, ibuprofen, indomethacin, dipyridamole, hydroxychloroquine and others that interfere with platelet aggregation reactions	Bleeding
Digitalis, tetracyclines, nicotine, antihistamines or IV nitroglycerine	Partial counteraction of the anticoagulant action of heparin sodium.
Corticosteroids or corticotropin	Risk of sodium retention

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions

Drug / Laboratory Interaction	Significance	Notes
Significant elevations of aminotransferase AST (SGOT) or Significant elevations of aminotransferase ALT (SGPT)	Aminotransferase determinations are important in the differential diagnosis of myocardial infarction, liver disease and pulmonary emboli, rises that might be caused by drugs (like heparin) should be interpreted with caution.	Hyperaminotransferasemia: Significant elevations of aminotransferase levels have occurred in a high percentage of patients (and healthy subjects) who have received heparin.

DOSAGE AND ADMINISTRATION

Dosing Considerations

The product should be administered under the supervision of a qualified health professional who is experienced in the use of anticoagulant agents. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

Small doses of heparin can alter tests for activated partial thromboplastin time (APTT). A baseline value for APTT should be obtained prior to administration of this solution.

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.

Recommended Dose and Dosage Adjustment

Maintenance of Catheter Patency

Although the rate of infusion of the 2 units/mL formulation is dependent upon the age, weight, clinical condition of the patient, and the procedure being employed, an infusion rate of 3 mL/hour has been found to be satisfactory.

Geriatric Use

Patients over 60 years of age may require lower doses of heparin. (See Precautions.)

Missed Dose

The product should only be administered under the supervision of a qualified health professional who is experienced in the use of anticoagulant agents, and missed doses are not to be expected.

Administration

Heparin Sodium is not effective by oral administration and Heparin Sodium in 0.9% Sodium Chloride Injection should not be given orally.

This product should be administered by continuous intravenous infusion. Do not use Heparin Sodium in 0.9% Sodium Chloride Injection as a “catheter lock flush” product.

(“Catheter lock flush” describes a procedure where a small volume of a saline or heparin solution is injected into a cannula after placement of the cannula, drug administration or blood sampling, and then the catheter is then capped. Heparin Sodium in 0.9% Sodium Chloride Injection is not suitable for this use. Use only products approved for catheter lock to perform catheter lock flush procedures.)

Confirm the choice of the correct heparin drug product and strength prior to administration of the drug to the patient (see Serious Warnings and Precautions Box). Heparin sodium injection products must not be confused with “catheter lock flush” products.

This product should not be infused under pressure.

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

Drug Compatibility

Because dosages of this drug are titrated to response no additives should be made to Heparin Sodium in 0.9% Sodium Chloride Injection.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Symptoms: Bleeding is the chief sign of heparin overdose. 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 the labeling of Protamine Sulfate Injection, USP products should be consulted.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Heparin inhibits reactions that lead to the clotting of blood and the formation of fibrin clots both *in vitro* and *in vivo*. Heparin acts at multiple sites in the normal coagulation system. Small amounts of heparin in combination with antithrombin III (heparin cofactor) can inhibit thrombosis by inactivating activated Factor X and inhibiting the conversion of prothrombin to thrombin. Once active thrombosis has developed, larger amounts of heparin can inhibit further coagulation by inactivating thrombin and preventing the conversion of fibrinogen to fibrin. Heparin also prevents the formation of a stable fibrin clot by inhibiting the activation of the fibrin stabilizing factor.

Pharmacodynamics

Bleeding time is usually unaffected by heparin. Clotting time is prolonged by full therapeutic doses of heparin; in most cases it is not measurably affected by low doses of heparin.

Heparin does not have fibrinolytic activity; therefore, it will not lyse existing clots.

Sodium, the major cation of the extracellular fluid, functions primarily in the control of water distribution, fluid balance, and osmotic pressure of body fluids. Sodium is also associated with chloride and bicarbonate in the regulation of the acid-base equilibrium of body fluid. Chloride, the major extracellular anion, closely follows the metabolism of sodium, and changes in the acid-base balance of the body are reflected in the chloride concentration.

Pharmacokinetics

Absorption:	Peak plasma levels of heparin are achieved 2-4 hours following subcutaneous administration, although there are considerable individual variations. Loglinear plots of heparin plasma concentrations with time for a wide range of dose levels are linear which suggests the absence of zero order processes.
Distribution:	The absence of a relationship between anticoagulant half-life and concentration half-life may reflect factors such as protein binding of heparin.
Metabolism:	Liver and the reticuloendothelial system are the sites of biotransformation. The biphasic elimination curve, a rapidly declining alpha phase ($t_{1/2} = 10$ minutes) and after the age of 40 a slower beta phase, indicates uptake in organs.

Special Populations and Conditions

Geriatrics: 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.

STORAGE AND STABILITY

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C); however, brief exposure up to 40°C does not adversely affect the product.

Invert container and carefully inspect the solution in good light for cloudiness, haze, or particulate matter. Any container which is suspect should not be used.

Storage in automated dispensing machines: Brief exposure up to 2 weeks to ultraviolet or fluorescent light does not adversely affect the product labeling legibility; prolonged exposure can cause fading of the red label. Rotate stock frequently.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Heparin Sodium in 0.9% Sodium Chloride Injection is supplied sterile and nonpyrogenic in EXCEL® Containers packaged 24 per case.

Canada DIN	REF	Size
Heparin Sodium 1,000 units in 0.9% Sodium Chloride Injection		
01935933	P8721-00	500 mL

Nonmedicinal ingredients:

Citric Acid Anhydrous USP,

Dibasic Sodium Phosphate Heptahydrate USP

The EXCEL® Container is Latex-free; PVC-free; and DEHP-free.

The plastic container is made from a multilayered film specifically developed for parenteral drugs. It contains no plasticizers and exhibits virtually no leachables. The solution contact layer is a rubberized copolymer of ethylene and propylene. The container is nontoxic and biologically inert. The container-solution unit is a closed system and is not dependent upon entry of external air during administration. The container is overwrapped to provide protection from the physical environment and to provide an additional moisture barrier when necessary.

The closure system has two ports; the one for the administration set has a tamper evident plastic protector. Refer to the Directions for Use of the container.

Directions for Use of EXCEL® Container

Do not admix with other drugs.

Caution: Do not use plastic container in series connection.

Do not remove overwrap until ready for use.

To Open

Tear overwrap down at notch and remove solution container. Check for minute leaks by squeezing solution container firmly. If leaks are found, discard solution as sterility may be impaired.

NOTE: Before use, perform the following checks:

- Inspect each container. Read the label. Ensure solution is the one ordered and is within the expiration date.
- Invert container and carefully inspect the solution in good light for cloudiness, haze, or particulate matter. Any container which is suspect should not be used.
- Use only if solution is clear and container and seals are intact.

Preparation for Administration

1. Remove plastic protector from sterile set port at bottom of container.
2. Attach administration set. Refer to complete directions accompanying set.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Heparin Sodium in 0.9% Sodium Chloride Injection

Chemical name: Heparin Sodium in 0.9% Sodium Chloride Injection

Molecular formula and molecular mass: Heparin is a heterogenous group of straight-chain anionic mucopolysaccharides, called glycosaminoglycans having anticoagulant properties. Although others may be present, the main sugars occurring in heparin are: (1) alpha-L-iduronic acid 2-sulfate, (2) 2-deoxy-2-sulfamino-alpha-D-glucose 6-sulfate, (3) beta-D-glucuronic acid, (4) 2-acetamido-2-deoxy-alpha-D-glucose, and (5) alpha-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.

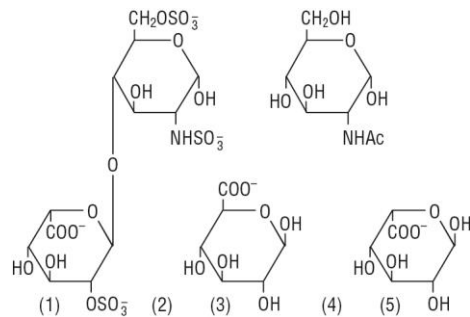
The formulas of the inactive ingredients are:

Ingredients	Molecular Formula	Molecular Weight
-------------	-------------------	------------------

Sodium Chloride USP	NaCl	58.44
Dibasic Sodium Phosphate Heptahydrate USP	$\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$	268.07
Citric Acid Anhydrous USP	$\text{CH}_2(\text{COOH})\text{C}(\text{OH})(\text{COOH})\text{CH}_2\text{COOH}$	192.12

Structural formula:

Structure of Heparin Sodium (representative subunits):



Physiochemical Properties: Heparin Sodium (2 units/mL) in 0.9% Sodium Chloride Injection is a sterile, nonpyrogenic solution prepared from Heparin Sodium USP (derived from porcine intestinal mucosa and standardized for use as an anticoagulant) in 0.9% Sodium Chloride Injection. It is to be administered by intravenous injection. The potency is determined by a biological assay using a USP reference standard based on units of heparin activity per milligram.

Each 100 mL contains 0.43 g Dibasic Sodium Phosphate•7H₂O USP and 0.037 g Citric Acid Anhydrous USP as a buffer system, 0.9 g Sodium Chloride USP, and Water for Injection USP qs.

pH: 7.0 (6.8-7.2)

Calculated Osmolarity: 360 mOsmol/liter

Concentration of Electrolytes (mEq/liter): Sodium 186; Chloride 154; Phosphate (HPO₄²⁻) 32; Citrate 6

IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

Heparin Sodium in 0.9% Sodium Chloride Injection

This leaflet is part III of a three-part “Product Monograph” published when Heparin Sodium in 0.9% Sodium Chloride Injection was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Heparin Sodium in 0.9% Sodium Chloride Injection. Contact your doctor or pharmacist if you have any questions about this drug.

ABOUT THIS MEDICATION

What the medication is used for:

Heparin Sodium in 0.9% Sodium Chloride Injection is used to keep catheters open.

What it does:

Heparin stops reactions that lead to the clotting of blood and the formation of fibrin clots. Once an active blood clot has developed, larger amounts of heparin can inhibit further clotting.

Peak levels of heparin are achieved 2-4 hours following intravenous administration, although there are considerable individual variations.

When it should not be used:

BEFORE you use Heparin Sodium in 0.9% Sodium Chloride Injection talk to your doctor if you have:

- reduction of blood platelets
- an uncontrollable active bleeding state (see **Warnings**), except when this is due to disseminated intravascular coagulation
- a hypersensitivity (allergy) to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

What the medicinal ingredient is:

Heparin Sodium in 0.9% Sodium Chloride Solution

What the important nonmedical ingredients are:

Dibasic Sodium Phosphate Heptahydrate USP
Citric Acid Anhydrous USP

For a full listing of nonmedicinal ingredients see Part I of the product monograph.

What dosage form it comes in:

Heparin Sodium 1,000 units in 0.9% Sodium Chloride Injection

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Fatal bleeding has occurred in infants and children due to medication errors in which 1 mL Heparin Sodium Injection vials were confused with 1 mL “catheter lock flush” vials.

Bleeding can occur at virtually any site in patients receiving heparin.

Increased resistance to heparin is frequently encountered in fever, blood clot, vein inflammation associated with a blood clot, infections with blood clotting tendencies, heart attack, cancer and in patients after surgery.

Heparin sodium should be used with extreme caution in disease states in which there is increased danger of bleeding. Some of the conditions in which increased danger of bleeding exists are:

- Infections of the heart and heart valves. Severe high blood pressure.
- During and immediately following (a) spinal tap or spinal anesthesia or (b) major surgery, especially involving the brain, spinal cord, or eye.
- Conditions associated with increased bleeding tendencies, such as hemophilia, thrombocytopenia (low platelets) and some vascular purpuras.
- Ulcers of the stomach and continuous tube drainage of the stomach or small intestine.
- Menstruation, liver disease with impaired blood clotting
- Heparin is not intended for Intramuscular Use
- Allergic reaction to this drug might happen, stop the medication and consult your doctor
- Platelet count should be tested and monitored.

Excessive administration of potassium-free solutions may result in significant hypokalemia (low potassium levels).

No additives should be made to Heparin Sodium in 0.9% Sodium Chloride Injection.

PROPER USE OF THIS MEDICATION

Usual dose:

The product should be administered under the supervision of a qualified health professional who is experienced in the use of anticoagulant agents and in the management of patients with venous thrombosis, pulmonary embolism, acute and chronic consumptive coagulopathies and peripheral arterial embolism. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to Canada Vigilance Program by one of the following 3 ways:

- **Report online at**
www.healthcanada.gc.ca/medeffect
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
 - Fax toll-free to 1-866-678-6789
 - Mail to: **Canada Vigilance Program
Health Canada
Postal Locator 1908C
Ottawa, Ontario
K1A 0K9**

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information relating to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, B. Braun of Canada, Ltd., at: 1-800-539-0801

This leaflet was prepared by B. Braun Medical Inc.

Last revised: June 1, 2020

EXCEL is a registered trademark of B. Braun Medical Inc.

