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PRODUCT MONOGRAPH

CIV HEPARIN SODIUM IN 5% DEXTROSE INJECTION

Solution, Heparin Sodium 20,000 units in 5% Dextrose Injection
Solution, Heparin Sodium 25,000 units in 5% Dextrose Injection

Prescribed

Therapeutic Classification: Heparin (Anticoagulant)

Manufactured by:

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

Date of Revision:
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Distributed by:

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Control # : 232670

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HEPARIN SODIUM IN 5% DEXTROSE INJECTION

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INDICATIONS AND CLINICAL USE

Heparin Sodium in 5% Dextrose Injection is indicated for:

- anticoagulant therapy
- prophylaxis and treatment of venous thrombosis and its extension
- prophylaxis and treatment of pulmonary embolism
- atrial fibrillation with embolization
- diagnosis and treatment of acute and chronic consumptive coagulopathies (disseminated intravascular coagulation)
- prevention of clotting in arterial and heart surgery
- prophylaxis and treatment of peripheral arterial embolism

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 5% Dextrose 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.
- solutions containing dextrose may be contraindicated in patients with hypersensitivity to corn products.

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.

General

Heparin is not intended for intramuscular use.

Do not use Heparin Sodium in 5% Dextrose Injection as a "catheter lock flush" product.

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.

This product contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

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.

Solutions containing dextrose without electrolytes should not be administered simultaneously with blood through the same infusion set because of the possibility of agglomeration.

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

Because dosages of this drug are titrated to response (see Dosage and Administration), no additives should be made to Heparin Sodium in 5% Dextrose 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 5% Dextrose Injection.

Endocrine and Metabolism

Solutions containing dextrose should be used with caution in patients with overt or known subclinical diabetes mellitus, or carbohydrate intolerance for any reason.

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/mm^3) 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/mm^3 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.

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 5% Dextrose Injection. It is also not known whether Heparin Sodium in 5% Dextrose Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Heparin Sodium in 5% Dextrose 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 occ urred 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.

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 reviewed[1]. 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

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.

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.

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

Heparin Sodium in 5% Dextrose Injection is indicated as a continuous intravenous infusion following an initial intravenous therapeutic dose of heparin sodium.

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.

The dosage of heparin sodium should be adjusted according to the patient's coagulation test results. When heparin sodium is administered by continuous intravenous infusion, coagulation tests should be performed approximately every 4 hours during the early stages of therapy. 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.

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.

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 5 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.

Recommended Dose and Dosage Adjustment

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 guidelines:

Method of Administration	Frequency	Recommended dose[1]
Continuous intravenous infusion	Initial dose	5,000 units by IV injection.
	Continuous	20,000 - 40,000 units/24 hours.

[1]Based on 150-lb. (68-kg) patient.

Pediatric Use

Follow recommendations of appropriate pediatric reference texts. In general, the following dosage schedule may be used as a guideline:

Initial Dose: 50 units/kg (IV, drip).

Maintenance Dose: 20,000 units/m^2/24 hours continuously.

Geriatric Use

Patients over 60 years of age may require lower doses of heparin. (See Warnings and 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 in 5% Dextrose Injection is for continuous intravenous use only. Do not use Heparin Sodium in 5% Dextrose Injection as a "catheter lock flush" product.

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

Heparin Sodium is not effective by oral administration and Heparin Sodium in 5% Dextrose Injection should not be given orally.

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 5% Dextrose Injection.

OVERDOSAGE

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

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 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.

Dextrose provides a source of calories. Dextrose is readily metabolized, may decrease losses of body protein and nitrogen, promotes glycogen deposition and decreases or prevents ketosis if sufficient doses are provided.

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.
Excretion:	The plasma half life is approximately 1½ hours, however the half life increases with increasing doses ranging from approximately 1 hour with a dose of 100 units/kg to approximately 2½ hours with a dose of 400 units/kg. The plasma half life may be prolonged in patients with cirrhosis or severe renal impairment. Patients with pulmonary embolism may have a more rapid clearance of heparin. Heparin is not removed by hemodialysis.

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 5% Dextrose Injection is supplied sterile and nonpyrogenic in EXCEL® Containers packaged 24 per case.

Canada DIN	REF	Size
Heparin Sodium 20,000 units in 5% Dextrose Injection		
02209713	P5671-00	500 mL
Heparin Sodium 25,000 units in 5% Dextrose Injection		
01935941	P5771-00	500 mL
Heparin Sodium 25,000 units in 5% Dextrose Injection		
02209721	P5872-00	250 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 5% Dextrose Injection

Chemical name: Heparin Sodium in 5% Dextrose Injection

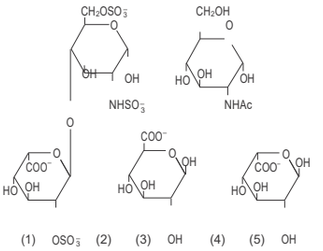
Molecular formula and molecular mass: Heparin is a heterogenous group of straight-chain anionic mucopolysaccharides, called glycosaminoglycans having anticoagulant properties. Although others may be present, the main sugars occurring in heparin are: (1) alpha-L-iduronic acid 2-sulfate, (2) 2-deoxy-2-sulfamino-alpha-D-glucose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

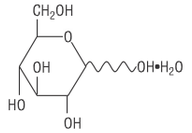
Ingredients	Molecular Formula	Molecular Weight
Dibasic Sodium Phosphate Heptahydrate USP	$Na_2HPO_4 \cdot 7H_2O$	268.07
Citric Acid Anhydrous USP	$CH_2(COOH)C(OH)(COOH)CH_2COOH$	192.12

Structural formula:

Structure of Heparin Sodium (representative subunits):



Structure of Hydrous Dextrose USP:



(M.W. 198.17)

Physiochemical Properties: Heparin Sodium in 5% Dextrose Injection is a sterile, nonpyrogenic solution prepared from heparin sodium (derived from porcine intestinal mucosa and standardized for use as an anticoagulant) and Hydrous Dextrose USP in Water for Injection USP. The potency is determined by a biological assay using a USP reference standard based on units of heparin activity per milligram.

Composition – Each 100 mL Contains:					Concentration of Electrolytes (mEq/liter)				
Solution	**Heparin Sodium USP**	**Hydrous Dextrose USP**	**Dibasic Sodium Phosphate Heptahydrate USP**	**Citric Acid Anhydrous USP**	**Sodium**	**Phosphate ($HPO_4^=$)**	**Citrate**	**pH**	**Calculated Osmolarity mOsmol/liter**
Heparin Sodium 20,000 units in 5% Dextrose Injection	4,000 units	5 g	0.41 g	0.093 g	38	30	15	5.6 (4.5-7.0)	315
Heparin Sodium 25,000 units in 5% Dextrose Injection	5,000 units	5 g	0.41 g	0.093 g	38	30	15	5.6 (4.5-7.0)	315
Heparin Sodium 25,000 units in 5% Dextrose Injection	10,000 units	5 g	0.41 g	0.093 g	38	30	15	5.6 (4.5-7.0)	315

Sodium Metabisulfite NF (antioxidant) <0.07 g
Water for Injection USP qs

IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

Heparin Sodium in 5% Dextrose Injection

This leaflet is part III of a three-part "Product Monograph" published when Heparin Sodium in 5% Dextrose 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 5% Dextrose 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 5% Dextrose Injection is indicated for:
- treatment to stop your blood clotting
- preventing and stopping the spread of blood clots in your veins
- preventing and stopping the spread of blood clots to your lungs
- preventing blood clots caused by abnormal heart beat patterns
- treatment of some disorders of blood clotting
- prevention of blood clotting during surgery
- prevention and treatment of blood clots in your arteries

What it does:

Heparin stops reactions that lead to the clotting of blood and the formation of 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 5% Dextrose Injection talk to your doctor if you have:
- severe reduction of of blood platelets
- an uncontrollable active bleeding state (see **Warnings**), except when this is due to disseminated intravascular coagulation
- a hypersensitivity or 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.
- a hypersensitivity (allergy) to corn products.

What the medicinal ingredient is:

Heparin Sodium in 5% Dextrose 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 1 of the product monograph.

What dosage forms it comes in:

Heparin Sodium 20,000 units in 5% Dextrose Injection
Heparin Sodium 25,000 units in 5% Dextrose Injection
Heparin Sodium 25,000 units in 5% Dextrose 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.

This product contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Excessive administration of potassium-free solutions may result in significant low concentrations of potassium in the blood.

No additives should be made to Heparin Sodium in 5% Dextrose 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.

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