NORMOSOL-R AND DEXTROSE- dextrose, sodium chloride, sodium acetate anhydrous, sodium gluconate, potassium chloride, and magnesium chloride injection, solution
Hospira, Inc.

Normosol®-R and 5% Dextrose Injection

MULTIPLE ELECTROLYTES AND 5% DEXTROSE INJECTION TYPE 1, USP

For Replacing Acute Losses of Extracellular Fluid

Flexible Plastic Container

R_x only

DESCRIPTION

Normosol-R and 5% Dextrose Injection is a sterile, nonpyrogenic solution of balanced electrolytes (with dextrose) in water for injection. The solution is administered by intravenous infusion for parenteral replacement of acute losses of extracellular fluid (with minimal carbohydrate calories).

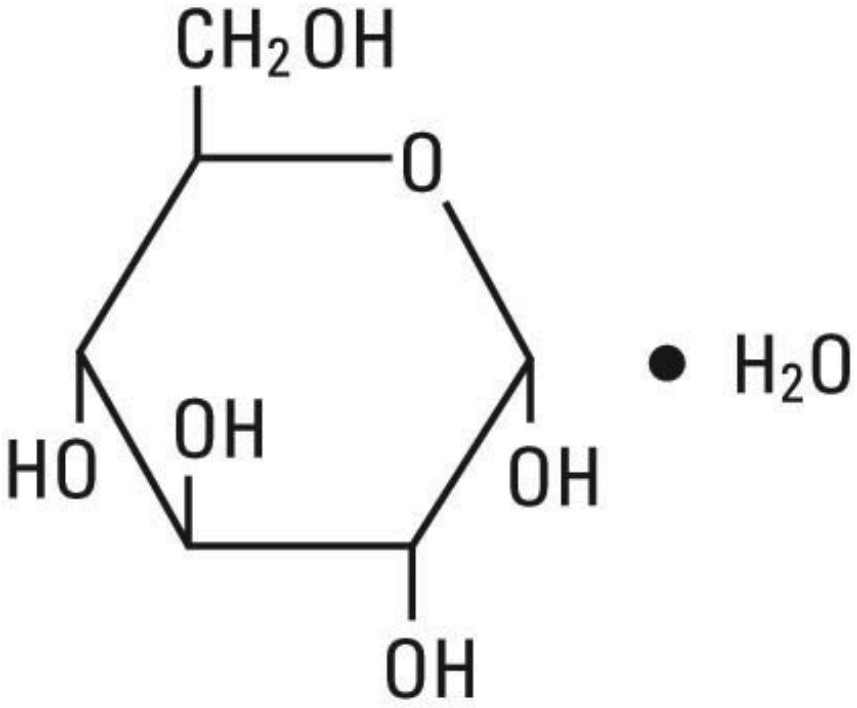
Each 100 mL of Normosol-R and 5% Dextrose Injection contains dextrose 5 g; sodium chloride 526 mg; sodium acetate, anhydrous 222 mg; sodium gluconate 502 mg; potassium chloride 37 mg; magnesium chloride, hexahydrate 30 mg; pH adjusted with hydrochloric acid.

See **TABLE** for summary of electrolyte content, caloric value and characteristics of this solution.

The solution contains no bacteriostat, antimicrobial agent or added buffer (except for pH adjustment) and is intended only for use as a single-dose injection. When smaller doses are required the unused portion should be discarded.

Normosol-R and 5% Dextrose Injection is a parenteral fluid, electrolyte and nutrient replenisher.

Dextrose, USP is chemically designated D-glucose monohydrate ($C_6H_{12}O_6 \cdot H_20$), a hexose sugar freely soluble in water. It has the following structural formula:

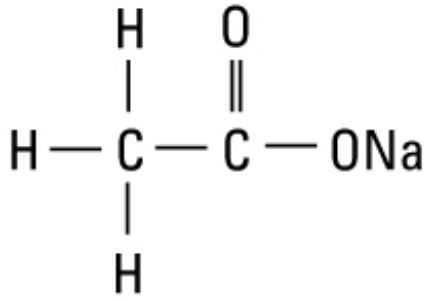


Sodium Chloride, USP is chemically designated NaCl, a white crystalline powder freely soluble in water.

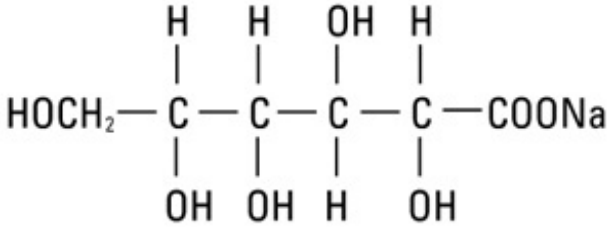
Potassium Chloride, USP is chemically designated KCl, a white granular powder freely soluble in water.

Magnesium Chloride, USP is chemically designated magnesium chloride hexahydrate ($MgCl_2 \cdot 6H_20$) deliquescent crystals very soluble in water.

Sodium Acetate, USP, is chemically designated sodium acetate anhydrous ($C_2H_3NaO_2$), a hygroscopic powder soluble in water. It has the following structural formula:



Sodium gluconate is chemically designated $C_6H_{11}NaO_7$, the normal sodium salt of gluconic acid soluble in water. It has the following structural formula:



Water for Injection, USP is chemically designated H_20.

The flexible plastic container is fabricated from a specially formulated polyvinylchloride. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials. Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

CLINICAL PHARMACOLOGY

When administered intravenously, Normosol-R and 5% Dextrose Injection provides water and electrolytes with carbohydrate calories for replacement of acute extracellular fluid losses without disturbing normal electrolyte relationships. The electrolyte composition approaches that of the principal ions of normal plasma (extracellular fluid). The electrolyte concentration is approximately isotonic in relation to the extracellular fluid (approx. 280 mOsmol/liter) and provides a physiologic sodium to chloride ratio, normal plasma concentrations of potassium and magnesium and two bicarbonate alternates, acetate and gluconate. Dextrose provides minimal calories and renders the solution hypertonic.

Solutions containing carbohydrate in the form of dextrose restore blood glucose levels and supply calories. Carbohydrate in the form of dextrose may aid in minimizing liver glycogen depletion and

exerts a protein-sparing action. Dextrose injected parenterally undergoes oxidation to carbon dioxide and water.

Sodium chloride in water dissociates to provide sodium (Na^+) and chloride (Cl^-) ions. Sodium (Na^+) is the principal cation of the extracellular fluid and plays a large part in the therapy of fluid and electrolyte disturbances. Chloride (Cl^-) has an integral role in buffering action when oxygen and carbon dioxide exchange occurs in the red blood cells. The distribution and excretion of sodium (Na^+) and chloride (Cl^-) are largely under the control of the kidney which maintains a balance between intake and output.

Potassium chloride in water dissociates to provide potassium (K^+) and chloride (Cl^-) ions. Potassium is the chief cation of body cells (160 mEq/liter of intracellular water). It is found in low concentration in plasma and extracellular fluids (3.5 to 5.0 mEq/liter in a healthy adult and child over 10 days old; 3.5 to 6.0 mEq/liter in a child less than 10 days old). Potassium plays an important role in electrolyte balance.

Normally about 80 to 90% of the potassium intake is excreted in the urine; the remainder in the stools and to a small extent, in the perspiration. The kidney does not conserve potassium well so that during fasting or in patients on a potassium-free diet, potassium loss from the body continues resulting in potassium depletion.

Magnesium chloride in water dissociates to provide magnesium (Mg^{++}) and chloride (Cl^-) ions. Magnesium is the second most plentiful cation of the intracellular fluids. It is an important cofactor for enzymatic reactions and plays an important role in neurochemical transmission and muscular excitability. Normal plasma concentration ranges from 1.5 to 2.5 or 3.0 mEq per liter. Magnesium is excreted solely by the kidney at a rate proportional to the plasma concentration and glomerular filtration.

Sodium acetate provides sodium (Na^+) and acetate (CH_3COO^-) ions, the latter anion (a source of hydrogen ion acceptors) serving as an alternate source of bicarbonate (HCO_3^-) by metabolic conversion in the liver. This has been shown to proceed readily even in the presence of severe liver disease. Thus, acetate anion exerts a mild systemic antiacidotic action that may be advantageous during fluid and electrolyte replacement therapy.

Sodium gluconate provides sodium (Na^+) and gluconate ($C_6H_{11}0_7^-$) ions. Although gluconate is a theoretical alternate metabolic source of bicarbonate ($HC0_3^-$) anion, a significant antiacidotic action has not been established. Thus, the gluconate anion serves primarily to complete the cation-anion balance of the solution.

Water is an essential constituent of all body tissues and accounts for approximately 70% of total body weight. Average normal adult daily requirement ranges from two to three liters (1.0 to 1.5 liters each for insensible water loss by perspiration and urine production).

Average normal pediatric daily requirements are based on the child’s weight as described in the table below:

Weight	Fluid Requirements
Up to 10 kg	100 mL/kg
11 to 20 kg	1,000 mL + 50 mL/kg for each
	kg above 10 kg
Above 20 kg	1,500 mL + 20 mL/kg for each
	kg above 20 kg

Water balance is maintained by various regulatory mechanisms. Water distribution depends primarily on the concentration of electrolytes in the body compartments and sodium (Na^+) plays a major role in maintaining physiologic equilibrium.

INDICATIONS AND USAGE

Normosol-R and 5% Dextrose Injection is indicated for *replacement* of acute extracellular fluid volume losses in surgery, trauma, burns or shock. Normosol-R and 5% Dextrose also can be used as an adjunct to restore a decrease in circulatory volume in patients with moderate blood loss. The solution is not intended to supplant transfusion of whole blood or packed red cells in the presence of uncontrolled hemorrhage or severe reductions of red cell volume.

CONTRAINDICATIONS

None known.

WARNINGS

Solutions containing sodium ions should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency and in clinical states in which there exists edema with sodium retention.

Solutions which contain potassium should be used with great care, if at all, in patients with hyperkalemia, severe renal failure and in conditions in which potassium retention is present.

In patients with diminished renal function, administration of solutions containing sodium or potassium ions may result in sodium or potassium retention. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function during fluid replacement with Normosol-R and 5% Dextrose.

Solutions containing acetate or gluconate ions should be used with great care in patients with metabolic or respiratory alkalosis. Acetate or gluconate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of these ions, such as severe hepatic insufficiency.

The intravenous administration of this solution can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary edema.

Elderly patients may be at increased risk for the development of fluid overloading and dilutional hyponatremia following Normosol-R and 5% Dextrose administration.

The risk of dilutional states is inversely proportional to the electrolyte concentrations of administered parenteral solutions. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of such solutions.

PRECAUTIONS

Normosol-R and 5% Dextrose Injection should be used with caution in severe renal impairment because of the danger of hyperkalemia. As with all intravenous solutions, care should be taken to avoid circulatory overload, especially in patients with cardiac or pulmonary disorders. Normosol-R and 5% Dextrose is not intended to correct acidosis or large deficits of individual electrolytes, nor to replace blood or plasma expanders when these are indicated.

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

Caution must be exercised in the administration of parenteral fluids, especially those containing sodium ions, to patients receiving corticosteroids or corticotropin.

Solutions containing acetate or gluconate ions should be used with caution, as excess administration may result in metabolic alkalosis.

Solutions containing dextrose should be used with caution in patients with known subclinical or overt

diabetes mellitus.

Do not administer unless solution is clear and container is undamaged. Discard unused portion.

Pregnancy Category C.

Animal reproduction studies have not been conducted with Normosol-R and 5% Dextrose Injection. It is also not known whether this solution can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. This solution should be given to a pregnant woman only if clearly needed.

Pediatric Use.

The safety and effectiveness in the pediatric population are based on the similarity of the clinical conditions of the pediatric and adult populations. In neonates or very small infants the volume of fluid may affect fluid and electrolyte balance.

Frequent monitoring of serum glucose concentrations is required when dextrose is prescribed to pediatric patients, particularly neonates and low birth weight infants.

In very low birth weight infants, excessive or rapid administration of dextrose injection may result in increased serum osmolality and possible intracerebral hemorrhage.

Geriatric Use.

Clinical studies of Normosol-R and 5% Dextrose did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in response between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Elderly patients have been shown to secrete higher levels of antidiuretic hormone than younger patients, which may increase the risk of fluid overloading, and dilutional hyponatremia in these patients. (See **WARNINGS**.)

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. (See **WARNINGS**.)

ADVERSE REACTIONS

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.

OVERDOSAGE

In the event of overhydration or solute overload, re-evaluate the patient and institute appropriate corrective measures. (See **WARNINGS**, **PRECAUTIONS** and **ADVERSE REACTIONS**.)

DOSAGE AND ADMINISTRATION

Normosol-R and 5% Dextrose Injection is administered by intravenous infusion. The amount to be infused is based on replacement of losses of extracellular fluid volume in the individual patient. Up to 3

times the volume of estimated blood loss during and after surgery can be given to correct circulatory volume when there is only a moderate loss of blood.

As reported in the literature, the dosage and constant infusion rate of intravenous dextrose must be selected with caution in pediatric patients, particularly neonates and low birth weight infants, because of the increased risk of hyperglycemia/hypoglycemia.

Drug Interactions

Additives may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic technique, mix thoroughly and do not store.

Normosol-R and 5% Dextrose solution does not contain calcium to avoid precipitation of calcium salts that may occur when certain drugs are added.

Parenteral drug products should be inspected visually for particulate matter or discoloration prior to administration, whenever solution and container permit. (See **PRECAUTIONS**.)

INSTRUCTIONS FOR USE

To Open:

Tear outer wrap at notch and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. If supplemental medication is desired, follow directions below before preparing for administration.

To Add Medication

1. Prepare additive port.
2. Using aseptic technique and an additive delivery needle of appropriate length, puncture resealable additive port at target area, inner diaphragm and inject. Withdraw needle after injecting medication.
3. The additive port may be protected by covering with an additive cap.
4. Mix container contents thoroughly.

To Administer

1. Attach administration set per manufacturer's instructions.
2. Regulate rate of administration per institutional policy.

WARNING: Do not use flexible container in series connections.

HOW SUPPLIED

Normosol-R and 5% Dextrose Injection (Multiple Electrolytes and 5% Dextrose Injection Type 1, USP) is supplied in a 1000 mL single-dose flexible plastic container (NDC No. 0409–7968–09).

TABLE

Electrolyte Content, Caloric Value and Characteristics

	Milliequivalents per Liter									
				$HC0^-_3$ (alternates)			Cal*	mOsmol/L	Tonicity	
	Na^+	K^+	Mg^{++}	Cl^-	Acetate	Gluconate	per Liter	(calc.)	(total contents)	pH
Normosol-R and 5% Dextrose	140	5	3	98**	27	23	185	547	Hypertonic	5.2 (4.0 to 6.5)

* Normosol-R and 5% Dextrose calories derived from dextrose (170) and gluconate (15).

**Not including hydrochloric acid.

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

®Normosol − multiple electrolyte solution, Hospira

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Hospira, Inc., Lake Forest, IL 60045 USA

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NORMOSOL-R AND DEXTROSE

dextrose, sodium chloride, sodium acetate anhydrous, sodium gluconate, potassium chloride, and magnesium chloride injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0409-7968
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DEXTROSE, UNSPECIFIED FORM (UNII: IY9XDZ35W2) (DEXTROSE, UNSPECIFIED FORM - UNII:IY9XDZ35W2)	DEXTROSE, UNSPECIFIED FORM	5 g in 100 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X) (SODIUM CATION - UNII:LYR4M0NH37,	SODIUM CHLORIDE	526 mg

CHLORIDE ION - UNII:Q32ZN48698)	SODIUM CHLORIDE	in 100 mL
SODIUM ACETATE ANHYDROUS (UNII: NVG71ZZ7P0) (SODIUM CATION - UNII:LYR4M0NH37)	SODIUM ACETATE ANHYDROUS	222 mg in 100 mL
SODIUM GLUCONATE (UNII: R6Q3791S76) (SODIUM CATION - UNII:LYR4M0NH37)	SODIUM GLUCONATE	502 mg in 100 mL
POTASSIUM CHLORIDE (UNII: 660YQ98I10) (POTASSIUM CATION - UNII:295O53K152)	POTASSIUM CHLORIDE	37 mg in 100 mL
MAGNESIUM CHLORIDE (UNII: 02F3473H9O) (MAGNESIUM CATION - UNII:T6V3LHY838)	MAGNESIUM CHLORIDE	30 mg in 100 mL

Inactive Ingredients

Ingredient Name	Strength
WATER (UNII: 059QF0KO0R)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0409-7968-09	12 in 1 CASE	09/16/2010	
1		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	NDA017609	09/16/2010	

Labeler - Hospira, Inc. (141588017)

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