PRESCRIBING INFORMATION

Sodium Chloride Injection USP 0.9 %

Solution, 0.9%, Intramuscular, Intravenous, Intraperitoneal and Subcutaneous

Isotonic Vehicle and Electrolyte Replenisher

Marcan Pharmaceuticals Inc.
2 Gurdwara Road, Suite #112
Ottawa, ON, K2E 1A2

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RECENT MAJOR LABEL CHANGES

None at the time of the most recent authorization.

TABLE OF CONTENTS

Sections or subsections that are not applicable at the authorization are not listed.

TABLE OF CONTENTS **2**
PART I: HEALTH PROFESSIONAL INFORMATION **3**
1 INDICATIONS **3**
2 CONTRAINDICATIONS **3**
4 DOSAGE AND ADMINISTRATION **3**
4.1 Dosing Considerations 3
4.3 Reconstitution 3
4.4 Administration 4
5 OVERDOSAGE **4**
6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING **4**
7 WARNINGS AND PRECAUTIONS **5**
7.1 Special Populations 7
7.1.1 Pregnant Women 7
7.1.3 Pediatrics 7
7.1.4 Geriatrics 7
8 ADVERSE REACTIONS **8**
8.1 Adverse Reaction Overview 8
8.5 Post-Market Adverse Reactions 8
9 DRUG INTERACTIONS **8**
10 CLINICAL PHARMACOLOGY **9**
10.1 Mechanism of Action 9
11 STORAGE, STABILITY AND DISPOSAL **9**
12 SPECIAL HANDLING INSTRUCTIONS **9**
PART II: SCIENTIFIC INFORMATION **10**
13 PHARMACEUTICAL INFORMATION **10**
17 SUPPORTING PRODUCT MONOGRAPHS **10**

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Sodium Chloride Injection USP 0.9% is indicated for:

- Sodium Chloride Injection USP 0.9 % is indicated as a source of water and electrolytes
- Sodium Chloride Injection USP 0.9 % can be used as a vehicle or diluent for compatible products for parenteral administration.
- Sodium Chloride Injection USP 0.9 % is also indicated for use as a priming solution in hemodialysis procedures.

2 CONTRAINDICATIONS

Sodium Chloride Injection USP 0.9 % is contraindicated in patients 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 Form, Composition and Packaging** section of the Prescribing Information. Sodium Chloride Injection USP 0.9 % is contraindicated in situations where administration of sodium or chloride could be clinically detrimental.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

As directed by the physician, dosage, rate and duration of administration are to be individualized and depend upon the indication for use, the patient's age, weight, clinical condition and concomitant treatment and on the patient's clinical and laboratory response to treatment.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration

Do not administer unless the solution is clear and the seal is intact.

Sodium Chloride Injection USP 0.9 % in clear glass vials are intended for Intramuscular, Intravenous, Intraperitoneal and Subcutaneous administration using sterile equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours.

4.3 Reconstitution

Additives may be incompatible with Sodium Chloride Injection USP 0.9 %. Compatibility of additives with Sodium Chloride Injection USP 0.9 % must be assessed before addition. Additives known, determined or suspected to be incompatible should not be used.

Before adding a substance or medication, verify that it is soluble and or stable in water and that the pH range of Sodium Chloride Injection USP 0.9 % is appropriate.

The instructions for use of medication to be added and other relevant literature must be consulted.

When introducing additives to Sodium Chloride Injection USP 0.9 %, aseptic technique must be used.

After addition, check for possible color change and/or the appearance of precipitates, insoluble complexes or crystals.

Mix the solution thoroughly when additives have been introduced. Do not store solutions containing additives.

4.4 Administration

When other electrolytes or medicines are added to this solution, the dosage and the infusion rate will also be dictated by the dose regimen of the additives.

For single use only.

Discard any unused portion.

5 OVERDOSAGE

An excessive volume of 0.9 % Sodium Chloride Injection USP may lead to hypernatremia (which can lead to CNS manifestations, including seizures, coma, cerebral edema and death) and sodium overload (which can lead to central and/or peripheral edema).

When assessing an overdose, any additives in the solution must also be considered.

Should overdose occur, prompt and careful clinical and laboratory assessment is essential. Effective therapeutic intervention based on the condition of the patient should be planned and executed as soon as possible.

The effects of an overdose may require immediate medical attention and treatment.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Sodium Chloride Injection USP 0.9 % is a sterile, nonpyrogenic solution for use as an isotonic vehicle, and liquid and electronic replenishment in single dose containers for Intramuscular, Intravenous, Intraperitoneal and Subcutaneous administration.

The composition, osmolarity, pH range and ionic concentration is provided in Table 1.

Table 1: The composition, osmolarity and pH of Sodium Chloride Injection USP 0.9 % in USP Type 1 glass vials.

Product	Volume (mL)	DIN	Composition & Concentration	Ionic Concentration (mmol/L)		Total Osmolarity mOsmol/kg	pH
			Sodium Chloride (mg/mL)	Na+	Cl-		
Sodium Chloride Injection USP 0.9 %	10, 20	Yet to be assigned	9	154	154	260-320	4.5-7.0

Table 1 shows the volume, composition, ionic concentration, osmolarity and pH range of 0.9% Sodium Chloride Injection USP.

The container is a single use clear USP Type I glass vial. The stopper is not made with natural rubber latex.

Table 2 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular, Intravenous, Intraperitoneal and Subcutaneous	Solution, 0.9 % 10 mL and 20 mL	Hydrochloric acid NF Nitrogen NF Sodium Hydroxide NF Water for Injection USP

Sodium Chloride Injection USP 0.9 % is available in clear glass single-dose vials of 10 ml and 20 ml.

Per mL: Medicinal ingredient: Sodium Chloride 9 mg. Non-medicinal ingredients: Hydrochloric Acid NF (for pH adjustment), Nitrogen NF and Sodium Hydroxide NF (for pH adjustment); Water for Injection (Q.S.).

7 WARNINGS AND PRECAUTIONS

General

Sodium Chloride Injection USP 0.9 % 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.
In patients with diminished renal function, administration of Sodium Chloride Injection USP 0.9% may result in sodium retention.
Intravenous administration of Sodium Chloride Injection USP 0.9 % may cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states, clinically relevant electrolyte disturbances, acid-base imbalance and/or central and peripheral edema. The risk of fluid and/or solute overload is directly proportional to the volume of the product intravenously administrated.
Excessive administration of potassium free solutions may result in significant hypokalemia.

The use of the intraperitoneal route permits more rapid introduction into the body of relatively larger quantities of fluid than is possible.

However, some of the risks with this procedure are:

1. If the solution is non-sterile and irritable, it may lead to ileus and peritoneal inflammation which may further develop into adhesions
2. Large volume can lead to pain, perforation of intestines, hemorrhage and respiratory distress

Carcinogenesis and Mutagenesis

Studies with Sodium Chloride Injection USP 0.9% have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

Hypersensitivity reactions

The hypersensitivity/infusion reactions reported with Sodium Chloride Injection USP 0.9 %

include hypotension, pyrexia, tremor, chill, urticaria, rash and pruritus.

Stop the infusion immediately if signs or symptoms of hypersensitivity reactions develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Risk of Fluid and/or Solute Overload and Electrolyte Disturbances
Depending on the volume and rate of infusion, intravenous administration of Sodium Chloride Injection USP 0.9 % can cause:

- fluid and/or solute overload resulting in overhydration/hypervolemia and, for example, congested states, including central and peripheral edema.
- clinically relevant electrolyte disturbances and acid-base imbalance.

In general, the risk of fluid/solute overload causing congested states and/or electrolyte disturbances is directly proportional to the volume of the products intravenously administrated.

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

Use in patients at risk for sodium retention, fluid overload and edema
Sodium Chloride Injection USP 0.9 % should be used with particular caution, if at all, in patients with or at risk for:

- Hypernatremia
- Hyperchloremia
- Metabolic acidosis
- Hypervolemia
- Conditions that may cause sodium retention, fluid overload and edema (central and peripheral), such as patients with:
  - primary hyperaldosteronism,
  - secondary hyperaldosteronism, associated with, for example:
    - hypertension,
    - congestive heart failure,
    - liver disease (including cirrhosis),
    - renal disease (including renal artery stenosis, nephrosclerosis) or
    - pre-eclampsia.
- Medications that may increase the risk of sodium and fluid retention, such as corticosteroids

Risk of Hyponatremia
Monitoring of serum sodium is important for all fluids. Sodium Chloride Injection USP 0.9 % has an osmolarity of 260-320 mOsmol/kg.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)), due to the risk of hospital-acquired hyponatremia.

Acute hyponatremia can lead to acute hyponatremic encephalopathy (brain edema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain edema are at particular risk of severe, irreversible and life-threatening brain injury.

Use in Patients with Severe Renal Impairment
Sodium Chloride Injection USP 0.9 % should be administered with particular caution, if at all, to patients with severe renal impairment. In such patients administration of Sodium Chloride Injection USP 0.9 % may result in sodium retention.

7.1 Special Populations
7.1.1 Pregnant Women
There are no adequate data from the use of Sodium Chloride Injection USP 0.9 % in pregnant or lactating women. Healthcare Practitioners should carefully consider the potential risks and benefits for each specific patient before administering 0.9 % Sodium Chloride Injection USP.

7.1.3 Pediatrics
Safety and effectiveness of Sodium Chloride Injection USP 0.9 % in pediatric patients have not been established by adequate and well controlled trials, however, the use of sodium chloride solutions in the pediatric population is referenced in the medical literature. The warnings, precautions and adverse reactions identified in the label copy should be observed in the pediatric population.
Plasma electrolyte concentrations should be closely monitored in the pediatric population because of their impaired ability to regulate fluids and electrolytes.

7.1.4 Geriatrics
Clinical studies of Sodium Chloride Injection USP 0.9 % 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 the responses between elderly and younger patients.

When selecting the type of infusion solution and the volume/rate of infusion for a geriatric patient, one should consider that geriatric patients are generally more likely to have cardiac, renal, hepatic, and other diseases or concomitant drug therapy.

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range.

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.

Monitoring and Laboratory Tests

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 or the rate of administration warrants such evaluation.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Adverse 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 and administration set for examination if deemed necessary.

8.5 Post-Market Adverse Reactions

The following adverse reactions have been reported in the post-marketing experience:

IMMUNE SYSTEM DISORDERS:
Hypersensitivity/infusion reactions, including Hypotension, Pyrexia, Tremor, Chills, Urticaria, Rash, Pruritus

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:
Infusion site reactions, such as Infusion site erythema, Injection site streaking, Burning sensation, Infusion site urticaria.
The following adverse reactions have been reported with other similar products:

- Hypernatremia
- Hyperchloremic metabolic acidosis
- Hyponatremia, which may be symptomatic
- Hyponatremic encephalopathy

9 DRUG INTERACTIONS

Drug Interactions Overview

Caution is advised when administering Sodium Chloride Injection USP 0.9 % to patients treated with drugs that may increase the risk of sodium and fluid retention, such as corticosteroids or corticotropin **[See also Warnings and Precautions - Use in patients at risk for sodium retention, fluid overload and edema.]**

Caution is advised in patients treated with lithium. Renal lithium clearance may be increased during administration of Sodium Chloride Injection USP 0.9 %, resulting in decreased lithium levels.

Caution is advised when administering Sodium Chloride Injection USP 0.9 % to patients treated with drugs leading to an increased vasopressin effect. The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hyponatremia following treatment with intravenous fluids.

[See Warnings and Precautions for Use and Adverse Reactions.]

Drugs stimulating vasopressin release such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3.4-methylenedioxy-N methamphetamine, ifosfamide, antipsycotics, opioids.

Drugs potentiating vasopressin action such as chlorpropamide, non steroidal anti-inflammatories (NSAIDS), cyclophosphamide.

Vasopressin analogues such as desmopressin, oxytocin, vasopressin, terlipressin.

Caution is advised when administering 0.9 % Sodium Chloride Injection USP to patients treated with drugs that may increase the risk of hyponatremia, such as diuretics and antiepileptics (e.g., oxcarbazepine).

Studies have not been conducted to evaluate additional drug/drug or drug/food interactions with 0.9% Sodium Chloride Injection USP.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Sodium Chloride Injection USP 0.9 % is a source electrolytes and water for hydration. It is capable of inducing diuresis depending on the clinical condition of the patient.

Solutions which are di-electrolytic are good for replacing or sustaining electrolytes. For ionic concentration, see Table 1.

11 STORAGE, STABILITY AND DISPOSAL

Sodium Chloride Injection 0.9 % USP, 10 mL and 20 mL must be stored at 20°C to 25°C (See “Controlled Room Temperature’’ in USP). Protect from freezing.

12 SPECIAL HANDLING INSTRUCTIONS

For single use only
Discard any unused portion.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Sodium Chloride

Chemical name: Sodium Chloride

Molecular formula and molecular mass: NaCl (58.44 g/mol)

Structural formula: Na-Cl

17 SUPPORTING PRODUCT MONOGRAPHS

1. 0.9 % Sodium chloride injection USP, solution, 232918, Product Monograph, Omega Laboratories Limited. JUL 09, 2020.
2. 0.9 % Sodium chloride injection USP, solution, 235120, Product Monograph, B. Braun Medical Inc. AUG 24, 2020.