PRESCRIBING INFORMATION

# 0.45% Sodium Chloride Injection, USP

Solution for Infusion

Intravenous Fluid and Electrolyte Replenisher

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# Prescribing Information

# 0.45% Sodium Chloride Injection, USP

## Summary Product Information

0.45% Sodium Chloride Injection, USP is a sterile, nonpyrogenic, hypotonic solution composed of sodium chloride (NaCl) and water. The composition, osmolarity and approximate pH of this product is shown in Table 1. The Viaflex plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic).

Table 1. Composition, osmolarity and pH of 0.45% Sodium Chloride Injection, USP

| Product | Volume (mL) | DIN | Composition & Concentration | Ionic Concentration (mmol/L) | | Total Osmolarity (mOsmol/L) | pH |
|---|---|---|---|---|---|---|---|
| | | | Sodium Chloride (g/L) | $Na^+$ | $Cl^-$ | | |
| 0.45% Sodium Chloride Injection, USP | 1000 | 00060186 | 4.5 | 77 | 77 | 154 | 4.5 – 7.0 |

Since osmolarity of this product (154 mOsmol/L) is only about half of that in human blood and extracellular fluid, administration of this product may reduce blood osmolarity and result in hemolysis.

The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g. di-2-ethylhexyl phthalate (DEHP), up to 5 parts per million. However, the safety of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.

### Actions

0.45% Sodium Chloride Injection, USP has a value as a source of water and electrolytes It is capable of inducing diuresis depending on the clinical conditions of the patient.

Solutions which are di-electrolytic or polyelectrolytic have value in maintaining or replenishing electrolytes. See Table 1 for ionic concentrations.

## Indications and Clinical Use

0.45% Sodium Chloride Injection, USP is indicated as a source of water and electrolytes.

0.45% Sodium Chloride Injection, USP used in a small volume (less than 100 mL) is also a vehicle or diluent for compatible products for parenteral administration.

## Contraindications

0.45% Sodium Chloride Injection, USP is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation of component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the Prescribing Information.

## Warnings and Precautions

## General

0.45% Sodium Chloride Injection, USP 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.

Excessive administration of this product may result in significant hypokalemia or hemolysis.

**Risk of Fluid and/or Solute Overload and Electrolyte Disturbances**

Depending on the volume and rate of infusion, intravenous administration of 0.45% Sodium Chloride Injection, USP 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.

0.45% Sodium Chloride Injection, USP has a risk resulting in hypotonic and/or dilutional states in the body. In general, the risk of resulting in fluid and/or solute overload and/or electrolyte disturbances is directly proportional to the volume of the product 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 with Severe Renal Impairment**

0.45% Sodium Chloride Injection, USP should be administered with particular caution, if at all, to patients with severe renal impairment. In such patients administration of 0.45% Sodium Chloride Injection, USP may result in sodium retention.

**Use in Patients at Risk for Sodium Retention, Fluid Overload and Edema**

In patients with diminished renal function, administration of solutions containing sodium ions may result in sodium retention.

0.45% Sodium Chloride Injection, USP should be used with particular caution, if at all, in patients with or at risk for:

- 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

**Hypersensitivity Reactions**

Hypersensitivity/infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus may occur.

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

**Hyponatremia**

Monitoring of serum sodium is particularly important for hypotonic fluids. 0.45% Sodium Chloride Injection, USP is hypotonic with an osmolarity of 154 mOsmol/L.

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 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.

The risk for hyponatremia is increased, for example,

- in children
- in elderly patients
- in women
- postoperatively
- in persons with psychogenic polydipsia
- in patients treated with medications that increase the risk of hyponatremia (such as certain antiepileptic and psychotropic medications).

The risk for developing hyponatremic encephalopathy is increased, for example,

- in pediatric patients (≤16 years of age)
- in women (in particular pre-menopausal women)
- in patients with hypoxemia
- in patients with underlying central nervous system disease

**Risk of Air Embolism**

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container.

Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

## Special Populations

**Pediatrics**

Rapid correction of hyponatremia and hypernatremia is potentially dangerous (risk of serious neurologic complications), see DOSAGE AND ADMINISTRATION.

Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes.

The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Acute hyponatraemia 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.

**Geriatrics**

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.

In elderly patients, the risk for hyponatremia is increased.

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.

**Pregnant or Nursing Women**

There are no adequate data from the use of 0.45% Sodium Chloride Injection, USP in pregnant or lactating women. Healthcare providers should carefully consider the potential risks and benefits for each specific patient before administering 0.45% Sodium Chloride Injection, USP.

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when 0.45% Sodium Chloride Injection, USP is administered to a nursing mother.

## Adverse Reactions

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

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

## Post-Marketing Adverse Reactions

The following adverse reactions have been reported in the postmarketing experience:

- Hyponatremia, which may be symptomatic

The following adverse reactions have been reported with other similar products:

- Hyperchloremic metabolic acidosis
- Hyponatremia, which may be symptomatic
- Hyponatremic encephalophathy
- Infusion site reactions, such as infusion site erythema, injection site streaking, burning sensation, infusion site urticaria.

## Drug Interactions

Caution is advised in patients treated with lithium. Renal lithium clearance may be decreased in the presence of hyponatremia, resulting in increased lithium levels.

Caution is advised when administering 0.45% Sodium Chloride Injection, USP 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 when administering 0.45% Sodium Chloride Injection, USP 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 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 0.45% Sodium Chloride Injection, USP to patients treated with drugs that may increase the risk of hyponatremia, such as diuretics and antiepileptics (e.g., oxcarbazepine).

## Dosage and Administration

As directed by a 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.

0.45% Sodium Chloride Injection, USP in **Viaflex** plastic container is intended for intravenous administration using sterile equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours.

Rapid correction of hyponatremia and hypernatremia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in intravenous fluid therapy.

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

Additives may be incompatible. Compatibility of additives must be checked before adding medication.

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 additions. When introducing additives to this solution, aseptic technique must be used.

Additives known or determined 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 0.45% Sodium Chloride Injection, USP is appropriate.

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

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

### Administration with Blood Products

Do not mix or administer 0.45% Sodium Chloride Injection, USP through the same administration set with whole blood or cellular blood components.

## Overdosage

An excessive volume of 0.45% Sodium Chloride Injection, USP may lead to:

- Hyponatremia (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). See also **Warnings and Precautions.**
- hypokalemia which may lead to cardiac arrhythmia, cardiac arrest, acute confusion state or death
- hemolysis

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.

## Storage

Store at 15°C to 25°C

## Special Handling Instructions

Additives known or determined 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 0.45% Sodium Chloride Injection, USP is appropriate.

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

When introducing additives to 0.45% Sodium Chloride Injection, USP, aseptic technique must be used.

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

Mix the solution thoroughly when additives have been introduced

Do not store solutions containing additives.

0.45% Sodium Chloride Injection, USP is for single use only.

Discard any unused portion.

## Dosage Form, Composition and Packaging

## How Supplied

Table 1 shows the composition, osmolarity, approximate pH, calories/litre and ionic concentration of 0.45% Sodium Chloride Injection, USP.

## Directions for use of Viaflex Plastic Container

WARNING: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air (approximately 15 mL) being drawn from the primary container before administration of the fluid from the secondary container is completed.

Do not remove unit from overwrap until ready to use.

**To Open**

Tear overwrap down side at slit and remove solution container. Visually inspect the container. If the outlet port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired. If supplemental medication is desired, follow directions below before preparing for administration. Some opacity of the plastic due to moisture absorption during sterilization process may be observed. This is normal and does not affect the solution quality and safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found discard solution as sterility may be impaired.

**Preparation for Administration**

1. Suspend container from eyelet support.
2. Remove plastic protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying set.

**To Add Medication**

1. Prepare medication site.

2. Using a syringe and 20 - 22 gauge needle, puncture resealable rubber plug at target area and inject. Multiple additions may be made in this manner.

3. Mix solution and medication thoroughly. For high density medications such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

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