PRESCRIBING INFORMATION

0.9% Sodium Chloride Injection, USP

In MINI-BAG and MINI-BAG PLUS (Viaflex) Plastic Containers

Solution for Infusion

Intravenous Fluid and Electrolyte Replenisher

Baxter Corporation
Mississauga, Ontario L5N 0C2
Canada

Date of Revision:
April 2, 2019

Submission Control No: 224943

Prescribing Information

0.9% Sodium Chloride Injection, USP
In MINI-BAG and MINI-BAG PLUS (VIAFLEX) Plastic Containers

Summary Product Information

0.9% Sodium Chloride Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in single dose containers for intravenous administration.

The composition, osmolarity, approximate pH range and ionic concentration of 0.9% Sodium Chloride Injection, USP are shown in Table 1.

Table 1. Composition, osmolarity and pH of 0.9% Sodium Chloride Injection, USP, in Mini-Bag and Mini-Bag Plus (Viaflex) plastic containers

Product	Volume (mL)	DIN	Composition & concentration	Ionic concentration (mmol/L)		Total osmolarity (mOsmol/L)	pH
			Sodium Chloride (g/L)	Na+	Cl-		
0.9% Sodium Chloride Injection, USP, in Mini-Bag and Mini-Bag Plus (Viaflex) plastic containers	25	00060208	9	154	154	308	4.5-7.0
	50						
	100						
	250						
	500						
	1000						

The MINI-BAG and MINI-BAG PLUS (Viaflex) plastic containers are fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic) with di-ethylhexyl phthalate (DEHP) as a plasticizer.

The MINI-BAG container contains a medication port (containing the injection site) and an administration port (containing a port protector). Additives may be introduced to the MINI-BAG container by inserting a needle through the injection site. The port protector is removed at the time of use to administer the contents of the MINI-BAG container.

The MINI-BAG Plus container is a standard diluent container with an integral drug vial adaptor. It allows for drug admixture after connection to a single dose powdered or liquid (up to 10 mL) vial having a 20 mm closure. A breakaway seal in the tube between the vial adaptor and the container is broken to allow transfer of the diluent into the vial and reconstitution of the drug. The reconstituted drug is then transferred from the vial into the container diluent and mixed to result in an admixture for delivery to the patient.

Water in a solution in the container can permeate through the plastic wall, but in an insufficient amount to significantly affect the solution. Before the product expires, a very small amount of chemical components of the plastic can be leached into the solution

in the container, such as up to 5 parts per million for DEHP. No safety issues of the plastic material were identified in USP biological tests in animals as well as by tissue culture toxicity studies.

Actions

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

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

Indications

0.9% Sodium Chloride Injection, USP is indicated as a source of water and electrolytes.

0.9% Sodium Chloride Injection, USP can be used as a vehicle or diluent for compatible products for parenteral administration.

0.9% Sodium Chloride Injection, USP is also indicated for use as a priming solution in hemodialysis procedures

Contraindications

0.9% Sodium Chloride Injection, USP 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.

Warnings and Precautions

General

0.9% 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.

In patients with diminished renal function, administration of 0.9% Sodium Chloride Injection, USP may result in sodium retention.

Intravenous administration of 0.9% Sodium Chloride Injection, USP 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.

Carcinogenesis and Mutagenesis

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

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus, have been reported with 0.9% Sodium Chloride Injection, USP.

Stop the infusion immediately if signs or symptoms of hypersensitivity/infusion 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 0.9% 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.

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

0.9% Sodium Chloride Injection, USP 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. 0.9% Sodium Chloride Injection, USP has an osmolarity of 308 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 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

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

Risk of Air Embolism

Do not connect flexible plastic containers of intravenous solutions in series connections. Such use could result in air embolism due to possible residual air being drawn from one container before administration of the fluid from a secondary container is completed.

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

Pregnancy and Lactation

There are no adequate data from the use of 0.9% Sodium Chloride Injection, USP 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.

Pediatrics

Safety and effectiveness of 0.9% Sodium Chloride Injection, USP 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.

Geriatrics

Clinical studies of 0.9% Sodium Chloride Injection, USP 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.

Adverse Reactions

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.

Post-marketing Adverse Reactions

The following adverse reactions have been reported in the post-marketing experience, listed by MedDRA System Organ Class (SOC), then, where feasible, by Preferred Term in order of severity.

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

Drug Interactions

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

Caution is advised when administering 0.9% 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 Special 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, antipsychotics, 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.

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.

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

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

0.9% Sodium Chloride Injection, USP in Viaflex plastic containers are intended for intravenous administration using sterile equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours.

Additives may be incompatible with 0.9% Sodium Chloride Injection, USP. Compatibility of additives with 0.9% Sodium Chloride Injection, USP 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 0.9% Sodium Chloride Injection, USP is appropriate.

0.9% Sodium Chloride Injection, USP in MINI-BAG Plus container should be used only with a single dose powdered or liquid (up to 10 mL) drug vial with a 20 mm closure.

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

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

After addition, check for a 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.

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.

Do not administer unless drug is completely dissolved and drug vial is empty for 0.9% Sodium Chloride Injection, USP in MINI-BAG Plus container.

Do not remove drug vial at any time prior to or during administration of 0.9% Sodium Chloride Injection, USP in MINI-BAG Plus container.

For single use only. After opening the MINI-BAG or MINI-BAG Plus container, the contents should be used immediately and should not be stored for a subsequent infusion. Do not reconnect any partially used MINI-BAG or MINI-BAG Plus containers. Discard any unused portion.

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.

Storage

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat.

Store at 15°C to 25°C

Special Handling Instructions

For single use only.

Discard any unused portion.

Dosage Form, Composition and Packaging

0.9% Sodium Chloride Injection USP in Viaflex plastic container is available in six different sizes, i.e. 25 ml, 50 ml, 100 ml, 250 ml, 500 ml and 1,000 ml.

Table 1 in the Summary Product Information section shows the volume, composition, ionic concentration, osmolarity and pH range of 0.9% Sodium Chloride Injection, USP in Viaflex Plastic Container.

Per 100 mL: Sodium Chloride 900 mg, Water for Injection

Directions for use of MINI-BAG (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. The overwrap is a moisture barrier.

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. Moisture and 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. If supplemental medication is desired, follow “To Add Medication” directions below.

Preparation for Administration

Caution: Do not use plastic containers in series connections.

Caution: Use only with a non-vented set or a vented set with the vent closed.

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

Additives may be incompatible.

To add medication before solution administration:

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.

To add medication during solution administration:

1. Close clamp on the set.

2. Prepare medication site.

3. Using syringe with 20 to 22 gauge needle, puncture resealable medication port and inject.

4. Remove container from IV pole and/or turn to an upright position.

5. Evacuate both ports by squeezing them while container is in the upright position.

6. Mix solution and medication thoroughly.

7. Return container to in-use position and continue administration.

Directions for use of MINI-BAG Plus (Viaflex) Plastic Container

WARNING: Do not use plastic containers in series connections. Such use could result in air embolism due to potential 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. The overwrap is a moisture barrier.

To Open

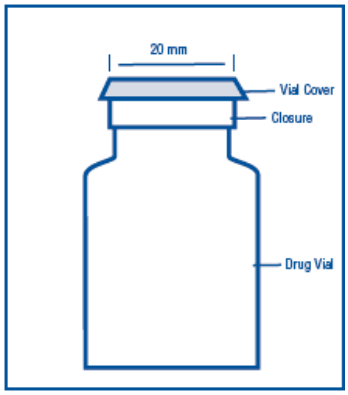
Tear overwrap down side at slit and remove solution container. Visually inspect the container. If the outlet port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired. Moisture and some opacity of

the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality and safety. The opacity will diminish gradually.

Prior to use, check that the vial adaptor cover is intact. Check for minute leaks by squeezing inner bag firmly. If leaks are found or if the vial adaptor cover is not intact, discard solution as sterility may be impaired.

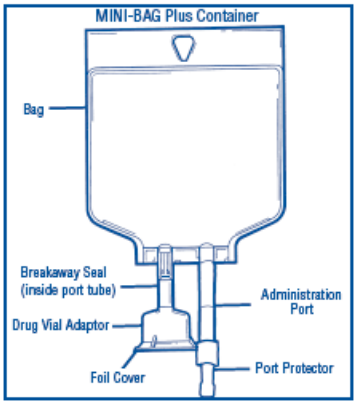
Assembly

1.



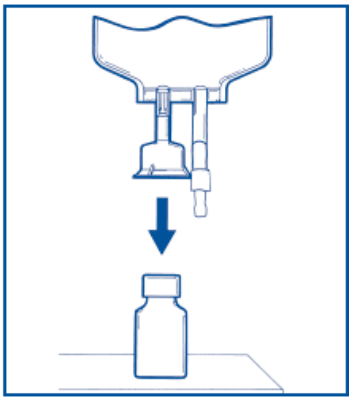
- Remove vial cover.
- Disinfect stopper.

2.



- Peel off foil cover.
- Inspect adaptor for moisture. Discard if found.

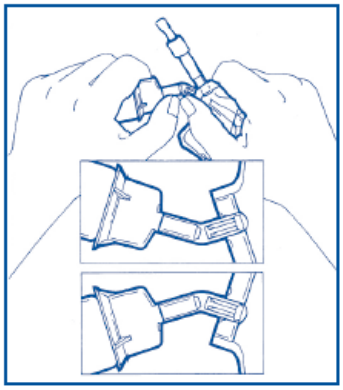
3.



- Place vial upright.
- Hold firmly.
- Push adaptor down until vial snaps in place.
- DO NOT TWIST.
- Pull vial to ensure fully seated.

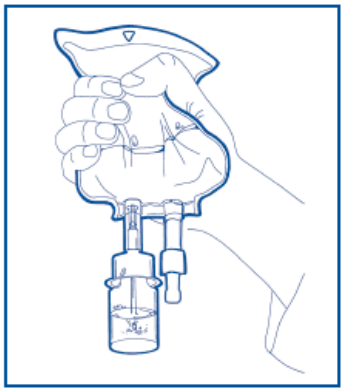
Reconstitution

4.



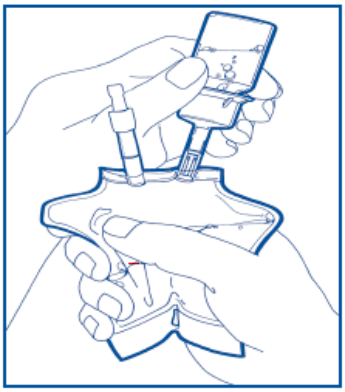
- Squeeze bag and check vial.
- Use only if vial fully seated and dry.
- Bend up then down to break seal.

5.



- For liquid drug vials, proceed directly to Step 6.
- **For powdered drug vials:** Hold bag with vial down.
- Squeeze solution into vial until **half full**.
- Shake to suspend drug in solution.

6.



- Hold bag with vial upside down.
- Squeeze bag to force air into vial.
- Release to drain suspended drug from vial.
- Repeat steps 5 and 6 until vial is **empty** of drug and solution is thoroughly mixed. **Ensure drug is completely dissolved. Do Not Remove Drug Vial.**

7.

Remove port protector. Attach administration set per its directions.

8.	Hang container on I.V. pole and prime set per directions. Ensure that vial is empty of drug and solution. Repeat step 6 if drug and solution remain in vial. Warning: Do not use in series connections.
9.	Administer medication per directions. Use within specified time for drug stability.

Baxter Corporation
Mississauga, ON L5N 0C2

Date of revision: April 2, 2019