Baxter

Sodium Chloride Injection, USP

in VIAFLEX Plastic Container

DESCRIPTION

Sodium Chloride Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in single dose containers for intravenous administration. It contains no antimicrobial agents. The nominal pH is 5.0 (4.5 to 7.0). Composition, osmolarity, and ionic concentration are shown below:

0.9% Sodium Chloride Injection, USP contains 9 g/L Sodium Chloride, USP (NaCl) with an osmolarity of 308 mOsmol/L (calc), pH adjusted with Sodium Hydroxide, USP. It contains 154 mEq/L sodium and 154 mEq/L chloride.

The VIAFLEX plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic). 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.

CLINICAL PHARMACOLOGY

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.

INDICATIONS AND USAGE

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

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

CONTRAINDICATIONS

None known.

WARNINGS

Hypersensitivity

Hypersensitivity and 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 a hypersensitivity reaction develop, such as tachycardia, chest pain, dyspnea and flushing. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Electrolyte Imbalances

Fluid Overload

Depending on the volume and rate of infusion, and the patient's underlying clinical condition, the intravenous administration of Sodium Chloride Injection, USP can cause fluid disturbances such as overhydration/hypervolemia and congested states, including pulmonary congestion and edema.

Avoid 0.9% Sodium Chloride Injection, USP in patients with or at risk for fluid and/or solute overloading. If use cannot be avoided, monitor fluid balance, electrolyte concentrations, and acid base balance, as needed and especially during prolonged use.

Hyponatremia

Sodium Chloride Injection, USP may cause hyponatremia. Hyponatremia can lead to acute hyponatremic encephalopathy 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 of hospital-acquired hyponatremia is increased in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH) treated with high volume of Sodium Chloride Injection, USP.

The risk for hyponatremia is increased in pediatric patients, elderly patients, postoperative patients, those with psychogenic polydipsia, and in patients treated with medications that increase the risk of hyponatremia (such as diuretics, certain antiepileptic and psychotropic medications). See **DRUG INTERACTIONS.**

Patients at increased risk for developing complications of hyponatremia such as hyponatremic encephalopathy, include pediatric patients, women (in particular pre-menopausal women), patients with hypoxemia, and patients with underlying central nervous system disease. Avoid Sodium Chloride Injection, USP in patients with or at risk for hyponatremia. If use cannot be avoided, monitor serum sodium concentrations.

Rapid correction of hyponatremia is potentially dangerous with risk of serious neurologic complications. Brain adaptations reducing risk of cerebral edema make the brain vulnerable to injury when chronic hyponatremia is too rapidly corrected, which is known as osmotic demyelination syndrome (ODS). To avoid complications, monitor serum sodium and chloride concentrations, fluid status, acid-base balance, and signs of neurologic complications.

Hypernatremia

Hypernatremia may occur with Sodium Chloride Injection, USP. Conditions that may increase the risk of hypernatremia, fluid overload and edema (central and peripheral), include 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); and pre-eclampsia.

Certain medications, such as corticosteroids or corticotropin, may also increase risk of sodium and fluid retention, see **DRUG INTERACTIONS.**

Avoid Sodium Chloride Injection, USP in patients with, or at risk for, hypernatremia. If use cannot be avoided, monitor serum sodium concentrations.

Rapid correction of hypernatremia is potentially dangerous with risk of serious neurologic complications. Excessively rapid correction of hypernatremia is also associated with a risk for serious neurologic complications such as osmotic demyelination syndrome (ODS) with risk of seizures and cerebral edema.

PRECAUTIONS

Patients with Severe Renal Impairment

Administration of Sodium Chloride Injection, USP in patients with or at risk of severe renal impairment, may result in hypernatremia and/or fluid overload (see **WARNINGS**). Avoid Sodium Chloride Injection, USP in patients with severe renal impairment or conditions that may cause sodium and/or potassium retention, fluid overload, or edema. If use cannot be avoided, monitor patients with severe renal impairment for development of these adverse reactions.

Drug Interactions

Other Products that Affect Fluid and/or Electrolyte Balance

Administration of Sodium Chloride Injection, USP to patients treated concomitantly with drugs associated with sodium and fluid retention may increase the risk of hypernatremia and volume overload. Avoid use of Sodium Chloride Injection, USP in patients receiving such products, such as corticosteroids or corticotropin. If use cannot be avoided, monitor serum electrolytes, fluid balance and acid-base balance.

Lithium

Renal sodium and lithium clearance may be increased during administration of 0.9% Sodium Chloride Injection, USP. Monitor serum lithium concentrations during concomitant use.

Other Drugs that Increase the Risk of Hyponatremia

Administration of Sodium Chloride Injection, USP in patients treated concomitantly with medications associated with hyponatremia may increase the risk of developing hyponatremia.

Avoid use of Sodium Chloride Injection, USP in patients receiving products, such as diuretics, and certain antiepileptic and psychotropic medications. Drugs that increase the vasopressin effect reduce renal electrolyte free water excretion and may also increase the risk of hyponatremia following treatment with intravenous fluids. If use cannot be avoided, monitor serum sodium concentrations.

Pregnancy

There are no adequate and well controlled studies with Sodium Chloride Injection, USP in pregnant women and animal reproduction studies have not been conducted with this drug. Therefore, it is not known whether Sodium Chloride Injection, USP can cause fetal harm when administered to a pregnant woman. Sodium Chloride Injection, USP should be given during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether this drug is present in human milk. Because many drugs are present in human milk, caution should be exercised when

Sodium Chloride Injection, USP is administered to a nursing woman.

Pediatric Use
The use of Sodium Chloride Injection, USP in pediatric patients is based on clinical practice. (See **DOSAGE AND ADMINISTRATION**).

Closely monitor plasma electrolyte concentrations in pediatric patients who may have impaired ability to regulate fluids and electrolytes. In very low birth weight infants, excessive or rapid administration of Sodium Chloride Injection, USP may result in increased serum osmolality and risk of intracerebral hemorrhage.

Children (including neonates and older children) are at increased risk of developing hyponatremia as well as for developing hyponatremic encephalopathy.

Geriatric Use
Geriatric patients are at increased risk of developing electrolyte imbalances. Sodium Chloride Injection, USP 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. Therefore, 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. Consider monitoring renal function in elderly patients.

ADVERSE REACTIONS

Post-Marketing Adverse Reactions
The following adverse reactions have been identified during post approval use of Sodium Chloride Injection, USP. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions have been reported in the post-marketing experience during use of 0.9% Sodium Chloride Injection, USP and include the following:

General disorders and administration site conditions: Infusion site erythema, injection site streaking, burning sensation, and infusion site urticaria

Hypersensitivity reactions: Hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus.

Metabolism and nutrition disorders: Hypernatremia, hyponatremia, hyperchloremic metabolic acidosis.

Nervous System Disorders: Hyponatremic encephalopathy

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

Excessive administration of:

- 0.9% Sodium Chloride Injection, USP can cause hypernatremia. Hypernatremia can lead to CNS manifestations, including seizures, coma, cerebral edema and death.
- Sodium Chloride Injection, USP can cause fluid overload (which can lead to pulmonary and/or peripheral edema). See **WARNINGS and ADVERSE REACTIONS.**

When assessing an overdose, any additives in the solution must also be considered. The effects of an overdose may require immediate medical attention and treatment.

Interventions include discontinuation of Sodium Chloride Injection, USP administration, dose reduction, and other measures as indicated for the specific clinical constellation (e.g., monitoring of fluid balance, electrolyte concentrations and acid base balance).

DOSAGE AND ADMINISTRATION

Important Preparation and Administration Instructions

- Sodium Chloride Injection, USP is intended for intravenous administration using sterile equipment.
- Prior to infusion, visually inspect the solution for particulate matter and discoloration. The solution should be clear, and there should be no precipitates. Do not administer unless solution is clear, and container is undamaged.
- To reduce the risk of air embolism, adhere to the following Sodium Chloride Injection, USP preparation instructions:
    - Use a non-vented infusion set or close the vent on a vented set.
    - Use a dedicated line without any connections (do not connect flexible containers in series).
    - The use of pressure infusion is **not** recommended as a method to increase flow rates. However, if pressure infusion is required, ensure that any air within the bag is fully evacuated prior to initiation of infusion.
- If using a pumping device to administer Sodium Chloride Injection, turn off the pump before the container is empty.

Dosing Information

The choice of product, dosage, volume, rate, and duration of administration is dependent upon the age, weight and clinical condition of the patient and concomitant therapy, and administration should be determined by a physician experienced in intravenous fluid therapy.

Introduction of Additives

Additives may be incompatible.

Evaluate all additions to the plastic container for compatibility and stability of the resulting preparation. Consult with a pharmacist, if available.

If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. After addition, if there is a discoloration and/or the appearance of precipitates, insoluble complexes or crystals, do not use. Do not store solutions containing additives. Discard any unused portion.

HOW SUPPLIED

The available sizes of each injection in VIAFLEX plastic containers are shown below:

Code	Size (mL)	NDC	Product Name
2B1322	250	0338-0049-02	0.9% Sodium Chloride Injection, USP
2B1323	500	0338-0049-03	
2B1324	1000	0338-0049-04	

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (25°C/77°F); brief exposure up to 40°C/104°F does not adversely affect the product.

DIRECTIONS FOR USE OF VIAFLEX PLASTIC CONTAINER

For Information on Risk of Air Embolism – see **DOSAGE AND ADMINISTRATION .**

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. 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. 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 directions below.

Preparation for Administration

1. Suspend container from eyelet support.
2. Remove 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 syringe with 19 to 22 gauge needle, puncture resealable medication port and inject.
3. Mix solution and medication thoroughly. For high density medication 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 19 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.

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Deerfield, IL 60015 USA
Made in Mexico

07-19-006-068

Rev. July 2024

Lactated Ringer's Injection, USP
in VIAFLEX Plastic Container

DESCRIPTION

Lactated Ringer's Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in single dose containers for intravenous administration. It contains no antimicrobial agents. Composition, osmolarity, pH, ionic concentration and caloric content are shown in Table 1.

Table 1

	Size (mL)	Composition (g/L)				Osmolarity (mOsmol/L) (calc)	pH	Ionic Concentration (mEq/L)					Caloric Content (kcal/L)
		Sodium Chloride, USP, (NaCl)	Sodium Lactate, ($C_3H_5NaO_3$)	Potassium Chloride, USP, (KCl)	Calcium Chloride, USP ($CaCl_2 \bullet 2H_2O$)			Sodium	**Potassium**	Calcium	Chloride	Lactate	
Lactated Ringer's Injection, USP	250 500 1000	6	3.1	0.3	0.2	273	6.5 (6.0 to 7.5)	130	**4**	2.7	109	28	9

The VIAFLEX plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic). 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.

CLINICAL PHARMACOLOGY

Lactated Ringer's 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.

Lactated Ringer's Injection, USP produces a metabolic alkalinizing effect. Lactate ions are metabolized ultimately to carbon dioxide and water, which requires the consumption of hydrogen cations.

INDICATIONS AND USAGE

Lactated Ringer's Injection, USP is indicated as a source of water and electrolytes or as an alkalinizing agent.

CONTRAINDICATIONS

Lactated Ringer's Injection, USP is contraindicated in:

- Newborns (≤28 days of age) receiving concomitant treatment with ceftriaxone, even if separate infusion lines are used due to the risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream.

- Patients older than 28 days, including adults, ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including Lactated Ringer's Injection, USP through the same infusion line (e.g., via a Y-connector). If the same infusion line is used for sequential administration, the line must be thoroughly flushed between infusions with a compatible fluid.

- Patients with known hypersensitivity to sodium lactate (see **WARNINGS**).

WARNINGS

Potassium Content

The potassium concentration in Lactated Ringer's Injection, USP is similar to the concentration in plasma; however, it is insufficient to produce a useful effect in case of severe potassium deficiency. Lactated Ringer's Injection, USP is not recommended for the treatment of severe hypokalemia.

Lactated Ringer's Injection, USP is not for the treatment of lactic acidosis or severe metabolic acidosis.

Hypersensitivity

Hypersensitivity reactions, including anaphylaxis, have been reported with Lactated Ringer's Injection, USP. Stop the infusion immediately if signs or symptoms of a hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Electrolyte Imbalances

Hyponatremia

Lactated Ringer's Injection, USP may cause hyponatremia. Hyponatremia can lead to acute hyponatremic encephalopathy 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 of hospital acquired hyponatremia is increased in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH) treated with high volume of Lactated Ringer's Injection, USP.

The risk for hyponatremia is increased in pediatric patients, elderly patients, postoperative patients, those with psychogenic polydipsia, and in patients treated with medications that increase the risk of hyponatremia (such as diuretics, certain antiepileptic and psychotropic medications). See **DRUG INTERACTIONS**.

Patients at increased risk for developing complications of hyponatremia such as hyponatremic encephalopathy, include pediatric patients, women (in particular, premenopausal women), patients with hypoxemia, and patients with underlying central nervous system disease. Avoid Ringer's Injection in patients with or at risk for hyponatremia. If use cannot be avoided, monitor serum sodium concentrations.

Rapid correction of hyponatremia is potentially dangerous with risk of serious neurologic complications. Brain adaptations reducing risk of cerebral edema make the brain vulnerable to injury when chronic hyponatremia is too rapidly corrected, which is known as osmotic demyelination syndrome (ODS). To avoid complications, monitor serum sodium and chloride concentrations, fluid status, acid-base balance, and signs of neurologic complications.

Fluid Overload

Depending on the volume and the rate of infusion, the intravenous administration of Lactated Ringer's Injection, USP can cause electrolyte disturbances such as overhydration and congested states, including pulmonary congestion and edema.

Avoid Lactated Ringer's Injection, USP in patients with or at risk for fluid and/or solute overloading. If use cannot be avoided, monitor fluid balance, electrolyte concentrations and acid base balance, as needed and especially during prolonged use.

Hyperkalemia

Potassium-containing solutions, including Lactated Ringer's Injection, USP, may increase the risk of hyperkalemia.

Patient's at increased risk of developing hyperkalemia include those:

- With conditions predisposing to hyperkalemia and/or associated with increased sensitivity to potassium, such as patients with severe renal impairment, acute dehydration, extensive tissue injury or burns, certain cardiac disorders such as

congestive heart failure.

- Treated concurrently or recently with agents or products that cause or increase the risk of hyperkalemia (see **DRUG INTERACTIONS**).

Avoid use of Lactated Ringer's Injection, USP in patients with, or at risk for, hyperkalemia. If use cannot be avoided, monitor serum potassium concentrations.

Alkalosis

Because lactate is metabolized to bicarbonate, administration of Lactated Ringer's Injection, USP may result in, or worsen, metabolic alkalosis. Avoid intravenous administration of Lactated Ringer's Injection, USP in patients with alkalosis or at risk for alkalosis.

PRECAUTIONS

Patients with Severe Renal Impairment

Administration of Lactated Ringer's Injection, USP in patients with or at risk of severe renal impairment, may result in hyperkalemia and/or fluid overload (see **WARNINGS**). Avoid Lactated Ringer's Injection, USP in patients with severe renal impairment or conditions that may cause sodium and/or potassium retention, fluid overload, or edema. If use cannot be avoided, monitor patients with severe renal impairment for development of these adverse reactions.

Hyperlactatemia

Lactated Ringer's Injection, USP should be used with caution in severe hepatic insufficiency, since lactate metabolism may be impaired. In addition, Lactated Ringer's Injection, USP may not produce its alkalinizing action in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. Consider when monitoring serum lactate levels.

Hypercalcemia

Lactated Ringer's Injection, USP contains calcium salts and may cause hypercalcemia. Avoid administration of Lactated Ringer's Injection, USP in patients with hypercalcemia or conditions predisposing to hypercalcemia; and in patients with calcium renal calculi or history of such calculi.

Hyperglycemia

Administration of solutions containing lactate should be used with caution in patients with impaired glucose tolerance and diabetes mellitus, as it may result in hyperglycemia.

Pediatric Use

Safety and effectiveness of Lactated Ringer's Injection, USP in pediatric patients have not been established by adequate and well controlled trials, however, the use of electrolyte 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.

Administration of a lactate-containing intravenous solution to infants should take into account that the metabolic capacity of the liver still matures during the first months of life, which also affects the biotransformation of lactate..

Pediatric patients are at increased risk of developing hyponatremia as well as for developing encephalopathy as a complication of hyponatremia (see **WARNINGS**).

Geriatric Use

Geriatric patients are at increased risk of developing electrolyte imbalances. Lactated Ringer's Injection, USP 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. Therefore, 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. Consider monitoring renal function in elderly patients.

Drug Interactions

Ceftriaxone

For information on interaction with ceftriaxone – see **CONTRAINDICATIONS**

Other Drugs that Increase the Risk of Hyponatremia

Administration of Lactated Ringer's Injection, USP to patients treated concomitantly with medications associated with hyponatremia may increase the risk of developing hyponatremia.

Avoid use of Lactated Ringer's Injection, USP in patients receiving products, such as diuretics, and certain antiepileptic and psychotropic medications. Drugs that increase the vasopressin effect reduce renal electrolyte free water excretion and may also increase the risk of hyponatremia following treatment with intravenous fluids. If use cannot be avoided, monitor serum sodium concentrations.

Other Products that Affect Fluid and/or Electrolyte Balance

Administration of Lactated Ringer's Injection, USP to patients treated concomitantly with drugs associated with sodium and fluid retention may increase the risk of hypernatremia and volume overload. Avoid use of Lactated Ringer's Injection, USP in patients receiving such products, such as corticosteroids or corticotropin. If use cannot be avoided, monitor serum electrolytes, fluid balance

and acid-base balance.

Drugs with pH Dependent Renal Elimination

Due to the alkalinizing action of lactate (formation of bicarbonate), Lactated Ringer's Injection, USP may interfere with the elimination of drugs with pH dependent renal elimination.

- Renal clearance of acidic drugs such as salicylates and barbiturates may be increased. Avoid use of Lactated Ringer's Injection, USP in patients receiving acidic drugs.

- Renal clearance of alkaline drugs, such as sympathomimetics (e.g., ephedrine, pseudoephedrine) and dextroamphetamine (dexamphetamine) sulfate, may be decreased. Avoid use of Lactated Ringer's Injection, USP in patients receiving sympathommimetics and dextroamphetamine.

Lithium

Renal sodium and lithium clearance may be increased during administration of Lactated Ringer's Injection, USP and result in decreased lithium concentrations. Avoid use of Lactated Ringer's Injection, USP in patients receiving drugs with pH dependent renal elimination. If use cannot be avoided, monitor serum lithium concentrations during concomitant use.

Other Products that Cause Hyperkalemia

Administration of Lactated Ringer's Injection, USP to patients treated concurrently or recently with products that are associated with hyperkalemia increases the risk of severe and potentially fatal hyperkalemia, in particular in the presence of other risk factors for hyperkalemia.

Digoxin

Administration of calcium may increase the effects of digitalis and lead to serious or fatal cardiac arrhythmia. In patients treated with digoxin, consider reducing the volume, and/or rate of administration.

Avoid use of Lactated Ringer's Injection, USP to patients receiving such products (e.g., potassium sparing diuretics , ACE inhibitors, angiotensin II receptor antagonists, or the immunosuppressants tacrolimus and cyclosporine. If use cannot be avoided, monitor serum potassium concentrations.

Other Drugs that Increase the Risk of Hypercalcemia

Avoid Lactated Ringer's Injection, USP in patients treated with thiazide diuretics or vitamin D, as these can increase the risk of hypercalcemia.

Pregnancy
Teratogenic Effects

Animal reproduction studies have not been conducted with Lactated Ringer's Injection,

USP. It is also not known whether Lactated Ringer's Injection, USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Lactated Ringer's Injection, USP should be given to a pregnant woman only if clearly needed.

For Hypersensitivity Reactions During Pregnancy – see **WARNINGS**

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential have not been performed with Lactated Ringer's Injection, USP. Studies to evaluate the possible impairment of fertility have not been performed.

Labor and Delivery

Studies have not been conducted to evaluate the effects of Lactated Ringer's Injection, USP on labor and delivery. Caution should be exercised when administering this drug during labor and delivery.

Nursing Mothers

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 Lactated Ringer's Injection, USP is administered to a nursing mother.

ADVERSE REACTIONS

Post-Marketing Adverse Reactions

The following adverse reactions associated with the use of Lactated Ringer's Injection, USP were identified in clinical trials or postmarketing reports. Because postmarketing reactions were reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency, reliably, or to establish a causal relationship to drug exposure.

Hypersensitivity and infusion reactions: angioedema, chest pain, chest discomfort, decreased heart rate, tachycardia, blood pressure decreased, respiratory distress, bronchospasm, dyspnea, cough, urticaria, rash, pruritus, erythema, flushing, throat irritation, paresthesias, hypoesthesia oral, dysgeusia, nausea, anxiety, pyrexia, headache, laryngeal edema and sneezing, infection at the site of injection, extravasation and infusion site anesthesia (numbness).

Metabolism and Nutrition Disorders: hyperkalemia, hyponatremia, hypervolemia.

General Disorders and Administration Site Conditions: phlebitis, infusion site inflammation, infusion site swelling, infusion site rash, infusion site pruritus, infusion site erythema, infusion site pain, infusion site burning.

Nervous System Disorders: hyponatremic encephalopathy.

OVERDOSAGE

Excessive administration of Lactated Ringer's Injection, USP can cause:

- hyperkalemia and hypernatremia, especially in patients with severe renal impairment.
- Metabolic alkalosis with or without hypokalemia.
- loss of bicarbonate with an acidifying effect.
- hypercalcemia.
- fluid overload (which can lead to pulmonary and/or peripheral edema). See **WARNINGS** and **ADVERSE REACTIONS**.

When assessing an overdose, any additives in the solution must also be considered. The effects of an overdose may require immediate medical attention and treatment. Interventions include discontinuation of Lactated Ringer's Injection, USP administration, dose reduction, and other measures as indicated for the specific clinical constellation (e.g., monitoring of fluid balance, electrolyte concentrations and acid base balance).

DOSAGE AND ADMINISTRATION

Important Preparation and Administration Instructions

- Lactated Ringer's Injection, USP is intended for intravenous administration using sterile equipment.
- Prior to infusion, visually inspect the solution for particulate matter and discoloration. The solution should be clear, and there should be no precipitates. Do not administer unless solution is clear, and container is undamaged.
- To reduce the risk of air embolism, adhere to the following preparation instructions for Lactated Ringer's Injection, USP:
    - Use a non-vented infusion set or close the vent on a vented set.
    - Use a dedicated line without any connections (do not connect flexible containers in series).

- The use of pressure infusion is **not** recommended as a method to increase flow rates. However, if pressure infusion is required, ensure that any air within the bag is fully evacuated prior to initiation of infusion.

- If using a pumping device to administer Lactated Ringer's Injection, turn off the pump before the container is empty.

- Do not administer Lactated Ringer's Injection, USP simultaneously with citrate anticoagulated/preserved blood through the same administration set because of the likelihood of coagulation precipitated by the calcium content of Lactated Ringer's Injection, USP.

Dosing Information

The choice of product, dosage, volume, rate, and duration of administration is dependent upon the age, weight and clinical condition of the patient and concomitant therapy, and administration should be determined by a physician experienced in intravenous fluid therapy.

Introduction of Additives

Additives may be incompatible.

Evaluate all additions to the plastic container for compatibility and stability of the resulting preparation. Consult with a pharmacist, if available.

Ceftriaxone is known to be incompatible with Lactated Ringer's Injection, USP due to precipitate formation. Ceftriaxone must not be mixed with Lactated Ringer's Injection, USP.If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. After addition, if there is a discoloration and/or the appearance of precipitates, insoluble complexes or crystals, do not use. Do not store solutions containing additives. Use content immediately after opening the container. Discard any unused portion.

HOW SUPPLIED

Lactated Ringer's Injection, USP in VIAFLEX plastic container is available as follows:

Code	**Size (mL)**	**NDC**
2B2322	250	0338-0117-02
2B2323	500	0338-0117-03
2B2324	1000	0338-0117-04

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (25°C); brief exposure up to 40°C does not adversely affect the product.

DIRECTIONS FOR USE OF VIAFLEX PLASTIC CONTAINER

For Information on Risk of Air Embolism – see *PRECAUTIONS*

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. 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. 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 directions below.

Preparation for Administration

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

To Add Medication

To add medication before solution administration

1. Prepare medication site.
2. Using syringe with 19 to 22-gauge needle, puncture medication port and inject.
3. Mix solution and medication thoroughly. For high density medication, 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 19 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.

Baxter Healthcare Corporation

Deerfield, IL 60015 USA

07-19-00-6067

Rev. July 2024

Sodium Chloride Injection, USP
in VIAFLEX Plastic Container

DESCRIPTION

Sodium Chloride Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in single dose containers for intravenous administration. It contains no antimicrobial agents. The nominal pH is 5.0 (4.5 to 7.0). Composition, osmolarity, and ionic concentration are shown below:

0.45% Sodium Chloride Injection, USP contains 4.5 g/L Sodium Chloride, USP (NaCl) and is hypotonic with an osmolarity of 154 mOsmol/L (calc). It contains 77 mEq/L sodium and 77 mEq/L chloride.

0.9% Sodium Chloride Injection, USP contains 9 g/L Sodium Chloride, USP (NaCl) with an osmolarity of 308 mOsmol/L (calc). It contains 154 mEq/L sodium and 154 mEq/L chloride.

The VIAFLEX plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic). 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.

CLINICAL PHARMACOLOGY

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.

INDICATIONS AND USAGE

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

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

CONTRAINDICATIONS

None known.

WARNINGS

Hypersensitivity

Hypersensitivity and infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus have been reported with 0.9% Sodium Chloride Injection, USP and may occur with 0.45% Sodium Chloride Injection, USP.

Stop the infusion immediately if signs or symptoms of a hypersensitivity reaction develop, such as tachycardia, chest pain, dyspnea and flushing. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Electrolyte Imbalances

Fluid Overload

Depending on the volume and rate of infusion, and the patient's underlying clinical condition, the intravenous administration of Sodium Chloride Injection, USP can cause fluid disturbances such as overhydration/hypervolemia and congested states, including pulmonary congestion and edema.

Avoid 0.9% Sodium Chloride Injection, USP in patients with or at risk for fluid and/or solute overloading. If use cannot be avoided, monitor fluid balance, electrolyte concentrations, and acid base balance, as needed and especially during prolonged use.

Hyponatremia

Sodium Chloride Injection, USP may cause hyponatremia. Hyponatremia can lead to acute hyponatremic encephalopathy 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 of hospital-acquired hyponatremia is increased in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH) treated with high volume of Sodium Chloride Injection, USP.

The risk for hyponatremia is increased in pediatric patients, elderly patients, postoperative patients, those with psychogenic polydipsia, and in patients treated with

medications that increase the risk of hyponatremia (such as diuretics, certain antiepileptic and psychotropic medications). See **DRUG INTERACTIONS.**

Patients at increased risk for developing complications of hyponatremia such as hyponatremic encephalopathy, include pediatric patients, women (in particular pre-menopausal women), patients with hypoxemia, and patients with underlying central nervous system disease. Avoid Sodium Chloride Injection, USP in patients with or at risk for hyponatremia. If use cannot be avoided, monitor serum sodium concentrations.

Rapid correction of hyponatremia is potentially dangerous with risk of serious neurologic complications. Brain adaptations reducing risk of cerebral edema make the brain vulnerable to injury when chronic hyponatremia is too rapidly corrected, which is known as osmotic demyelination syndrome (ODS). To avoid complications, monitor serum sodium and chloride concentrations, fluid status, acid-base balance, and signs of neurologic complications.

Hypernatremia

Hypernatremia may occur with Sodium Chloride Injection, USP. Conditions that may increase the risk of hypernatremia, fluid overload and edema (central and peripheral), include 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); and pre-eclampsia.

Certain medications, such as corticosteroids or corticotropin, may also increase risk of sodium and fluid retention, see **DRUG INTERACTIONS**.

Avoid Sodium Chloride Injection, USP in patients with, or at risk for, hypernatremia. If use cannot be avoided, monitor serum sodium concentrations.

Rapid correction of hypernatremia is potentially dangerous with risk of serious neurologic complications. Excessively rapid correction of hypernatremia is also associated with a risk for serious neurologic complications such as osmotic demyelination syndrome (ODS) with risk of seizures and cerebral edema.

PRECAUTIONS

Patients with Severe Renal Impairment

Administration of Sodium Chloride Injection, USP in patients with or at risk of severe renal impairment, may result in hypernatremia and/or fluid overload (see **WARNINGS**). Avoid Sodium Chloride Injection, USP in patients with severe renal impairment or conditions that may cause sodium and/or potassium retention, fluid overload, or edema. If use cannot be avoided, monitor patients with severe renal impairment for development of these adverse reactions.

Drug Interactions

Other Products that Affect Fluid and/or Electrolyte Balance

Administration of Sodium Chloride Injection, USP to patients treated concomitantly with drugs associated with sodium and fluid retention may increase the risk of hypernatremia and volume overload. Avoid use of Sodium Chloride Injection, USP in patients receiving such products, such as corticosteroids or corticotropin. If use cannot be avoided, monitor serum electrolytes, fluid balance and acid-base balance.

Lithium

Renal sodium and lithium clearance may be decreased during administration of 0.45% Sodium Chloride Injection, USP. Monitor serum lithium concentrations during concomitant use.

Renal sodium and lithium clearance may be increased during administration of 0.9% Sodium Chloride Injection, USP. Monitor serum lithium concentrations during concomitant use.

Other Drugs that Increase the Risk of Hyponatremia

Administration of Sodium Chloride Injection, USP in patients treated concomitantly with medications associated with hyponatremia may increase the risk of developing hyponatremia.

Avoid use of Sodium Chloride Injection, USP in patients receiving products, such as diuretics, and certain antiepileptic and psychotropic medications. Drugs that increase the vasopressin effect reduce renal electrolyte free water excretion and may also increase the risk of hyponatremia following treatment with intravenous fluids. If use cannot be avoided, monitor serum sodium concentrations.

Pregnancy

There are no adequate and well controlled studies with Sodium Chloride Injection, USP in pregnant women and animal reproduction studies have not been conducted with this drug. Therefore, it is not known whether Sodium Chloride Injection, USP can cause fetal harm when administered to a pregnant woman. Sodium Chloride Injection, USP should be given to a during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

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

Pediatric Use

The use of Sodium Chloride Injection, USP in pediatric patients is based on clinical practice. (See **DOSAGE AND ADMINISTRATION**).

Closely monitor plasma electrolyte concentrations in pediatric patients who may have impaired ability to regulate fluids and electrolytes. In very low birth weight infants, excessive or rapid administration of Sodium Chloride Injection, USP may result in increased serum osmolality and risk of intracerebral hemorrhage.

Children (including neonates and older children) are at increased risk of developing hyponatremia as well as for developing hyponatremic encephalopathy.

Geriatric Use

Geriatric patients are at increased risk of developing electrolyte imbalances. Sodium Chloride Injection, USP 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. Therefore, 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. Consider monitoring renal function in elderly patients.

ADVERSE REACTIONS

Post-Marketing Adverse Reactions

The following adverse reactions have been identified during post approval use of Sodium Chloride Injection, USP. Because these reactions are reported voluntarily from a

population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions have been reported in the post-marketing experience during use of Sodium Chloride Injection, USP and include the following:

*General disorders and administration site condition*s: Infusion site erythema, injection site streaking, burning sensation, and infusion site urticaria

Hypersensitivity reactions: Hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus.

Metabolism and nutrition disorders: Hypernatremia*, hyponatremia, hyperchloremic metabolic acidosis.

Nervous System Disorders: Hyponatremic encephalopathy

* Adverse reaction of hyponatremia is only related to 0.9% Sodium Chloride Injection, USP

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

Excessive administration of:

- 0.45% Sodium Chloride Injection, USP can cause hyponatremia and hypernatremia. Both hypo- and hypernatremia can lead to CNS manifestations, including seizures, coma, cerebral edema and death.
- 0.9% Sodium Chloride Injection, USP can cause hypernatremia.
- Sodium Chloride Injection, USP can cause fluid overload (which can lead to pulmonary and/or peripheral edema). See **WARNINGS and ADVERSE REACTIONS**.

When assessing an overdose, any additives in the solution must also be considered. The effects of an overdose may require immediate medical attention and treatment.

Interventions include discontinuation of Sodium Chloride Injection, USP administration, dose reduction, and other measures as indicated for the specific clinical constellation (e.g., monitoring of fluid balance, electrolyte concentrations and acid base balance).

DOSAGE AND ADMINISTRATION

Important Preparation and Administration Instructions

- Sodium Chloride Injection, USP is intended for intravenous administration using sterile equipment.
- Prior to infusion, visually inspect the solution for particulate matter and discoloration. The solution should be clear, and there should be no precipitates. Do not administer unless solution is clear, and container is undamaged.
- To reduce the risk of air embolism, adhere to the following preparation instructions for Lactated Ringer's Injection, USP:
    - Use a non-vented infusion set or close the vent on a vented set.
    - Use a dedicated line without any connections (do not connect flexible containers in series).
    - The use of pressure infusion is **not** recommended as a method to increase flow rates. However, if pressure infusion is required, ensure that any air within the bag is fully evacuated prior to initiation of infusion.
    - If using a pumping device to administer Sodium Chloride Injection, turn off the pump before the container is empty.
    - Do not mix or administer 0.45% Sodium Chloride Injection, USP through the same administration set with whole blood or cellular blood components.

Dosing Information

The choice of product, dosage, volume, rate, and duration of administration is dependent upon the age, weight and clinical condition of the patient and concomitant therapy, and administration should be determined by a physician experienced in intravenous fluid therapy.

Introduction of Additives

Additives may be incompatible.

Evaluate all additions to the plastic container for compatibility and stability of the resulting preparation. Consult with a pharmacist, if available.

If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. After addition, if there is a discoloration and/or the appearance of precipitates, insoluble complexes or crystals, do not use. Do not store solutions containing additives. Discard any unused portion.

HOW SUPPLIED

The available sizes of each injection in VIAFLEX plastic containers are shown below:

Code	Size (mL)	NDC	Product Name
2B1313	500	0338-0043-03	0.45% Sodium Chloride Injection, USP
2B1314	1000	0338-0043-04	
2B1300	25 Quad Pack	0338-0049-10	0.9% Sodium Chloride Injection, USP
	50		
2B1306	Single pack	0338-0049-41	
2B1301	Quad pack	0338-0049-11	
2B1308	Multi pack	0338-0049-31	
	100		
2B1307	Single pack	0338-0049-48	
2B1302	Quad pack	0338-0049-18	
2B1309	Multi pack	0338-0049-38	
2B1322	250	0338-0049-02	
2B1323	500	0338-0049-03	
2B1324	1000	0338-0049-04	

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (25°C/77°F); brief exposure up to 40°C/104°F does not adversely affect the product.

DIRECTIONS FOR USE OF VIAFLEX PLASTIC CONTAINER

For Information on Risk of Air Embolism – see **DOSAGE AND ADMINISTRATION**.

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. 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. 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 directions below.

Preparation for Administration

1. Suspend container from eyelet support.
2. Remove 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 syringe with 19 to 22 gauge needle, puncture resealable medication port and inject.
3. Mix solution and medication thoroughly. For high density medication 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 19 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.

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Deerfield, IL 60015 USA
Printed in USA

Distributed in Canada by
Baxter Corporation
Mississauga, ON L5N 0C2

07-19-00-6066

Rev. July 2024