

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 ₃ H ₅ NaO ₃)	Potassium Chloride, USP, (KCl)	Calcium Chloride, USP (CaCl ₂ •2H ₂ O)			Sodium	Potassium	Calcium	Chloride	Lactate	
Lactated Ringer's Injection, USP	250	6	3.1	0.3	0.2	273	6.5 (6.0 to 7.5)	130	4	2.7	109	28	9
	500												
	1000												

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 alkalizing 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 alkalizing 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, administered ceftriaxone simultaneously 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.

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported with Lactated Ringer's Injection, USP (see **ADVERSE REACTIONS**). 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 **PRECAUTIONS, Drug Interactions and Pediatric Use**.

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 Lactated Ringer's 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.

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.

Patients 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 **PRECAUTIONS, 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 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.

Patients with Hepatic Impairment

In patients with severe hepatic impairment, lactate metabolism may be impaired and Lactated Ringer's Injection, USP may not produce alkalization. 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

Avoid administration of solutions containing lactate in patients with impaired glucose tolerance and diabetes mellitus, as it may result in hyperglycemia.

Monitoring of Serum Lactate Levels

Administration of Lactated Ringer's Injection, USP may result in an iatrogenic increase in serum lactate levels and interfere with interpretation of serum lactate levels in patients with severe metabolic acidosis including lactic acidosis.

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 liver and kidneys are still maturing during the first year of life, which also affects the biotransformation and renal excretion 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.

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.

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.

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 lithium. If use cannot be avoided, monitor serum lithium concentrations during concomitant use.

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 of Lactated Ringer's Injection, USP.

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.

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 may be increased. Renal clearance of alkaline drugs may be decreased.

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.
- fluid overload (which can lead to pulmonary and/or peripheral edema).
- metabolic alkalosis with or without hypokalemia.

- loss of bicarbonate with an acidifying effect.
- hypercalcemia.

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 Administration Instructions

- Lactated Ringer's Injection, USP is intended for intravenous administration using sterile equipment.
- Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container.
- Set the vent to the closed position on a vented intravenous administration set to prevent air embolism.
- Use a dedicated line without any connections to avoid air embolism.
- Do not pressurize intravenous solutions contained in flexible plastic containers to increase flow rates in order to avoid air embolism due to incomplete evacuation of residual air in the container.
- 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.
- 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 **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

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.

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