

PRESCRIBING INFORMATION

Potassium Chloride in Lactated Ringer's Injection, USP

Sodium chloride 6.0 g/L, Sodium lactate 3.1 g/L, Potassium chloride 1.8 g/L and Calcium chloride 0.2 g/L

Sterile solution

IV Fluid and Electrolyte Replenisher

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Potassium Chloride in Lactated Ringer's Injection, USP in Plastic Container

VIAFLEX Container

Description

Potassium Chloride in Lactated Ringer's Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in a single dose container for intravenous administration. Each litre of 20 mmols Potassium Chloride in Lactated Ringer's Injection, USP contains a total of 24 mmols of Potassium Chloride, USP. Each litre of 40 mmols Potassium Chloride in Lactated Ringer's Injection, USP contains a total of 44 mmols of Potassium Chloride, USP. It contains no antimicrobial agents. Composition, osmolarity, pH and ionic concentration are shown in Table 1. The VIAFLEX plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic). VIAFLEX on the container indicates the presence of a drug additive in a drug vehicle. The VIAFLEX plastic container system utilizes the same container as the VIAFLEX plastic container system. 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

Potassium Chloride in Lactated Ringer's Injection, USP has value as a source of water and electrolytes. It is capable of inducing diuresis on the clinical condition of the patient.

Potassium Chloride in 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.

Potassium is the chief cation of body cells (160 mEq/litre of intracellular water) and is concerned with the maintenance of body fluid composition and electrolyte balance. Potassium participates in carbohydrate utilization and protein synthesis, and is critical in the regulation of nerve conduction and muscle contraction, particularly in the heart. Chloride, the major extracellular anion, closely follows the metabolism of sodium. Changes in the acid-base balance of the body are reflected by changes in the chloride concentration. Normally, about 80 – 90% of the potassium intake is excreted in the urine, the remainder in the stool and to a small extent, in the perspiration. The kidney does not conserve potassium well so that during fasting, or in patients on a potassium free diet, potassium loss from the body continues, resulting in potassium depletion. A deficiency of either potassium or chloride will lead to a deficit of the other.

Indications and Usage

Potassium Chloride in Lactated Ringer's Injection, USP is indicated as a source of water and electrolytes.

Contraindications

Potassium Chloride in Lactated Ringer's Injection, USP is contraindicated in diseases where high potassium levels may be encountered, and in patients with hyperkalemia, renal failure and in conditions in which potassium retention is present. As for other calcium-containing infusion solutions, concomitant administration of ceftriaxone and Potassium Chloride in Lactated Ringer's Injection, USP is contraindicated in newborns (\leq 28 days of age), even if separate infusion lines are used (risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream).

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

Potassium Chloride in Lactated Ringer's Injection, USP is contraindicated in patients with a known hypersensitivity to sodium lactate.

Special Warnings and Precautions for Use

Potassium Chloride in Lactated Ringer's Injection, USP is not for use in patients with hyperkalemia and is not for the treatment of lactic acidosis or severe metabolic acidosis.

Warnings and Precautions

Administration of Citrate Anticoagulated/Preserved Blood

Due to the risk of coagulation precipitated by its calcium content, Potassium Chloride in Lactated Ringer's Injection, USP must not be added to or administered simultaneously through the same tubing with citrate anticoagulated/preserved blood.

Hypersensitivity Reactions

The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Risk of Hyponatremia

Monitoring of serum sodium is particularly important for hypotonic fluids. Potassium Chloride in Lactated Ringer's Injection, USP has an osmolality of 312 mOsmol/L.

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

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

Risk of Fluid and/or Solute Overload and Electrolyte Disturbances

Depending on the volume and rate of infusion, the intravenous administration of Potassium Chloride in Lactated Ringer's Injection, USP can cause clinically relevant electrolyte disturbances, acid-base imbalance, fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration and, for example, congested states, including pulmonary congestion and edema. The risk of dilutional states is inversely proportional to the electrolyte concentrations of the injection. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of Potassium Chloride in Lactated Ringer's Injection, USP.

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

Use in Patients with or at Risk for Hyperkalemia

Potassium Chloride in Lactated Ringer's Injection, USP should be used with great caution, if at all, in patients with congestive heart failure, potassium retention, hyperkalemia or conditions predisposing to hyperkalemia (such as adrenocortical insufficiency, acute dehydration, or extensive tissue injury or burns) and in patients with cardiac disease.

Use in patients with or at Risk for Alkalosis

Potassium Chloride in Lactated Ringer's Injection, USP should be administered with particular caution, if at all, to patients with alkalosis or at risk for alkalosis. Because lactate is metabolized to bicarbonate, administration may result in, or worsen, metabolic alkalosis.

Use in Patients with Hypervolemia or Overhydration, or Conditions that Cause Sodium Retention and Edema

Potassium Chloride in Lactated Ringer's Injection, USP should be administered with particular caution, if at all, to hypervolemic or overhydrated patients and patients with conditions that may cause sodium retention, fluid overload and edema, such as patients with primary hyperaldosteronism, secondary hyperaldosteronism (associated with e.g., hypertension, congestive heart failure, renal artery stenosis, or nephrosclerosis), or preeclampsia.

Use in Patients with Severe Renal Impairment

Potassium Chloride in Lactated Ringer's Injection, USP should be administered with particular caution, if at all, to patients with severe renal insufficiency. In such patients, administration of Potassium Chloride in Lactated Ringer's Injection, USP may cause sodium and/or potassium retention and life-threatening hyperkalemia.

General Precautions:

The use of potassium salts in patients with cardiac disease, renal disease, adrenal insufficiency or any condition which impairs potassium excretion, requires careful attention. Acid base balance should be monitored, including serum electrolytes, ECG and clinical status.

Potassium should be used with caution in diseases associated with heart block since serum potassium may increase the degree of block.

Potassium therapy should be guided by serial electrocardiograms, especially in patients receiving digitalis. Serum potassium levels are not necessarily indicative of tissue potassium levels.

Potassium Chloride in Lactated Ringer's Injection, USP should be used with great care in patients with metabolic or respiratory alkalosis. Excess administration of Potassium Chloride in Lactated Ringer's Injection, USP may result in metabolic alkalosis.

Risk of Air Embolism

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

Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism

if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers. If the administration is controlled by a pumping device, care must be taken to discontinue pumping action before the container runs dry or air embolism may result.

Use in Patients with or at Risk for Increased Lactate Levels or with Impaired Lactate Utilization

Potassium Chloride in Lactated Ringer's Injection, USP should be administered with particular caution, if at all, to patients with conditions associated with increased lactate levels or an impaired lactate utilization, such as severe hepatic insufficiency.

Hyperlactatemia can develop in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. In addition, Potassium Chloride in Lactated Ringer's Injection, USP may not produce its alkalinizing action in patients with severe hepatic insufficiency, since lactate metabolism may be impaired.

Lactate-containing solutions should be administered with particular caution to neonates and infants less than 6 months of age.

Use in Patients with or at Risk for Hypercalcemia

Solutions containing calcium salts should be used with caution in patients with:

- hypercalcemia or conditions predisposing to hypercalcemia, such as patients with severe renal impairment and granulomatous diseases associated with increased calcitriol synthesis such as sarcoidosis.
- calcium renal calculi or a history of such calculi.

Use in patients with Type 2 Diabetes

Lactate is a substrate for gluconeogenesis. This should be taken into account when Potassium Chloride in Lactated Ringer's Injection, USP is used in patients with type 2 diabetes.

Use in Pediatric Patients

Safety and Effectiveness of Potassium Chloride in Lactated Ringer's Injection, USP in children 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.

Lactate-containing solutions should be administered with particular caution to neonates and infants less than 6 months of age.

Use in Geriatric Patients

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

Interactions With Other Medicinal Products and Other Forms of Interaction

- Ceftriaxone: See Contraindications.
- Caution is advised when administering Potassium Chloride in Lactated Ringer's 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 IV 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 Potassium Chloride in Lactated Ringer's Injection, USP to patients treated with drugs that may increase the risk of hyponatremia, such as diuretics and antiepileptics (e.g., oxcarbazepine).
- Caution is advised when administering Potassium Chloride in Lactated Ringer's Injection, USP to patients treated with drugs that may increase the risk of sodium and fluid retention, such as corticosteroids and carbenoxolone.
- Extreme caution is advised with the simultaneous administration of Potassium Chloride in Lactated Ringer's Injection, USP to patients receiving drugs that may increase the risk of sodium and fluid retention, such as corticosteroids, corticotrophin and carbenoxolone. Caution is advised when administering Potassium Chloride in Lactated Ringer's Injection, USP to patients treated with drugs for which renal elimination is pH dependent. Due to the alkalinizing action of lactate (formation of bicarbonate), Potassium Chloride in Lactated Ringer's Injection, USP may interfere with the elimination of such drugs.
 - Renal clearance of acidic drugs such as salicylates, barbiturates, and lithium may be increased.
 - Renal clearance of alkaline drugs, such as sympathomimetics (e.g., ephedrine, pseudoephedrine), dextroamphetamine (dexamphetamine) sulfate, and fenfluramine (phenfluramine) hydrochloride may be decreased.

- Because of its potassium content, Potassium Chloride in Lactated Ringer's Injection, USP should be administered with caution in patients treated with agents or products that can cause hyperkalemia or increase the risk of hyperkalemia, such as potassium-sparing diuretics (e.g. amiloride, spironolactone or triamterene), with angiotensin converting enzyme (ACE) inhibitor (e.g. enalapril, lisinopril), angiotensin II receptor antagonists, or the immunosuppressants tacrolimus and cyclosporine. Administration of potassium in patients treated with such medications can produce severe and potentially fatal hyperkalemia, particularly in patients with severe renal insufficiency.
- Administration of calcium may increase the effects of digitalis and lead to serious or fatal cardiac arrhythmia. Therefore, larger volumes or faster infusion rates should be used with caution in patients treated with digitalis glycosides.
- Caution is advised when administering Potassium Chloride in Lactated Ringer's Injection, USP to patients treated with thiazide diuretics or vitamin D, as these can increase the risk of hypercalcemia.

Pregnancy and Lactation

There are no adequate data from the use of Potassium Chloride in Lactated Ringer's Injection, USP in pregnant or lactating women. The potential risks and benefits for each specific patient should be carefully considered before using Potassium Chloride in Lactated Ringer's Injection, USP in pregnant or lactating women.

Pregnancy Category C. Animal reproduction studies have not been conducted with Potassium Chloride in Lactated Ringer's Injection, USP. It is also not known whether Potassium Chloride in Lactated Ringer's Injection, USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Potassium Chloride in Lactated Ringer's Injection, USP should be given to pregnant woman only if clearly needed.

Adverse Reactions

Adverse Reactions from Clinical Trials

There are no data available on adverse reactions from Baxter-sponsored clinical trials conducted with Potassium Chloride in Lactated Ringer's Injection, USP.

Post-marketing Adverse Reactions

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

IMMUNE SYSTEM DISORDERS: Hypersensitivity/infusion reactions, including Anaphylactic/Anaphylactoid reactions, and the following manifestations: 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

METABOLISM AND NUTRITION DISORDERS: Hyperkalemia

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site reactions, including Phlebitis, Infusion site inflammation, Infusion site swelling, Infusion site rash, Infusion site pruritus, Infusion site erythema, Infusion site pain, Infusion site burning

Reactions reported with the use of potassium-containing solutions include nausea, vomiting, abdominal pain and diarrhea. Severe adverse effects reported with potassium preparations have been hyperkalemia and arrhythmias (see overdose).

Class Reactions

Other adverse reactions reported with similar products are: Hyponatremia, Hyponatremic encephalopathy, Infusion site anesthesia (numbness) (reported with Lactated Ringer's and 5% Dextrose Injection)

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.

Overdose Symptoms and Treatment

An excessive volume or too high a rate of administration of Potassium Chloride in Lactated Ringer's Injection, USP may lead to fluid and sodium overload with a risk of edema (peripheral and/or pulmonary), particularly when renal sodium excretion is impaired.

- Excessive administration of lactate may lead to metabolic alkalosis. Metabolic alkalosis may be accompanied by hypokalemia.
- Excessive administration of potassium may lead to the development of hyperkalemia, especially in patients with severe renal impairment.
- Excessive administration of calcium salts may lead to hypercalcemia.
- 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.

The signs and symptoms of potassium intoxication include parathesis of the extremities, areflexia, muscular or respiratory paralysis, mental confusion, weakness, hypotension, cardiac arrhythmias, heart block, electrocardiographic abnormalities and cardiac arrest. Potassium deficits result in disruption of neuromuscular function, and intestinal ileus and dilatation.

However, hyperkalemia is usually asymptomatic and may be manifested only by an increased serum potassium concentration and characteristic ECG changes (peaking of T-waves, loss of P-waves, depression of S-T segment and

prolongation of the QT interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest. Should any of these manifestations occur, discontinue administration immediately. In the event of fluid overload during parenteral therapy, reevaluate the patient's condition and institute appropriate corrective treatment. In the event of overdose with potassium-containing solutions, discontinue the infusion immediately and institute corrective therapy to reduce serum potassium levels.

Treatment of hyperkalemia includes the following:

1. Dextrose Injection, USP 10% or 25% containing 10 units of crystalline insulin per 20 grams of dextrose administered intravenously, 300 to 500 mL per hour.
2. Absorption and exchange of potassium using sodium or ammonium cycle cation exchange resin, orally and as a retention enema.
3. Hemodialysis and peritoneal dialysis.

The use of potassium-containing foods or medications must be eliminated. In cases of patients receiving digoxin, too rapid lowering of plasma potassium concentration can cause digoxin toxicity.

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 as well as laboratory response to treatment.

Potassium Chloride in Lactated Ringer's Injection, USP is intended for intravenous administration using sterile and nonpyrogenic equipment.

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. Use of a final filter is recommended during administration of all parenteral solutions, where possible.

When making additions to Potassium Chloride in Lactated Ringer's Injection, USP, aseptic technique must be used. Mix the solution thoroughly when additives have been introduced. Do not store solutions containing additives (see Incompatibilities).

Incompatibilities

Ceftriaxone must not be mixed with calcium-containing solutions including Potassium Chloride in Lactated Ringer's Injection, USP. See also Contraindications.

Additives may be incompatible. Complete information is not available. Those additives known to be incompatible must not be used. Consult with pharmacist, if available. If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique.

As with all parenteral solutions, compatibility of the additives with the solution must be assessed before addition, by checking for a possible color change and/or the appearance of precipitates, insoluble complexes or crystals. Before adding a substance or medication, verify that it is soluble and/or stable in water and that the pH range of Potassium Chloride in Lactated Ringer's Injection, USP is appropriate.

The instructions for use of the medication to be added and other relevant literature must be consulted. Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

How Supplied

Potassium Chloride in Lactated Ringer's Injection, USP in VIAFLEX plastic containers is available as shown in Table 1. Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Store at 15°C to 25°C.

Directions for use of VIAFLEX Plastic Container

Warning: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed. **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. After opening the container, the contents should be used immediately and should not be stored for a subsequent infusion. Do not reconnect any partially used containers.

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 plastic protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying set.

To Add Medication:

Warning: Additives may be incompatible.

To add medication before solution administration:

1. Prepare medication site.
2. Using syringe with 19 to 22 gauge needle, puncture re-sealable 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 re-sealable 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.

* Normal physiologic osmolarity range is approximately 280 to 310 mOsmol/L. Administration of substantially hypertonic solutions (> 600 mOsmol/L) may cause vein damage.

Table 1

Potassium chloride in Lactated Ringers' Inj. USP	mL	Composition (g/L)				mOsmol/L	pH	Ionic Concentration (mmol/L)					Caloric Content
		Sodium Chloride USP	Sodium Lactate	Potassium Chloride USP	Calcium chloride USP			Sodium	Potassium	Calcium	Chloride	Lactate	
20 mmols	1000	6.0	3.1	1.8	0.2	2	6.5	130	24	1.4	129	28	9
							6.0 – 7.5						
40 mmols	1000	6.0	3.1	3.3	0.2	353	6.5	130	44	1.4	149	28	9
							6.0 – 7.5						

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