PRESCRIBING INFORMATION

Lactated Ringer’s and 5% Dextrose Injection, USP
In Viaflex Plastic Container

Parenteral Replenisher

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Lactated Ringer’s and 5% Dextrose Injection, USP in VIAFLEX Plastic Container

SUMMARY PRODUCT INFORMATION

Lactated Ringer’s and 5% Dextrose Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment and caloric supply in a single dose container for intravenous administration. It contains no antimicrobial agents. The composition, osmolarity and approx. pH are shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Composition (g/L)</th>
<th>Ionic Concentration (mmol/L)</th>
<th>Caloric Content (kcal/L)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Dextrose Hydr. USP</td>
<td>Sodium Chloride, USP</td>
<td>Sodium Lactate</td>
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<tr>
<td>Lactated Ringer’s and 5% Dextrose Injection, USP</td>
<td>500</td>
<td>50</td>
<td>6.0</td>
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<td></td>
<td>1000</td>
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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.

ACTIONS

Lactated Ringer’s and 5% Dextrose Injection, USP has value as a source of water, electrolytes and calories. It is capable of inducing diuresis depending on the clinical conditions of the patient.

Lactated Ringer’s and 5% Dextrose 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 CLINICAL USE

Lactated Ringer’s and 5% Dextrose Injection, USP is indicated as a source of water, electrolytes and calories, or as an alkalinizing agent.

CONTRAINDICATIONS

Lactated Ringer’s and 5% Dextrose Injection, USP is contraindicated in the following conditions:

- Patients with hypersensitive to any ingredient in the formulation or component of the container. For more information, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section.

- Concomitant administration of ceftriaxone in newborns (≤ 28 days of age), even if separate infusion lines are used due to risk of fatal ceftriaxone-calcium salt precipitation in the neonate’s bloodstream.

- Simultaneous administration of ceftriaxone through the same infusion line (e.g., via Y-port/Y-site) in patients older than 28 days of age. If the same infusion line is used for sequential administration, the line must be thoroughly flushed between infusions with a compatible fluid.
WARNINGS AND PRECAUTIONS

General
Although Lactated Ringer’s and 5% Dextrose Injection, USP has a potassium concentration similar to the concentration in plasma, it is insufficient to produce a useful effect in case of severe potassium deficiency; therefore, it should not be used for this purpose.

Lactated Ringer’s and 5% Dextrose Injection, USP is not for use for the treatment of lactic acidosis or severe metabolic acidosis.

Administration of Citrate Anticoagulated/Preserved Blood
Due to the risk of coagulation precipitated by its calcium content, Lactated Ringer’s and 5% Dextrose Injection, USP must not be added to or administered simultaneously through the same administration set as 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. Solutions containing dextrose should be used with caution, if at all, in patients with known allergy to corn or corn products.

Risk of Fluid and/or Solute Overload and Electrolyte Disturbances
Depending on the volume and rate of infusion, intravenous administration of Lactated Ringer’s and 5% Dextrose Injection, USP can cause clinically relevant electrolyte disturbances and acid-base imbalance, fluid and/or solute overload 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 Lactated Ringer’s and 5% Dextrose Injection, USP. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of Lactated Ringer’s and 5% Dextrose Injection, USP.

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

Use in Patients with or at Risk for Hyperkalemia
Lactated Ringer’s and 5% Dextrose Injection, USP should be administered with particular caution, if at all, to patients with hyperkalemia or conditions predisposing to hyperkalemia (such as severe renal impairment or 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
Lactated Ringer’s and 5% Dextrose 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
Lactated Ringer’s and 5% Dextrose Injection, USP should be administered with particular caution, if at all, to hypervolemic or overhydrated patients.

Lactated Ringer’s and 5% Dextrose Injection, USP should be administered with particular caution, if at all, to 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 nephroclerosis), or preeclampsia.

Use in Patients with Severe Renal Impairment
Lactated Ringer’s and 5% Dextrose Injection, USP should be administered with particular caution, if at all, to patients with severe renal impairment. In such patients, administration of Lactated Ringer’s and 5% Dextrose Injection, USP may result in sodium and/or potassium retention.
**Risk of Air Embolism**
Do not use plastic containers in series connections. Such use could result in air embolism due to residual air (approximately 15 mL) being drawn from the primary container before administration of the fluid from the secondary container is completed.

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.

**Use in Patients with or at Risk for Hyperglycemia**
Solutions containing dextrose should be used with caution in patients with impaired glucose tolerance or diabetes mellitus. Lactate is a substrate for gluconeogenesis. This should be taken into account when Lactated Ringer's and 5% Dextrose Injection, USP is used in patients with type 2 diabetes.

Because Lactated Ringer's and 5% Dextrose Injection, USP contains dextrose and lactate (which is metabolized to glucose), administration that exceeds the metabolic capacity for glucose may lead to hyperglycemia.

Hyperglycemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after acute ischemic strokes. Caution is recommended in using dextrose-containing solutions in such patients.

Early hyperglycemia has been associated with poor outcomes in patients with severe traumatic brain injury. Dextrose-containing solutions should, therefore, be used with caution in patients with head injury, in particular during the first 24 hours following the trauma.

Newborns – especially those born premature and with low birth weight - are at increased risk of developing hypo- or hyperglycemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycemic control in order to avoid potential long term adverse effects. (see SPECIAL POPULATIONS - PEDIATRICS)

If hyperglycemia occurs, the rate of dextrose administration should be reduced and/or insulin administered, or the insulin dose adjusted.

**Use in Patients with or at Risk for Increased Lactate Levels or with Impaired Lactate Utilization**
Lactated Ringer's and 5% Dextrose Injection, USP should be administered with particular caution, if at all, to patients with conditions associated with increased lactate levels or impaired lactate utilization, such as severe hepatic insufficiency.

Hyperlactatemia (i.e., high lactate levels) can develop in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. In addition Lactated Ringer's and 5% Dextrose 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.

**Osmolarity**
The addition of 5% dextrose to the electrolyte solution renders Lactated Ringer's and 5% Dextrose Injection, USP hypertonic, having an osmolarity of 524 mOsm/L. The normal physiologic serum osmolarity range is approximately 280 to 310 mOsmol/L. Administration of substantially hypertonic solutions may cause venous irritation, including phlebitis. Hyperosmolar solutions should be administered with caution, if at all, to patients with hyperosmolar states.

**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.
Special Populations

Pediatrics
Safety and effectiveness of Lactated Ringer's and 5% Dextrose 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.

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy and should be determined by the consulting physician experienced in pediatric intravenous fluid therapy.

Newborns – especially those born premature and with low birth weight - are at increased risk of developing hypo- or hyperglycemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycemic control in order to avoid potential long term adverse effects. Hypoglycemia in the newborn can cause prolonged seizures, coma and brain damage. Hyperglycemia has been associated with intraventricular hemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stay, and death.

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

Geriatrics
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.

Pregnant or Nursing Women
Animal reproduction studies have not been conducted with Lactated Ringer's and 5% Dextrose Injection, USP. It is also not known whether Lactated Ringer's and 5% Dextrose Injection, USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Lactated Ringer's and 5% Dextrose 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 Lactated Ringer's and 5% Dextrose 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, Bronchospasm, Dyspnea, Cough, Urticaria, Rash, Pruritus, Erythema, Nausea, Pyrexia

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site reactions, including Infusion site pruritus, Infusion site erythema, Infusion site anesthesia (numbness)

Other Reactions
Other adverse reactions reported with Lactated Ringer's Injection and Sodium Lactate Injection are:

- Other manifestations of hypersensitivity/infusion reactions: Decreased heart rate, Tachycardia, Blood pressure decreased, Respiratory distress, Flushing, Throat irritation, Paresthesias, Hypoesthesia oral, Dysgeusia, Anxiety, Headache

- Hyperkalemia
- Other infusion site reactions: Phlebitis, Infusion site inflammation, Infusion site swelling, Infusion site rash, Infusion site pain, Infusion site burning

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

**DRUG INTERACTIONS**

Co-administration of this product and ceftriaxone increase the risk of ceftriaxone-calcium salt precipitation in the body which may result in serious clinical outcomes (see CONTRAINDICATIONS).

Caution must be exercised in the administration of Lactated Ringer's and 5% Dextrose Injection, USP to patients treated with drugs that may increase the risk of sodium and fluid retention, such as corticosteroids, corticotrophin and carbenoxolone.

Caution is advised when administering Lactated Ringer's and 5% Dextrose Injection, USP to patients treated with drugs for which renal elimination is pH dependent. Due to the alkalinizing action of lactate (formation of bicarbonate), Lactated Ringer's and 5% Dextrose 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, Lactated Ringer's and 5% Dextrose 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 (amiloride, spironolactone, triamterene), with ACE inhibitors, 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 a faster infusion rates should be used with caution in patients treated with digitalis glycosides.
- Caution is advised when administering Lactated Ringer's and 5% Dextrose Injection, USP to patients treated with thiazide diuretics or vitamin D, as these can increase the risk of hypercalcemia.

**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.

Lactated Ringer's and 5% Dextrose Injection, USP is intended for intravenous administration using sterile and nonpyrogenic equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours. The infusion rate should not exceed the patient's ability to utilize glucose in order to avoid hyperglycemia. The infusion rate of intravenous solutions containing dextrose should be selected with caution in children (See SPECIAL POPULATIONS – PEDIATRICS).

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.

When making additions to Lactated Ringer's and 5% Dextrose Injection, USP, aseptic technique must be used. Mix the solution thoroughly when additives have been introduced. Do not store solutions containing additives.

Ceftriaxone must not be mixed with calcium-containing solutions including Lactated Ringer's and 5% Dextrose Injection, USP. See also DRUG INTERACTIONS.
Additives may be incompatible with Lactated Ringer's and 5% Dextrose Injection, USP. Complete information is not available. Those additives known to be incompatible should not be used. 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. Before adding a substance or medication, verify that it is soluble and/or stable in water and that the pH range of Lactated Ringer's and 5% Dextrose Injection, USP is appropriate. After addition, check for a possible color change and/or the appearance of precipitates, particulate matter or crystals.

Thorough and careful mixing of any additive is mandatory. Do not store solutions containing additives. The instructions for use of the medication to be added and other relevant literature must be consulted.

OVERDOSAGE

An excessive volume or too high a rate of administration of Lactated Ringer's and 5% Dextrose 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.

Excessive administration of a dextrose-containing solution may lead to hyperglycemia, hyperosmolarity, osmotic diuresis, and dehydration.

When assessing overdose, any additives in the solution must also be considered.

Interventions include discontinuation of Dextrose Injection, USP administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

Clinically significant overdose of Dextrose Injection, USP may, therefore, constitute a medical emergency.

Dosage Form, Composition and Packaging

How Supplied
See Summary Product Information, Table 1 which shows the ionic composition, osmolarity, approx. pH and volume of Lactated Ringers and 5% Dextrose Injection, USP. The presence of the catalogue code number indicates that the injection is available in that size.

Directions for use of VIAFLEX Plastic Container:
WARNING: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air (approximately 15 mL) being drawn from the primary container before administration of the fluid from the secondary container is completed. Do not remove unit from overwrap until ready to use. 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.

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

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

To Add Medication:

1. Prepare medication site.
2. Using a syringe and a 20 – 22 gauge needle, puncture resealable rubber plug at target area and inject. Multiple additions may be made in this manner.
3. Mix solution and medication thoroughly. For high density medications such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

Storage

Store between 15ºC and 25ºC.