1.3 Summary of product characteristics, labellin and package leathlet.

1.3.1 Summary of product characteristics (SPC)

1-Name of the Medicinal Product :

1.1 Product Name
Lactated Ringer's Injection

1.2 Strength
500ml

1.3 Pharmaceutical Dosage Form
Liquid injection

2-Quality and Quantitative Composition :

2.1 Qualitative Declaration

Active ingredient: Sodium Lactate: 500ml:1.55g
Sodium Chloride: 500ml:3.00g
Potassium Chloride: 500ml:0.15g
Calcium Chloride: 500ml:0.10g

Inactive ingredient: Water of Injection：q.s. to 500ml

2.2 Quantitative Declaration

Each bottle of 500ml solution for injection contains:
Sodium Lactate: 500ml:1.55g
Sodium Chloride: 500ml:3.00g
Potassium Chloride: 500ml:0.15g
Calcium Chloride: 500ml:0.10g

3-Pharmaceutical Form : Clear, colorless liquid.

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4-Clinical Particulars

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

4.2 Posology and method of administration

- Recommended doses :

As directed by a physician. Dosage is dependent upon the age, weight and clinical condition of the patient as well as laboratory determinations. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Use of a final filter is recommended during administration of all parenteral solutions, where possible. Do not administer unless solution is clear and seal is intact. All injections in glass containers are intended for intravenous administration using sterile equipment. Additives may be incompatible. Complete information is not available. Those additives known to be incompatible should 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. Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

4.3 Contraindications

Solutions containing lactate are NOT FOR USE IN THE TREATMENT OF LACTIC ACIDOSIS.

4.4 Special warning and precautions for use

Solutions containing calcium ions should not be administered simultaneously through the same administration set as blood because of the likelihood of coagulation.

Solutions which contain potassium should be used with great care, if at all, in patients with hyperkalemia, severe renal failure and in conditions in which potassium retention is present.

Solutions containing sodium ions should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency and in clinical states in which there exists edema with sodium retention.

In patients with diminished renal function, administration of solutions containing sodium or potassium ions may result in sodium or potassium retention.

Solutions containing lactate ions should be used with great care in patients with metabolic or respiratory alkalosis. The administration of lactate ions should be done with great care where there is an increased level or an impaired utilization of lactate ions, as in severe hepatic insufficiency.

The intravenous administration of this solution can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary edema. The risk of dilutional states is inversely proportional to the electrolyte concentrations of administered parenteral solutions.

The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of such solutions.

PRECAUTIONS

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 warrants such evaluation.

Caution must be exercised in the administration of parenteral fluids, especially those containing sodium ions, to patients receiving corticosteroids or corticotropin.

Potassium containing solutions should be used with caution in the presence of cardiac disease, particularly in digitalized patients or in the presence of renal disease.

Solutions containing lactate ions should be used with caution as excess administration may result in metabolic alkalosis.

Do not administer unless solution is clear and container is undamaged. Discard unused portion.

4.5 Interaction with other medicinal products and other forms of Interactions

Additives may be incompatible. Consult additive manufacturer. When introducing additives, use aseptic technique, mix thoroughly and do not store.

The presence of calcium limits their compatibility with certain drugs that form precipitates of calcium salts, and also prohibits their simultaneous infusion through the same administration set as blood because of the likelihood of coagulation.

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

4.4 Pregnancy and lactation

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.

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 woman.

4.7 Effects on ability to drive and use machine

None

4.8 Undesirable effects

Allergic reactions or anaphylactoid symptoms such as localized or generalized urticaria and pruritis; periorbital, facial, and/or laryngeal edema; coughing, sneezing, and/or difficulty with breathing have been reported during administration of this

injection. The reporting frequency of these signs and symptoms is higher in women during pregnancy. Reactions which may occur because of the solution or the technique of administration include febrile response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of infection, extravasation, and hypervolemia.

4.9 Overdose and special antidotes .
Overdosage may cause ion unbalance in body.

5-Pharmacological Properties :

5.1 Pharmacodynamic Properties

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.

5.2 Pharmacokinetic Properties
Lactated Ringer's Solution has value as a source of water and electrolytes. It is capable of inducing diuresis depending on the clinical condition of the patient. It produces a metabolic alkalinizing effect. Lactate ions are metabolized ultimately to carbon dioxide and water, which requires the consumption of hydrogen cations.

5.3 Preclinical safety Data
When administered intravenously, Lactated Ringer's Injection provides a source of water and electrolytes. The electrolyte content resembles that of the principal ionic constituents of normal plasma and the solution therefore is suitable for parenteral replacement of extracellular losses of fluid and electrolytes.
Calcium chloride in water dissociates to provide calcium (Ca^{++}) and chloride (Cl^{-}) ions. They are normal constituents of the body fluids and are dependent on various physiologic mechanisms for maintenance of balance between intake and output. Approximately 80% of body calcium is excreted in the feces as insoluble salts; urinary excretion accounts for the remaining 20%.
Potassium chloride in water dissociates to provide potassium (K^{+}) and chloride (Cl^{-}) ions. Potassium is found in low concentration in plasma and extracellular fluids (3.5 to 5.0 mEq/liter in a healthy adult). It is the chief cation of body cells (160 mEq/liter of intracellular water). Potassium plays an important role in electrolyte balance. Normally about 80 to 90% of the potassium intake is excreted in the urine; the remainder in the stools 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.
Sodium chloride in water dissociates to provide sodium (Na^+) and chloride (Cl^-) ions. Sodium (Na^+) is the principal cation of the extracellular fluid and plays a large part in the therapy of fluid and electrolyte disturbances. Chloride (Cl^-) has an integral role in buffering action when oxygen and carbon dioxide exchange occurs in the red blood cells. The distribution and excretion of sodium (Na+) and chloride (Cl^-) are largely under the control of the kidney which maintains a balance between intake and output.
Sodium lactate provides sodium (Na^+) and lactate ($C_3H_5O_3^-$) ions. The lactate anion is in equilibrium with pyruvate and has an alkalizing effect resulting from simultaneous removal by the liver of lactate and hydrogen ions. In the liver, lactate is metabolized to glycogen which is ultimately converted to carbon dioxide and water by oxidative metabolism. The sodium (Na^+) ion combines with bicarbonate ion produced from carbon dioxide of the body and thus retains bicarbonate to combat metabolic acidosis (bicarbonate deficiency). The normal plasma level of lactate ranges from 0.9 to 1.9 mEq/liter.
Water is an essential constituent of all body tissues and accounts for approximately 70% of total body weight. Average normal adult daily requirement ranges from two tothree liters (1.0 to 1.5 liters each for insensible water loss by perspiration and urine production).
Water balance is maintained by various regulatory mechanisms. Water distribution depends primarily on the concentration of electrolytes in the body compartments and sodium (Na^+) plays a major role in maintaining physiologic equilibrium.

6-Pharmaceutical Particulars :

6.1 List of excipients
Water for injection, HCl/NaOH
6.2 Incompatibilities
Some additives may be incompatible. Consult with pharmacist. When introducing additives, use aseptic techniques. Mix thoroughly. Do not store.
6.3 Shelf life
3 years

6.4 Special precautions for storage
Keep sealed.

6.5 Nature and contents of container
PP bottle