Summary of Product Characteristic

1. Name of the Medicinal Product

1.1 Product Name

Lactated Ringer's Injection USP

1.2 Strength

Each 100 mL contains:-

Sodium chloride	600 mg	Potassium chloride	30 mg
Sodium lactate	310 mg	Calcium chloride, dihydrate	20 mg

1.3 Pharmaceutical Dosage Form

Solution for infusion

2. Quality and Quantitative Composition

2.1 Qualitative Declaration

Sodium chloride	Potassium chloride
Sodium lactate	Calcium chloride, dihydrate

2.2 Quantitative Declaration:

Each 100 mL contains:-

Sodium chloride	600 mg	Potassium chloride	30 mg
Sodium lactate	310 mg	Calcium chloride, dihydrate	20 mg

3. Pharmaceutical Form

Clear, colorless sterile solution for infusion

4. Clinical Particulars

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

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.

The recommended dosage is 20 mL/kg of Lactated Ringer's Injection USP.

Alternatively, daily maintenance (not including pathologic ongoing loss) fluid requirements may be roughly estimated as follows:

Less than 10 kg	= 100 mL/kg/d
10-20 kg	= 1000 + 50 mL/kg/d for each kg over 10 kg
Greater than 20 kg	= 1500 + 20 mL/kg/d for each kg over 20 kg

Administration rate:

The infusion rate is usually 40 mL/kg/ over 1-2 hours.

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.

Mode of Administration

- 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.

4.3 Contraindication

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).

4.4 Special warning and precautions for use

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.

4.5 Interaction with other medicinal products and other forms of 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.

4.6 Pregnancy and lactation

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.

4.7 Effects on ability to drive and use machine

No additional data of relevance.

4.8 Undesirable effects

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.

4.9 Overdose

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).

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 conditions 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

No additional data of relevance.

5.3 Preclinical Safety data

No additional data of relevance.

6. Pharmaceutical Particulars

6.1 List of excipients

Water for injection

6.2 Incompatibilities

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.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Storage below 30°C

6.5 Nature and contents of container

Plastic containers (Polypropylene) size 100 mL with or without paper box of 1, 10, 12, 20, 24, 36, 50, 60, 80, 100, 120, 150 and 200 bottles.

Plastic containers (Polypropylene) size 250, 500 and 1000 mL with or without paper box of 1, 10, 12, 20, 24, 36, 50 and 60 bottles.

6.6 Special precautions for disposal and other handling

After opening the container, the contents should be used immediately and should not be stored for a subsequent.

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

7. Marketing Authorization Holder

ABLE MEDICAL COMPANY LIMITED

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8. Marketing Authorization Numbers

2A 15222/63

9. Date of authorization

28 December, 2020

10. Date of revision of the text

07 December, 2020