Summary of Product Characteristic

1. Name of the Medicinal Product

1.1 Product Name

Acetate Ringer's Injection

1.2 Strength

Each 100 mL contains:-

Sodium chloride	600 mg	Potassium chloride	30 mg
Sodium acetate, trihydrate	380 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 acetate, trihydrate	Calcium chloride, dihydrate

2.2 Quantitative Declaration:

Each 100 mL contains:-

Sodium chloride	600 mg	Potassium chloride	30 mg
Sodium acetate, trihydrate	380 mg	Calcium chloride, dihydrate	20 mg

3. Pharmaceutical Form

Clear, colorless sterile solution for infusion

4. Clinical Particulars

4.1 Therapeutic indications

Replacement of extracellular fluid and electrolyte loss or short-term volume replacement (alone or in association with colloid).

4.2 Posology and method of administration

Posology

The infusion rate and volume depend on the age, weight, clinical condition (e.g. burns, surgery, head-injury, infections), and concomitant therapy should be determined by the consulting physician experienced in paediatric intravenous fluid therapy (see sections 4.4. and 4.8). Fluid balance and serum electrolytes should be monitored before and during administration (see sections 4.4, 4.5, 4.6 and 4.8).

Recommended dosage:

The amount of Acetate Ringer's Injection needed to temporary restore blood volume is 3 to 5 times the volume of lost blood.

Adults, Adolescents and older patients (age 12 years and over):

The recommended dosage for longer treatment is:

- For adults, the elderly and adolescents (age 12 years and over): 500 ml to 3 litres/24h.

Paediatric population

- 0 - 10 kg body weight: 100 ml/kg/24h
- 10-20 kg body weight: 1000 ml + (50 ml/ kg over 10 kg) / 24h
- > 20 kg body weight: 1500 ml + (20 ml/ kg over 20 kg) / 24h

Administration rate:

The infusion rate is usually 40 ml/kg/24h in adults.

In paediatric patients the infusion rate is 5 ml/kg/h in average but the value varies.

- 6-8 ml/kg/h for 0 - 10 kg body weight
- 4-6 ml/kg/h for 10-20 kg body weight
- 2-4 ml/kg/h for > 20 kg body weight

Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes.

Mode of Administration

The administration is performed by intravenous route. Due to its iso-osmolality, this solution can be administered through a peripheral vein. Use only if the solution is clear, without visible particles and if the container is undamaged. Administer immediately following the insertion of infusion set. Do not remove unit from overwrap until ready for use. The inner bottle maintains the sterility of the product. 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 the 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.

The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system. Additives may be introduced before infusion or during infusion through the injection site. For instructions on preparing the product for administration, see section 6.6.

4.3 Contraindication

The solution is contraindicated in patients presenting with:

- Known hypersensitivity to the product or any ingredients in the formulation
- Extracellular hyperhydration or hypervolemia

As for other calcium-containing infusion solutions, treatment with ceftriaxone and Acetate Ringer's Injection is contraindicated in preterm newborn infants and term newborn infants (≤28 days of age), even if separate infusion lines are used (risk of fatal ceftriaxone calcium salt precipitation in the neonate's bloodstream).

4.4 Special warning and precautions for use

Cases of fatal reactions with calcium-ceftriaxone precipitates in lungs and kidneys in premature and full-term newborn infants aged less than 1 month have been described. In patients of any age ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions even via different infusion lines or different infusion sites.

However, in patients older than 28 days of age ceftriaxone and calcium-containing solutions may be administered sequentially one after another if infusion lines at different sites are used or if the infusion lines are replaced or thoroughly flushed between infusions with physiological salt-solution to avoid precipitation.

Sequential infusions of ceftriaxone and calcium-containing products must be avoided in case of hypovolaemia.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure and in patients presenting with oedema, ascitic cirrhosis or renal insufficiency.

Hyponatraemia

Treatment with intravenous fluids having a lower sodium concentration than the patient's serum sodium may cause hyponatremia (see section 4.2). Children, patients with reduced cerebral compliance, patients with non-osmotic vasopressin release (e.g. in acute illness, trauma, post-operative stress, central nervous system diseases), and patients exposed to vasopressin agonists and other drugs that can lower serum sodium (see section 4.5) are at particular risk of acute hyponatraemia. Acute hyponatraemia can lead to acute brain oedema and life-threatening brain injury.

The patient's clinical status and laboratory parameters (fluid balance, blood and urine electrolytes as well as acid-base balance) must be monitored during use of this solution. The plasma electrolyte levels such as natraemia, chloraemia, kalaemia, magnesaemia, calcaemia must be closely monitored.

Paediatric population:

Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes.

Solutions containing potassium salts should be administered with caution to patients with cardiac diseases, hyperkalaemia or conditions that can lead to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration, or extensive tissue destruction as occurs with severe burns (see also in 4.5 “Interactions with other medicinal products and other forms of interaction”).

Although Acetate Ringer’s Injection has a potassium concentration similar to the concentration in plasma, it is insufficient to produce a useful effect in case of severe potassium insufficiency and therefore it should not be used for this purpose.

Calcium chloride is irritant, therefore care should be taken to prevent extravasation during intravenous injection. Solutions containing calcium should be given cautiously to patients with hypercalcemia or patients with impaired renal function, or disease associated with elevated vitamin D concentrations such as sarcoidosis or calcium renal calculi or history of such calculi to patients receiving digitalis therapy (see also in 4.5 “Interactions with other medicinal products and other forms of interaction”). In case of concomitant blood transfusion and because of the presence of calcium, Acetate Ringer’s Injection must not be administered via the same infusion system because of the risk of coagulation.

Infusion of Acetate Ringer’s Injection may cause metabolic alkalosis because of the presence of acetate ions and should be administered with particular caution to patents with alkalosis or at risk for alkalosis. However; it is not suitable to treat severe metabolic or respiratory acidosis. During long-term parenteral treatment, a convenient nutritive supply must be given to the patient.

Geriatric use:

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/or other diseases, and/or concomitant drug therapy.

4.5 Interaction with other medicinal products and other forms of interactions

Interaction with ceftriaxone

- Concomitant treatment with ceftriaxone and Acetate Ringer's Injection is contraindicated in preterm newborn infants and term newborn infants (≤28 days of age), even if separate infusion lines are used (risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream) (see Section 4.3).
- In patients of any age ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions even via different infusion lines or different infusion sites (See Section 4.4).

Drugs that can increase the risk for hyponatremia

Drugs that can lower serum sodium may increase the risk of acquired hyponatraemia following treatment with intravenous fluids inappropriately balanced to the need of the patient in terms of fluid volume and sodium content (see sections 4.2, 4.4, 4.6 and 4.8). Examples are diuretics, non-steroid anti-inflammatory drugs (NSAIDs), antipsychotics, selective serotonin reuptake inhibitors, opioids, antiepileptics, oxytocin, and chemotherapy.

Suxamethonium and potassium, when administered concomitantly, may result in considerable hyperkalaemia, thereby intensifying their negative effects on cardiac rhythm. Therefore, concomitant administration of Acetate Ringer's Injection and drugs containing the above mentioned substances, is not recommended.

The effect on potassium and/or sodium retention of certain drugs should be considered such as: Corticoids/Steroids, Potassium-sparing diuretics, Angiotensin converting enzyme inhibitors (ACEi) angiotensin II receptor antagonists, Tacrolimus, Cyclosporin.

Calcium increases the risk of toxic effects of digitalis glycosids. Alkalisation of the urine by bicarbonate resulting from acetate metabolism, will increase the elimination of certain drugs (such as - salicylates, lithium, barbiturates) and will decrease elimination of kinidin and sympathomimetics (such as amphetamine, dextro amphetamine sulfate, ephedrine and pseudoephedrine).

Acetate Ringer's Injection should be administered with caution in patients treated with thiazide diuretics or vitamin D, as these can increase the risk of hypercalcemia.

4.6 Pregnancy and lactation

Acetate Ringer's Injection can be used during pregnancy and lactation. When Acetate Ringer's Injection is administrated to pregnant women during labour, particularly if administered in combination with oxytocin, there may be an increased risk for hyponatraemia (see section 4.4, 4.5 and 4.8).

4.7 Effects on ability to drive and use machine

There is no information on the effects of Acetate Ringer's Injection on the ability to operate an automobile or other heavy machinery.

4.8 Undesirable effects

During administration of Acetate Ringer's Injection, the following adverse reactions have been reported in the post-marketing experience, listed by MedDRA System Organ Class, then by preferred term in order of severity, where feasible:

Tabulated list of adverse reactions

MedDRA System Organ Class	**Common (>1/100, <1/10)**	**Rare (>1/10000,<1/1000)**	**Very rare (<1/10000)**	**Not known**
Immune system disorders	-		-	Hypersensitivity reactions, allergic reactions or anaphylactic/anaphylactoid symptoms; Urticaria
Metabolism and nutrition disorders		-		Hyponatremia Overhydration Electrolyte disturbances
Nervous system disorders	-	-	Seizure that may be precipitated by the alkalosis induced by acetate	Hyponatraemic encephalopathy
Cardiac disorders	Heart failure in patient with cardiac disorder	Tachycardia, bradycardia	-	-
Respiratory, thoracic and mediastinal disorders	Pulmonary oedema	-	-	-
General disorders and administration site conditions	Febrile reaction, infection at the site of injection, local pain or	Chest tightness, chest pain.	-	-

	reaction, vein irritation, venous thrombosis or phlebitis extending from the site of injection, extravasation,			

Adverse reactions may be associated with medications added to the solution.

4.9 Overdose

Excessive administration of Acetate Ringer's Injection can cause:

- Fluid and sodium overload with a risk of edema (peripheral and/or pulmonary), particularly when renal sodium excretion is impaired
- Hyperkalemia, especially in patients with severe renal impairment
- Hypercalcemia
- Hyperchloremia
- A loss of bicarbonate with an acidifying effect
- Hypermagnesemia

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 Acetate Ringer's Injection administration, dose reduction, and other measures as indicated for the specific clinical constellation.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Electrolytes - ATC code: B05BB01

Acetate Ringer's Injection has approximately the same electrolyte composition as the extracellular fluid. The product is used for corrections of disturbances in the serum electrolyte balance and in the acid-base balance. Electrolytes are given to receive or to keep normal osmotic conditions in the extracellular as well as the intracellular compartment. Acetate is oxidized into bicarbonate, mainly in the muscles and peripheral tissues and gives a weak alkalising effect. Due to the amount of metabolisable anions, Acetate Ringer's Injection is suitable for patients with a tendency to acidosis.

5.2 Pharmacokinetic properties

The acetates in Acetate Ringer's Injection are metabolised by muscles and peripheral tissues to bicarbonate.

When medication is added to Acetate Ringer's Injection, the overall pharmacokinetics of the solution will depend on the nature of the drug used.

5.3 Preclinical Safety data

There are no preclinical data considered relevant to clinical safety beyond data included in other sections of the SPC.

6. Pharmaceutical Particulars

6.1 List of excipients

Water for injection

6.2 Incompatibilities

Incompatibility of the medicinal product to be added with the solution in Acetated Ringer's Injection must be assessed before addition. The instruction for use of the medicinal product to be added must be consulted.

Before adding a drug, verify it is soluble and stable in water at the pH of Acetated Ringer's Injection (pH 6.0 to 7.5).

Acetated Ringer's Injection should not be mixed with products containing carbonates, sulfates or phosphates.

Ceftriaxone: See sections 4.3 and 4.4 for more information.

Acetated Ringer's Injection is incompatible with the following agents due to precipitate formation (includes but is not limited to):

- Amphotericin B
- Cortisone
- Erythromycin lactobionate
- Etamivan
- Ethyl alcohol
- Thiopental sodium
- Disodium edetate

6.3 Shelf life

2 years

In-use shelf-life:

Chemical and Physical stability of any additive at the pH of Acetated Ringer's Injection should be established prior to use.

From a microbiological point of view, the diluted product must be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours.

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

When additive is used, verify isotonicity prior to parenteral administration. Thorough and careful aseptic mixing of any additive is mandatory. Solutions containing additives should be used immediately and not stored. Adding other medication or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In case of adverse reaction, infusion must be stopped immediately.

Discard after single use.

Discard any unused portion.

Do not reconnect partially used bottles.

7. Marketing Authorization Holder

ABLE MEDICAL COMPANY LIMITED

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Mahasarakham 44160, Thailand

8. Marketing Authorization Numbers

1A 15221/63

9. Date of authorization

28 December, 2020

10. Date of revision of the text

07 December, 2020