Summary of Product Characteristics

1. Name of the medicinal product

Compound Sodium Lactate intravenous infusion BP

2. Qualitative and quantitative composition

Each 1ml contains;

Sodium lactate: 3.2 mg

Sodium chloride: 6.0 mg

Potassium chloride: 0.4 mg

Calcium chloride dihydrate: 0.27 mg

For full list of excipients see section 6.1

3. Pharmaceutical form

Solution for infusion.

A clear, colourless solution

4. Clinical particulars

4.1 Therapeutic indications

Compound Sodium Lactate intravenous infusion (Ringer Lactate solution) is used in the following indications:

- Restoration of extracellular fluid and electrolyte balances or replacement of extracellular fluid loss where isotonic concentrations of electrolytes are sufficient.
- Short term volume replacement (alone or in association with colloid) incase of hypovolemia or hypotension.
- Regulation or maintenance of metabolic acidosis balance and/ortreatment of mild to moderate metabolic acidosis (except lacticacidosis)
- As a vehicle for intravenous drug delivery, if the drugs are compatible with the solutions

4.2 Posology and method of administration

Adults, the Elderly and Children:

Dosage, rate, and duration of administration are to be individualized and depend upon theindication for use, the patient's age, weight, clinical condition, and concomitant treatment,and on the patient's clinical and laboratory response to treatment.

Recommended dosage:

The amount of Compound Sodium Lactate solution needed to restore normal blood volume is3 to 5 times the volume of lost blood.

The recommended dosage is:

- For adults : 500 ml to 3Liters /24h
- For infants, toddlers and children : 20 ml to 100 ml / kg / 24 h

Administration rate:

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

In paediatric patients the infusion rate is 5mg/kg/hron average but the value varies with age: 6-8 ml/kg/ h forinfants, 4-6 ml/kg/h for toddlers, and 2-4 ml/kg/h for schoolchildren. In children with burns, the dose is on average 3.4 ml/kg/per cent burn at 24 h post-burn and 6.3 ml/kg/per cent burn at 48 h.

In severely head-injured children the dose is on average 2850 ml/m2 . Infusion rate and total volume can behigher in surgery or in case of need. Note: infants and toddlers: aged from 28 days to 23 months (a toddler is an infant who can walk) - children and schoolchildren: aged from 2 years to 11 years.

Use in pediatric patients

The safety and efficacy of Compound Sodium Lactate solution in children has not beenestablished by adequate and well-controlled trials; however, the use of electrolyte solutions inthe pediatric population is referenced in the medical literature. Lactate-containing solutionsshould be administered with particular caution to neonates and infants less than 6 months ofage.

Pediatric infusion rates are 5 ml/kg/h in average but the value varies with age:

- infants: 6-8 mL/kg/h,
- toddlers: 4-6 mL/kg/h
- children: 2-4 mL/kg/h .

In children with burns, the dose is on average 3.4 mL/kg/per cent burn at 24 h post-burn and6.3 mL/kg/per cent burn at 48 h.

In severely head-injured children the dose is on average 2850 mL/m².

Infusion rate and total volume can be higher in surgery or in case of need.

Note:

- infants and toddlers: aged from 28 days to 23 months (a toddler is an infant who can walk)
- children: age from 2 to 11 years

Use in geriatric patients

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

Method of administration:

The solution is for intravenous administration through a sterile and non-pyrogenicadministration set using aseptic technique. The equipment should be primed with thesolution in order to prevent air entering the system.

The solution should be inspected visually for particulate matter and discoloration prior toadministration. Do not administer unless the solution is clear, free from visible particles andthe seal is intact. Do not remove unit from overwrap until ready for use. The inner bagmaintains the sterility of the solution. Administer immediately following the insertion ofinfusion set.

Do not connect flexible plastic containers in series in order to avoid air embolism due topossible residual air contained in the primary container. Pressurizing intravenous solutionscontained in flexible plastic containers to increase flow rates can result in air embolism if theresidual air in the container is not fully evacuated prior to administration. Use of a ventedintravenous 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 usedwith flexible plastic containers.

Additives may be introduced before infusion or during infusion through the injection site.

When making additions to Compound Sodium Lactate solution, aseptic technique must beused. Mix the solution thoroughly when additives have been introduced. Do not storesolutions containing additives.

Monitoring

Fluid balance and plasma electrolytes concentrations (sodium, potassium, calcium and chlorides) must bemonitored during administration.

4.3 Contraindications

As for other calcium-containing infusion solutions, concomitant administration of ceftriaxoneand Compound Sodium Lactate solution is contraindicated in newborns (≤28 days of age),even if separate infusion lines are used (risk of fatal ceftriaxone-calcium salt precipitation inthe neonate’s bloodstream).

Compound Sodium Lactate solution is also contraindicated in patients with

- A known hypersensitivity to sodium lactate.

- Extracellular hyperhydration or hypervolemia
- Severe renal insufficiency (with oliguria/anuria)
- Uncompensated cardiac failure
- Hyperkalemia
- Hypercalcaemia
- Metabolic alkalosis
- Ascitic cirrhosis
- Severe metabolic acidosis
- Conditions associated with increased lactate levels (hyperlactatemia) including lactic acidosis, or impaired lactate utilization, such as severe hepatic insufficiency.
- Concomitant digitalis therapy

4.4 Special warnings and precautions for use

Hypersensitivity reactions

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 hypovolemia.

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

High volume infusion must be used under specific monitoring in patients with cardiacor pulmonary failure.

The patient's clinical status and laboratory parameters (blood and urine electrolytes aswell as acid-base balance) must be monitored during use of this solution. The plasmapotassium level of the patient must be particularly closely monitored in patients atrisk of hyperkalaemia.

Solutions containing sodium chloride should be carefully administered to patientswith hypertension, heart failure, peripheral or pulmonary oedema, impaired renalfunction, pre-eclampsia, aldosteronism, or other conditions associated with sodium retention.

Solutions containing potassium salts should be administered with caution to patientswith cardiac disease or conditions predisposing to hyperkalemia such as renal oradrenocortical insufficiency, acute dehydration, or extensive tissue destruction asoccurs with severe burns.

Although Ringer Lactate solution has a potassium concentration similar to theconcentration in plasma, it is insufficient to produce a useful effect in case of severepotassium insufficiency and therefore it should not be used for this purpose.

Calcium chloride is irritant, therefore care should be taken to prevent extravasationduring intravenous injection and intramuscular injection must be avoided. Solutionscontaining calcium salts should be given cautiously to patients with impaired renalfunction, or disease associated with elevated vitamin D concentrations such assarcoidosis. They should be avoided in patients with calcium renal calculi, or ahistory of renal calculi. In case of concomitant blood transfusion and because of thepresence of calcium, Ringer lactate solution must not be administered via the sameinfusion system because of the risk of coagulation.

Ringer lactate solution may cause metabolic alkalosis because of the presence oflactate ions.

Ringer lactate solution may not produce its alkalinizing action in patients with liverinsufficiency since lactate metabolism may be impaired.

The solution containing lactate should be administered with particular care toneonates less than 3 months old.

During long term parenteral treatment, a convenient nutritive supply must be given tothe patient.

4.5 Interaction with Other Medicinal Products And Other Forms Of Interaction

Interaction with ceftriaxone

Concomitant treatment with ceftriaxone and Ringer's Solution for Infusion 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 older than 28 days (including adults), ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including Ringer's Solution for Infusion (See Section 4.4) even via different infusion lines or different infusion sites (see section 6.2)

Interaction associated with sodium:

Corticoids/Steroids and carbenoxolone which are associated with the retention of sodium and water (with oedema and hypertension).

Interactions associated with calcium:

Infusion in association with digitalis cardiac glycosides is contra-indicated because of the risk of severe to fatal cardiac arrhythmia particularly in the case of hypokalaemia

Care should be taken in the concurrent use of thiazide diuretics or vitamin D because of the risk of hypercalcaemia resulting from reduced urinary clearance of calcium.
Bisphosphonates, fluoride, some fluoroquinolones and tetracyclines which are less absorbed (lower availability) when administered with calcium.

Interactions associated with potassium:

Care should be taken in concurrent use of drugs containing potassium and drugs which have the potential for inducing hyperkalaemia, such as potassium-sparing diuretics given alone or in combination (such as spironolactone, triamterene, amiloride, potassium canrenoate), ACE inhibitors, angiotensin-II receptor antagonists, tacrolimus and ciclosporin.
- Digitalis glycosides (digitalis cardiotonics) whose effects are enhanced by the presence of calcium andmay lead to serious or fatal cardiac arrhythmia. - Thiazide diuretics or vitamin D which can lead to hypercalcaemia when co-administered with calcium. For information on incompatibilities between this and other products, please see section 6.2

Interaction associated with lactate (which is metabolized into bicarbonate):

Acidic drugs such as salicylates, barbiturates and lithium whose renal clearance is increased because of the alkalinisation of urine by the bicarbonate resulting from lactate metabolism.

Alkaline drugs, notably sympathomimetics (e.g. ephedrine, pseudoephedrine) and stimulants (e.g. dexamphetamine sulphate, phenfluramine hydrochloride) whose halflife is prolonged (slowest elimination).

4.6 Fertility, Pregnancy and Lactation

Ringer Lactate solution can be used safely during pregnancy and lactation as long as the electrolyte- and fluid balance is controlled.

It is reminded that calcium crosses the placenta and is distributed into breast milk.

When a medication is added, the nature of the drug and its use during pregnancy and lactation have to be considered separately

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

During administration of Compound Sodium Lactate intravenous infusion, the following undesirable effectshave been reported as:

- very common:

Allergic reactions or anaphylactic/anaphylactoid symptoms such as localized or generalized urticaria, skin rash & erythema and itching/pruritus; skin swelling,periobial facial and/or laryngeal oedema (Quincke's oedema).

Nasal congestion, coughing, sneezing, bronchospasm and/or difficulty breathing

- common:

Chest tightness, chest pain, with tachycardia or bradycardia

Pruritus has been reported to occur in about 10% of patients receiving Ringer Lactate.

Hyperhydration and heart failure are very common in patients with cardiac disorderor pulmonary oedema

Electrolytes disturbances have been very commonly reported too.

Lactate infusions commonly induce feelings of anxiety, and a few cases of panicattack have been reported

Seizure may be precipitated by the alkalosis induced by lactate but this is uncommon.

Adverse reactions may be associated with the technique of administration includingfebrile response, infection at the site of injection, local pain or reaction, veinirritation, venous thrombosis or phlebitis extending from the site of injection,extravasation, and hypervolemia.

Adverse reactions may be associated to the medications added to the solution; thenature of the additive will determine the likelihood of any other undesirable effects.

In case of undesirable effect(s), the infusion must be discontinued

Reporting of suspected adverse drug reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals areasked to report any suspected adverse reactions

4.9 Overdose

Overuse or too fast administration may lead to water and sodium overload with a risk of oedema, particularly when there is a defective renal sodium excretion. In this case extra renal dialysis may be necessary.

Excessive administration of potassium may lead to the development of hyperkalemia, especially in patients with renal impairment. Symptoms include paresthesia of the extremities, muscle weakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest, and mental confusion.

Excessive administration of calcium salts may lead to hypercalcemia. Symptoms of hypercalcemia may include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi, and, in severe cases, cardiac arrhythmias and coma. Too rapid intravenous injection of calcium salts may also lead to many of the symptoms of hypercalcemia as well as to chalky taste, hot flushes, and peripheral vasodilatation. Mild asymptomatichypercalcemia will usually resolve on stopping administration of calcium and other contributory drugs such as vitamin D. If hypercalcemia is severe, urgent treatment (such as loop diuretics, hemodialysis, calcitonin, bisphosphonates, trisodium edetate) is required.

Excessive administration of sodium lactate may lead to hypokalemia and metabolic alkalosis, especially in patients with impaired renal function. Symptoms may include mood changes, tiredness, shortness of breath, muscle weakness, and irregular heartbeat. Muscle hypertonicity, twitching, and tetany may develop especially in hypocalcemic patients. Treatment of metabolic alkalosis associated with bicarbonate overdose consists mainly of appropriate correction of fluid and electrolyte balance.

Replacement of calcium, chloride, and potassium may be of particular importance.

When overdose is related to medications added to the solution infused, the signs andsymptoms of over infusion will be related to the nature of the additive being used. Inthe event of accidental over infusion, treatment should be discontinued and the patientshould be observed for the appropriate signs andsymptoms related to the drugadministered. The relevant symptomatic and supportive measures should be providedas necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group –Plasma substitutes and infusion solutions / electrolytes

ATC Code:B05BB01

Compound sodium lactate intravenous infusion is an isotonic solution of electrolytes. The constituents ofCompound sodium lactate intravenous infusion and their concentrations are designed to match those of plasma.The pharmacodynamic properties of this solution are those of its components (water, sodium, potassium, calcium, and chloride). The main effect of Ringer's Solution for Infusion is the expansion of the extracellularcompartment including both the interstitial and intravascular fluids. Ions, such as sodium, circulate through the cell membrane using various mechanisms of transport among which is the sodium pump (Na + /K + -ATPase). Sodium plays an important role in neurotransmission and cardiac electrophysiology, and also in its renal metabolism. Potassium is essential for numerous metabolic and physiological processes including nerve conduction, muscle contraction, and acid-base regulation. A normal concentration of potassium in plasma is about 3.5 to 5.0 mmoles per litre. Potassium is predominantly an intracellular cation, primarily found in muscle; only about 2% is present in the extracellular fluid. The passage of potassium into the cells and retention against the concentration gradient requires active transport via the Na + /K + -ATPase enzyme. Approximately 99% of calcium is incorporated into the skeleton. The remaining 1% is found in body tissuesand fluids, and is essential for normal nerve conduction, muscle activity, and blood coagulation. Chloride is mainly an extracellular anion found in low concentration in bone and in

high concentration in some components of connective tissue such as collagen. Intracellular chloride is in high concentration in redblood cells and gastric mucosa. The balance of anions and cations are regulated by the kidneys. Reabsorptionof chloride generally follows reabsorption of sodium

The main effect of Compound sodium lactate intravenous infusion is the expansion of the extracellular compartmentincluding both the interstitial fluid and the intravascular fluid.

The lactate is metabolized into bicarbonate, mainly in the liver, and produces analkalinising effect on the plasma.

In healthy volunteers receiving Compound sodium lactate intravenous infusion, central venous pressure changes wereassociated with a secretion of atrial natriuretic peptide.

In healthy volunteers, Compound sodium lactate intravenous infusion decreased serum osmolality, increased bloodpH, and the time until first urination was shorter than that with normal saline.

There is no significant change in glucagon, norepinephrine, epinephrine, bloodglucose and insulin levels in aortic surgery patients receiving Ringer Lactate.

When medication is added to Compound sodium lactate intravenous infusion, the overall pharmacodynamics of thesolution will depend on the nature of the drug used.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of the Compound sodium lactate intravenous infusion are those of the ions itscomposition includes (sodium, potassium, calcium and chloride).

Infusion of Compound sodium lactate intravenous infusion in normal hemodynamically stable adults does not increasecirculating lactate concentrations.

The lactate in Compound sodium lactate intravenous infusion is metabolized by both oxidation andgluconeogenesis, predominantly in the liver, and bicarbonate is generated by bothprocesses over 1-2 h.

When medication is added to Compound sodium lactate intravenous infusion, the overall pharmacokinetics of thesolution will depend on the nature of the drug used.

The volume and the ionic composition of the extracellular and the intracellular compartments are as follows; After injection of Sodium (24Na), the half-life is 11 to 13 days for 99% of the injected Na and one year for the remaining 1%. The distribution varies according to tissues: it is fast in muscles, liver, kidney, cartilage and skin; it is slow in erythrocytes and neurons; it is very slow in the bone. Sodium is predominantly excreted by the kidney, but there is extensive renal reabsorption. Small amounts of sodium are lost in the faeces and sweat. Factors influencing

potassium transfer between intracellular and extracellular fluid such as acid-base disturbances can distort the relationship between plasma concentrations and total body stores. Potassium is excreted mainly by the kidneys; it is secreted in the distal tubules in exchange of sodium or hydrogen ions. The capacity of the kidneys to conserve potassium is poor and some urinary excretion of potassium continues even when there is severe depletion. Some potassium is excreted in the faeces and small amountsmay also be excreted in sweat. The concentration of calcium in plasma is regulated by parathyroid hormone, calcitonin, and vitamin D. About 47% of calcium in plasma is in the ionized physiologically active form, about 6% is complexed with anions such as phosphate or citrate, and the remainder is bound to proteins, principally albumin. If the plasma-albumin concentration is raised (as in dehydration) or reduced (as is common in malignancy) it willaffect the proportion of ionized calcium. Thus, the total plasma-calcium concentration is commonly adjusted for plasma albumin. Excess of calcium is predominantly excreted renally. Unabsorbed calcium is eliminated in the faeces, together with that secreted in the bile and pancreatic juice. Minor amounts are lost in sweat, skin, hair, and nails. Calcium crossess the placenta and is distributed into breast milk.

5.3 Preclinical Safety data

Preclinical safety data of Ringer's Solution for Infusion in animals are not relevant since its constituents arephysiological components of animal and human plasma. Toxic effects are not to be expected under the condition of clinical application. The safety of potential additives should be considered separately**.**

6. Pharmaceutical particulars

6.1 List of excipients

- Water For Injections BP.

6.2 Incompatibilities

Ceftriaxone must not be mixed with calcium-containing solutions including Compound Sodium Lactate solution.

As with all parenteral solutions additives may be incompatible. Compatibility of the additiveswith the Compound Sodium Lactate solution and Viaflo container must be assessed beforeaddition. After addition of the additive, incompatibility may become visible by a possiblecolour change and/or the appearance of precipitates, insoluble complexes or crystals.

The Instructions for Use of the medication to be added and other relevant literature must beconsulted.

Before adding a substance or medication, verify that it is soluble and/or stable in water andthat the pH range of Compound Sodium Lactate solution is appropriate (pH 5.0 to 7.0).

When making additions to Compound Sodium Lactate solution, aseptic technique must beused. Mix the solution thoroughly when additives have been introduced. Do not storesolutions containing additives.

As guidance, the following medications are incompatible with the Compound Sodium Lactate solution (***non-exhaustive listing***):

Medications incompatible with Compound Sodium Lactate Solution;

Aminocaproic acid

Amphotericin B

Metaraminol tartrate

Cefamandole

Ceftriaxone

Cortisone acetate

Diethylstilbestrol

Etamivan

Ethyl alcohol

Phosphate and carbonate solutions

Oxytetracycline

Thiopental sodium

Versenate disodium

Medications with partial incompatibility with Compound Sodium Lactate Solution:

Tetracycline stable for 12 hours

Ampicillin sodium

concentration of 2%-3% stable for 4 hours

concentration >3% must be given within 1 hour

Minocycline stable for 12 hours

Doxycycline stable for 6 hoursAdditives known or determined to be incompatible should not be used.

6.3 Shelf life

36 months when unopened

Use immediately on removal from overwrap.

6.4 Special precautions for storage

Do not store above 30^0C and do not freeze.

6.5 Nature and contents of container

Pack sizes: 500 mL/250mL.

The bottles are made from Low Density Polyethylene plastic; the bottles are then overwrapped with a protective plastic pouch.

6.6 Special precautions for disposal and other handling

For single use only

Solution containing visible solid particles should not be used.

Do not use unless the solution is clear and the container undamaged

Do not connect in series and purge the infusion system to remove all air because ofthe risk of air embolism.

Discard any unused solution.

Verify the integrity of the container and the site for attachment.

For slow infusion only

Preparation for administration

Use sterile material for preparation and administration. • Suspend container from eyelet support. • Use an aseptic method to set up the infusion. • Attach administration set. Refer to directions of the accompanying set for connection, priming of the setand administration of the solution.

Techniques for injection of additive medications

Warning:Additives may be incompatible. When additive is used, verify isotonicity prior to parenteral administration. Thorough and careful asepticmixing of any additive is mandatory. Solutions containing additives should be used immediately and not stored.

To add medication before administration

• Disinfect medication site.

• Using syringe with 19 to 22-gauge needle, puncture re-sealable medication port and inject.

•Mix solution and medication thoroughly. For high-density medication such as potassium chloride, tapthe ports gently while ports are upright and mix.

Caution: Do not store bags containing added medications. To add medication during administration • Close clamp on the set • Disinfect medication site. • Using syringe with 19 to 22-gauge needle, puncture resealable medication port and inject. • Remove container from IV pole and/or turn to an upright position. • Evacuate both ports by tapping gently while the container is in an upright position. • Mix solution and medication thoroughly. • Return container to in use position, re-open the clamp and continue administration.

7. Marketing authorisation holder

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8. Marketing authorisation number

N/A

9. Date of first authorisation/renewal of the authorisation

Oct 2019

10. Date of revision of the text

July 2023.