SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Compound Sodium Lactate Solution for Infusion BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative Composition:

Each100 ml contains

Sodium lactate Solution BP

Eq. to sodium Lactate

Sodium Chloride BP

Potassium Chloride BP

Calcium Chloride Dihydrate

Water for injection BP

3. PHARMACEUTICAL FORM

Solution for Infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Compound Sodium Lactate solution is used in the following indications:

- Restoration of extracellular fluid and electrolytes balances or replacement of extracellular fluid loss where isotonic concentrations of electrolytes are sufficient
- Short term volume replacement (alone or in association with colloid) in case of hypovolemia or hypotension.
- Regulation or maintenance of metabolic acidosis balance and/or treatment of mild to moderate metabolic acidosis (except lactic acidosis)

4.2 Posology and method of administration

Posology

Adults, the Elderly and Children:

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 and laboratory response to treatment.

Recommended dosage:

The amount of Compound Sodium Lactate solution needed to restore normal blood volume is 3 to 5 times the volume of lost blood.

The recommended dosage is:

- Foradults: 500 ml to 3 L/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.

Use in paediatric patients

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

Paediatric infusion rates is 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 and 6.3mL/kg/per cent burn at 48 h.

In severely head-injured children the dose is on average 2850 mL/m^2.

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-pyrogenic administrationset using aseptic technique. The equipment should be primed with the solution in order toprevent 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 and

theseal is intact. Do not remove unit from overwrap until ready for use. The inner bag maintains thesterility of the solution. Administer immediately following the insertion of infusion set.Do not connect flexible plastic containers in series in order to avoid air embolism due to possibleresidual air contained in the primary container. Pressurizing intravenous solutions contained inflexible plastic containers to increase flow rates can result in air embolism if the residual air inthe container is not fully evacuated prior to administration. Use of a vented intravenousadministration set with the vent in the open position could result in air embolism. Ventedintravenous administration sets with the vent in the open position should not be used withflexible plastic containers.Additives may be introduced before infusion or during infusion through the injection site. Whenmaking additions to Compound Sodium Lactate solution, aseptic technique must be used. Mixthe solution thoroughly when additives have been introduced. Do not store solutions containingadditives.For information on incompatibilities and preparation of the product with additives.

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), evenif separate infusion lines are used (risk of fatal ceftriaxone-calcium salt precipitation in theneonate's bloodstream). For patients over 28 days of age.

Compound Sodium Lactate solution is also contraindicated in patients with

- A known hypersensitivity to sodium lactate.
- Extracellular hyperhydration or hypervolaemia
- Severe renal insufficiency (with oliguria/anuria)
- Uncompensated cardiac failure
- Hyperkalaemia
- Hypercalcaemia
- Metabolic alkalosis
- Ascitic cirrhosis
- Severe metabolic acidosis
- Conditions associated with increased lactate levels (hyperlactataemia) including lactic acidosis,or impaired lactate utilization, such as severe hepatic insufficiency.
- Concomitant digitalis therapy

4.4 Special warnings and precautions for use

Liver disease:

Caution is needed in patients with severe hepatic impairment. The dose of metronidazole shouldbe reduced as necessary. Metronidazole is mainly metabolised by hepatic oxidation. Substantialimpairment of Metronidazole clearance may occur in the presence of advanced hepaticinsufficiency. The risk/benefit ratio of using Metronidazole to treat trichomoniasis in suchpatients should be carefully considered (for dosage adjustment see section 4.2). Plasma levels ofMetronidazole should be closely monitored.

Caution is needed in patients with hepatic encephalopathy. Patients with severe hepaticencephalopathy metabolize metronidazole slowly, with resultant accumulation of metronidazole.This may cause exacerbation of CNS adverse effects. The dose of metronidazole should bereduced as necessary.

Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome withvery rapid onset after treatment initiation in patients with Cockayne syndrome have beenreported with products containing metronidazole for systemic use. In this population,metronidazole should therefore be used after careful benefit-risk assessment and only if noalternative treatment is available. Liver function tests must be performed just prior to the start oftherapy, throughout and after end of treatment until liver function is within normal ranges, oruntil the baseline values are reached. If the liver function tests become markedly elevated duringtreatment, the drug should be discontinued.

Patients with Cockayne syndrome should be advised to immediately report any symptoms ofpotential liver injury to their physician and stop taking metronidazole.

Active Central Nervous System disease:

Metronidazole should be used with caution in patients with active disease of the Peripheral andCentral Nervous System. Severe neurological disturbances (including seizures and peripheraland optic neuropathies) have been reported in patients treated with metronidazole. Stopmetronidazole treatment if any abnormal neurologic symptoms occur such as ataxia, dizziness,confusion or any other CNS adverse reaction. The risk of aggravation of the neurological stateshould be considered in patients with fixed or progressive paraesthesia, epilepsy and activedisease of the central nervous system except for brain abscess.

Encephalopathy has been reported in association with cerebellar toxicity characterized by ataxia,dizziness, dysarthria, and accompanied by CNS lesions seen on magnetic resonance imaging(MRI). CNS symptoms and CNS lesions, are generally reversible within days to weeks upondiscontinuation of metronidazole.

Aseptic meningitis can occur with metronidazole. Symptoms can start within hours of doseadministration and generally resolve after metronidazole therapy is discontinued.

Blood Dyscrasias

Metronidazole should be used with caution in patients with evidence or history of blood dyscrasia as a granulocytosis; leukopenia and neutropenia have been observed followingmetronidazole administration.

Renal Disease:

Metronidazole is removed during haemodialysis and should be administered after the procedureis finished.Patients with renal impairment, including patients receiving peritoneal dialysis, should bemonitored for signs of toxicity due to the potential accumulation of toxic metronidazolemetabolites.

Sodium restricted patients:

This medicinal product contains 13.5 mmol (310 mg) sodium per 100 mL. To be taken intoconsideration by patients on a controlled sodium diet.

Alcohol:

Patients should be advised to discontinue consumption of alcoholic beverages or alcoholcontainingproducts before, during, and up to 72hours after taking metronidazole because of adisulfram-like effect (abdominal cramps, nausea, headaches, flushing, vomiting and tachycardia).

ntensive or prolonged Metronidazole therapy:

As a rule, the usual duration of therapy with i.v Metronidazole or other imidazole derivatives isusually less than 10 days. This period may only be exceeded in individual cases after a very strictbenefit-risk assessment. Only in the rarest possible case should the treatment be repeated.Limiting the duration of treatment is necessary because damage to human germ cells cannot beexcluded.

Intensive or prolonged Metronidazole therapy should be conducted only under conditions ofclose surveillance for clinical and biological effects and under specialist direction. If prolongedtherapy is required, the physician should bear in mind the possibility of peripheral neuropathy orleucopenia. Both effects are usually reversible.

In case of prolonged treatment, occurrence of undesirable effects such as paraesthesia, ataxia,dizziness and convulsive crises should be checked. High dose regimes have been associated withtransient epileptiform seizures.

Monitoring:

Due to increased risk for adverse reactions, regular clinical and laboratory monitoring (includingblood count) are advised in cases of high-dose, prolonged or repeated treatment, in case ofantecedents of blood dyscrasia, in case of severe infection and in severe hepatic insufficiency.

4.5 Interaction with other medicinal products and other forms of interaction

< **Interaction related to the presence of sodium:**

Caution is advised when administering Compound Sodium Lactate solution to patients treatedwith drugs that may increase the risk of sodium and fluid retention (with oedema andhypertension), such as corticosteroids.

Interaction related to the presence of potassium:

Because of its potassium content, Compound Sodium Lactate solution should be administeredwith caution in patients treated with agents or products that can cause hyperkalaemia or increasethe risk of hyperkalaemia, such as

- Potassium-sparing diuretics (amiloride, spironolactone, triamterene, alone or in association).
- Angiotensin converting enzyme inhibitors (ACEi) and angiotensin II receptor antagonists
- Tacrolimus, cyclosporine

Administration of potassium in patients treated with such medications can produce severe andpotentially fatal hyperkalaemia, particularly in patients with severe renal insufficiency.

Interaction related to the presence of calcium:

Administration of calcium may increase the effects of digitalis and lead to serious or fatal cardiacarrhythmia. Therefore, larger volumes or a faster infusion rates should be used with caution inpatients treated with digitalis glycosides.

- Caution is advised when administering Compound Sodium Lactate solution to patients treatedwith thiazide diuretics or vitamin D, as these can increase the risk of hypercalcaemia.
- Bisphosphonates, fluoride, some fluoroquinolones and tetracyclines which are less absorbed(lower availability) when administered with calcium.

Interaction related to the presence of lactate (which is metabolized into bicarbonate):

Caution is advised when administering Compound Sodium Lactate solution to patients treatedwith drugs for which renal elimination is pH dependent. Due to the alkalinizing action of lactate(formation of bicarbonate), Compound Sodium Lactate solution may interfere with theelimination of such drugs.

- Renal clearance of acidic drugs such as salicylates, barbiturates, and lithium may be increasedbecause of the alkalinisation of urine by the bicarbonate resulting from lactate metabolism.
- Renal clearance of alkaline drugs, such as sympathomimetics (e.g. ephedrine, pseudoephedrine)and stimulants (e.g. dexamphetamine sulfate, phenfluramine hydrochloride) may be decreased

4.6 Fertility, pregnancy and lactation

Compound Sodium Lactate solution can be used safely during pregnancy and lactation as long asthe 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 lactationhas to be considered separately.

4.7 Effects on ability to drive and use machines

The following adverse reactions (listed by MedDRA System Organ Class) have been reportedspontaneously during the post-market experience.

Immune System Disorders	Hypersensitivity/Infusion reactions including Anaphylactic/Anaphylactoid reaction, possiblymanifested by one or more of the following symptoms: Angioedema, Chest pain, Chest discomfort, Decreasedheart rate, Tachycardia, Blood pressure decreased,Respiratory distress, Bronchospasm, Dyspnea, Cough,Urticaria, Rash, Pruritus, Erythema, Flushing, Throatirritation, Paresthesias, Hypoesthesia oral, Dysgeusia, Nausea, Anxiety, Pyrexia, Headache
Metabolism and Nutrition Disorders	Hyperkalaemia
General Disorders and Administration Site Conditions	Infusion Site Reactions manifested by one or more ofthe following symptoms: Phlebitis, Infusion siteinflammation, Infusion site swelling, Infusion siterash, Infusion site pruritus, Infusion site erythema,Infusion site pain, Infusion site burning

The following adverse reactions have been reported spontaneously during the use of othersodium-lactate containing solutions:

• Hypersensitivity: Laryngeal oedema (Quincke'soedema), skin swelling, nasal congestion,Sneezing

• Electrolyte disturbances

• Hypervolaemia

• Panic Attack

• Other infusion site reactions: Infection at the site of injection, Extravasation, Infusion siteanesthesia (numbness)

4.8 Undesirable effects

An excessive volume or too high a rate of administration of Compound Sodium Lactate solutionmay lead to fluid and sodium overload with a risk of oedema (peripheral and/or pulmonary),particularly when renal sodium excretion is impaired. In this case extra renal dialysis may benecessary.

Excessive administration of potassium may lead to the development of hyperkalaemia, especiallyin patients with renal impairment. Symptoms include paresthesia of the extremities, muscleweakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest, and mental confusion.Excessive administration of calcium salts may lead to hypercalcaemia. Symptoms ofhypercalcaemia may include anorexia, nausea, vomiting, constipation, abdominal pain, muscleweakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi, and, insevere cases, cardiac arrhythmias and coma. Too rapid intravenous injection of calcium saltsmay also lead to many of the symptoms of hypercalcaemia as well as to chalky taste, hot flushes,and peripheral vasodilatation. Mild asymptomatic hypercalcaemia will usually resolve onstopping administration of calcium and other contributory drugs such as vitamin D. Ifhypercalcaemia is severe, urgent treatment (such as loop diuretics, haemodialysis, calcitonin,bisphosphonates, trisodiumedetate) is required.

Excessive administration of lactate may lead to metabolic alkalosis. Metabolic alkalosis may beaccompanied by hypokalaemia, Symptoms may include mood changes, tiredness, and shortness ofbreath, muscle weakness, and irregular heartbeat. Muscle hypertonicity, twitching, and tetanymay develop especially in hypocalcaemic patients. Treatment of metabolic alkalosis due tobicarbonate overdose consists mainly of appropriate correction of fluid and electrolyte balance.Replacement of calcium, chloride, and potassium may be of particular importance.

4.9 Overdose

When overdose is related to medications added to the solution infused, the signs and symptomsof over infusion will be related to the nature of the additive being used. In the event of accidentalover infusion, treatment should be discontinued and the patient should be

observed for theappropriate signs and symptoms related to the drug administered. The relevant symptomatic andsupportive measures should be provided as necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group (ATC code): B05BB01 “Electrolytes”

Compound Sodium Lactate solution is an isotonic solution of electrolytes. The constituents of Compound Sodium Lactate Solution and their concentrations are designed to match those ofplasma.The pharmacological properties of the Compound Sodium Lactate solution are those of itscomponents (sodium, potassium, calcium, chloride and lactate). The main effect of CompoundSodium Lactate Solution is the expansion of the extracellular compartment including both theinterstitial fluid and the intravascular fluid.The lactate is metabolised into bicarbonate, mainly inthe liver, and produces an alkalinising effect on the plasmaIn healthy volunteers receiving Compound Sodium Lactate Solution, central venous pressurechanges were associated with a secretion of atrial natriuretic peptideIn healthy volunteers,

Compound Sodium Lactate Solution decreased serum osmolality, increased blood pH, and thetime until first urination was shorter than that with normal saline. There is no significant changein glucagon, norepinephrine, epinephrine, blood glucose and insulin levels in aortic surgerypatients receiving Compound Sodium Lactate Solution. When medication is added to CompoundSodium Lactate Solution, the overall pharmacodynamics of the solution will depend on thenature of the drug used.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of the Compound Sodium Lactate solution are those of the ionsits composition includes (sodium, potassium, calcium and chloride).

Infusion of Compound Sodium Lactate Solution in normal hemodynamically stable adults doesnot increase circulating lactate concentrations.

The pharmacokinetics of D-lactate and L-lactate are similar. The lactate in Compound SodiumLactate solution is metabolized by both oxidation and gluconeogenesis, predominantly in theliver, and bicarbonate is generated by both processes over 1-2 h. When medication is added toCompound Sodium Lactate Solution, the overall pharmacokinetics of the solution will depend onthe nature of the drug used.

5.3 Preclinical safety data

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection BP

6.2 Incompatibilities

6.3 Shelf life

36 Months from the date of manufacture

6.4 Special precautions for storage

Store in a cool & dry place. Protected from light

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

500 ml and 1000 ml Plastic Bottles.

6.6 Special precautions for disposal <and other handling>

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

5798/REN/2018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16.04.2014
Date of latest renewal: 25.05.2020

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Date: 12.07.2023