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DIRECTIONS FOR USE

B. Braun Melsungen AG · 34209 Melsungen, Germany

Compound Sodium Lactate Solution for Infusion

1 NAME OF THE MEDICINAL PRODUCT

Compound Sodium Lactate Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution contain

Sodium chloride	6.00 g
Sodium lactate solution (50% w/w) (equivalent to sodium lactate, 3.12 g)	6.24 g
Potassium chloride	0.40 g
Calcium chloride dihydrate	0.27 g
Electrolyte concentrations:	
Sodium	131 mmol/l
Potassium	5.4 mmol/l
Calcium	1.8 mmol/l
Chloride	112 mmol/l
Lactate	28 mmol/l

Excipients

For -the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion,

Clear, colourless aqueous solution

Theoretical osmolarity:	277 mOsm/l
Acidity (titration to pH 7.4):	< 1 mmol/l
pH:	5.0 – 7.0

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Fluid substitution under the conditions of undisturbed acid-base balance or mild acidosis
- Isotonic and hypotonic dehydration
- Short-term intravascular volume replacement
- Vehicle solution for compatible electrolyte concentrates and drugs.

4.2 Posology and method of administration

Posology

The dosage of the solution depends on the fluid and electrolyte requirements of the patient, his/her age, weight, clinical condition and physiological (acid-base) status. Fluid balance, serum electrolytes and acid-base balance may need to be monitored before and during administration, with particular attention to serum sodium in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonist drugs, due to the risk of hospital acquired hyponatraemia (see sections 4.4, 4.5 and 4.8).

Monitoring of serum sodium is particularly important for hypotonic fluids.

Compound Sodium Lactate osmolarity once infused: 277 mOsm/l

The recommended dosages are:

Adults and adolescents

Maximum daily dose

Up to 40 ml per kg body weight (BW) per day, corresponding to 5.24 mmol sodium per kg BW per day and max. 0.22 mmol potassium per kg BW per day.

Maximum infusion rate:

The infusion rate should be adjusted according to the patient's clinical condition.

The infusion rate should normally not exceed the following values: 5 ml per kg BW per hour

Paediatric population

Recommended dosage for infants and children:

20 ml – 100 ml per kg BW per day, corresponding to 2.6 - 13 mmol sodium per kg BW per day and 0.108 – 0.54 mmol potassium per kg BW per day.

Maximum infusion rate

on average 5 ml per kg BW per hour, but the value varies with age:

6 – 8 ml per kg BW per hour for infants[1]

4 – 6 ml per kg BW per hour for toddlers[1]

2 - 4 ml per kg BW per hour for schoolchildren[2]

[1] infants and toddlers: age range 28 days to 23 months

[2] schoolchildren: age range 2 years to 11 years

Elderly patients

Basically the same dosage as for adults applies, but caution should be exercised in patients suffering from further diseases like cardiac insufficiency or renal insufficiency that may frequently be associated with advanced age.

Patients with burns

In order to calculate fluid requirements of patients with burns according to Parkland the following values may be used as guidance:

Adults

During the first 24 h Compound sodium lactate is administered in an amount of 4 ml/kg BW/%burn.

Children

During the first 24 h Compound sodium lactate is administered in an amount of 3 ml/kg BW/% burn.

The following volume is added as maintenance for children according to their weight:

- for children weighing 0 – 10 kg the amount is 4 ml/kg BW/h;
- for children weighing 10 – 20 kg the amount is 40 ml/ h + 2 ml/kg BW/h;
- for children weighing more than 20 kg, the amount is 60 ml/h + 1 ml/kg BW/h.

Use as vehicle solution

If Compound Sodium Lactate is used as vehicle solution for compatible electrolyte concentrates and medicinal products, the instructions for use relating to the medicinal product to be added must be observed.

Short-term volume replacement

In order to reconstitute normal blood volume values approximately a volume that is 3-5 fold higher than the amount of lost blood has to be administered.

Method of administration

Intravenous use

Precautions regarding pressure infusion, see section 4.4.

4.3 Contraindications

- Impairment of lactate utilisation with hyperlactataemia (see also section 4.4)
- Hyperhydration

This solution is not indicated for the treatment of severe metabolic acidosis.

4.4 Special warnings and precautions for use

This solution should only be administered with particular caution in the following conditions:

- hypertonic dehydration
- hyperkalaemia
- hypernatraemia
- hyperchloraemia
- hypercalcaemia
- hepatic insufficiency

High volume infusions must only be used under specific monitoring in patients with cardiac, renal or pulmonary failure lung or brain oedema, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia (see below).

Hyponatraemia Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, burns, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of hypotonic fluids.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Children, women in the fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, cerebral contusion and brain oedema) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia.

Lactate utilisation may be impaired in the presence of hypoxia or hepatic insufficiency.

Compound sodium lactate contains an amount of potassium that is similar to that of the physiological concentration of potassium in human blood. Nevertheless it is not suitable for the treatment of patients with severe potassium deficiency.

As the solution contains metabolisable ions (e.g. lactate) it may cause metabolic alkalosis. Therefore the solution has to be administered with caution in patients with metabolic alkalosis.

Solutions containing **sodium chloride** should be administered with caution to patients with

- cardiac insufficiency, peripheral oedema or extracellular hyper hydration,
- hypertension, impaired renal function, present or imminent eclampsia, aldosteronism or other conditions or treatment (e. g. corticoids/steroids) associated with sodium retention (see also section 4.5).

Solutions containing **potassium** salts should be administered with caution to patients with cardiac disease, conditions predisposing to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration, or extensive tissue destruction as occurs with severe burns.

Because of the presence of **calcium**:

- Care should be taken to prevent extravasation during intravenous infusion.
- The solution should be given cautiously to patients with impaired renal function or diseases associated with elevated vitamin D concentrations such as sarcoidosis. Thus administration of calcium containing solutions should be avoided in patients with nephroliths or with a history of nephroliths.
- In case of concomitant blood transfusion, the solution must not be administered via the same infusion set.

Patients with chronic hyponatraemia:

Too rapid correction of serum sodium levels must be avoided in patients with chronic hyponatraemia as rapid increases of serum sodium levels may in rare cases lead to osmotic adverse effects, e.g. the osmotic demyelinisation syndrome.

Paediatric patients

The solution should be administered only with special care to newborns younger than 3 months.

Use as vehicle solution

Please note: If this solution is used as vehicle solution the safety information of the additive provided by the respective manufacturer has to be taken into account.

Clinical monitoring should include checks of serum electrolyte levels, acid-base balance and water balance.

Serum lactate should be monitored carefully and if lactate accumulates during infusion, the dosage and infusion rate should be reduced or administration of the solution should eventually be discontinued.

In case of pressure infusion, which may be necessary in vital emergencies, all air must be removed from the plastic container and the infusion set before the solution is administered.

4.5 Interactions with other medicinal products and other forms of interaction

Administration of Compound Sodium Lactate in accordance with the recommended indications and contraindications does not increase the plasma concentrations of the electrolytes contained in it. In case there is a rise of any electrolyte's concentration due to other reasons the following interactions should be considered.

- Related to sodium
  Corticoids/steroids and carbenoxolone may be associated with the retention of sodium and water (with oedema and hypertension).
- Related to potassium
  Suxamethonium, potassium-sparing diuretics (amilorid, spironolactone, triamteren, alone or in association), ACE inhibitors (e.g. captopril, enalapril), Angiotensin II receptor antagonists (e.g. valsartan, losartan), tacrolimus, cyclosporine may increase the concentration of potassium in the plasma and lead to potentially fatal hyperkalaemia notably in case of renal failure increasing the hyperkalaemic effect.
- Related to calcium
  - *Digitalis glycosides* (cardiac glycosides) may undergo enhancement of their effects during hypercalcaemia and lead to serious or fatal cardiac arrhythmia.
  - Thiazid-diuretics and Vitamin D administered simultaneously with calcium may induce hypercalcaemia.
- If bisphosphonates, fluorides, several fluorchinolones and tetracyclines are administered simultaneously with calcium containing solutions the bioavailablility (reduced absorption) of above named medicinal products may be reduced.

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- Related to lactate
  The administration of **bicarbonate or bicarbonate precursor** like lactate leads to **alkalinisation of the urine** with increased renal clearance of acidic drugs (e.g. salicylic acid).The half life of basic medicinal products – especially sympathomimetics (e.g. ephedrine, pseudoephedrine) and stimulants (e.g. dexamphetaminesulphate, fenfluramine hydrochloride) will be prolonged if lactate containing solutions are administered simultaneously.
- Drugs leading to an increased vasopressin effect

The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i.v. fluids (see sections 4.2, 4.4 and 4.8).

- Drugs stimulating vasopressin release include: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics
- Drugs potentiating vasopressin action include: Chlorpropamide, NSAIDs, cyclophosphamide
- Vasopressin analogues include: Desmopressin, oxytocin, vasopressin, terlipressin
- Other medicinal products increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is a limited amount of data (less than 300 pregnancy outcomes) from the use of the components of Compound Sodium Lactate in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As all components of Compound Sodium Lactate are naturally present in the body and their biochemical properties are well known the product can be used as indicated.

Compound Sodium Lactate should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see section 4.4, 4.5 and 4.8).

Caution should be exercised in toxaemia of pregnancy.

Breast-feeding

Calcium is excreted in human milk, but at therapeutic doses of Compound Sodium Lactate no effects on the breastfed newborns/infants are anticipated. Therefore Compound Sodium Lactate can be used during breast-feeding..

Fertility

No special precautions.

4.7 Effects on ability to drive and use machines

This medicinal product has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects are listed according to their frequencies as follows:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (cannot be estimated from the available data)

Metabolism and nutrition disorders:
Not known: Hospital Acquired Hyponatraemia

Neurological disorders:
Not known: Hyponatraemic encephalopathy

Hospital acquired hyponatraemia may cause irreversible brain injury and death due to development of acute hyponatraemic encephalopathy (see sections 4.2 and 4.4).

4.9 Overdose

Symptoms

Overdose may result in hyperhydration with increased skin tension, venous congestion, oedema - possibly also lung or brain oedema -, electrolyte and acid-base imbalances as well as serum hyperosmolarity.

Treatment

Cessation of infusion, administration of diuretics with continuous monitoring of serum electrolytes, correction of electrolyte and acid-base imbalances.
In severe cases of overdose dialysis may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Solutions affecting the electrolyte balance, electrolytes
ATC-Code: B05B B01

Mechanism of action

The solution contains the essential ions present in extracellular fluid. Therefore the pharmacodynamic properties of the ions contained in it (sodium, potassium, calcium, chloride, lactate) are the same as in normal physiology.

Lactate is a key substrate in intermediary metabolism. Inter alia, it is oxidised to bicarbonate, exerting a mild alkalinising effect.

Pharmacodynamic effect

Compound Sodium Lactate has a similar electrolyte composition as the extracellular fluid (neglecting some very minor differences). It is used for correction of serum electrolyte and acid-base imbalances. Electrolytes are administered in order to achieve or to maintain a normal osmotic situation in both the extra- and the intracellular space.

Due to its distribution (see below) the solution has a short haemodynamic effect.

On account of the proportion of metabolisable anions Compound Sodium Lactate is particularly indicated in patients with a tendency to acidosis.

5.2 Pharmacokinetic properties

Absorption

Since the ingredients of Compound Sodium Lactate are infused intravenously their bioavailability is 100 %.

Distribution

Administration of Compound Sodium Lactate directly results in replenishment of the interstitial space which amounts to about 2/3 of the extracellular space. Only 1/3 of the administered volume stays in the intravascular space. Thus the solution has a short haemodynamic effect.

Biotransformation, elimination

Potassium, sodium, and chloride are mainly excreted in urine but small amounts are lost via the skin and also the intestinal tract. Especially surgery results in increased urinary excretion of potassium while water and sodium is retained.

Calcium is mainly excreted via the functioning kidneys. Small amounts are lost via the skin, hair, and nails. Calcium passes the placenta and is excreted into breast-milk.

Lactate is converted to bicarbonate and CO_2, both are normal body constituents. Plasma concentrations of bicarbonate and lactate are regulated by the kidneys and the plasma concentration of CO_2 is regulated by the lung. Lactate metabolism is impaired in states of hypoxia and in liver insufficiency.

5.3 Preclinical safety data

Non-clinical data for the individual components of Compound Sodium Lactate reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections

6.2 Incompatibilities

Medicinal products containing oxalate, phosphate, or carbonate/bicarbonate may cause precipitation upon mixing with Compound Sodium Lactate.

No other medicinal product or substance should be added to the fluid unless known to be compatible and dilution took place under aseptic conditions.

6.3 Shelf life

- unopened

3 years

- after first opening

Not applicable, see section 6.6

- after admixture of additives

From the microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 30 °C.
For storage conditions after admixture of additives to medicinal product, see section 6.3.

6.5 Nature and contents of container

- Bottles of low-density polyethylene (LD-PE), contents: 500 ml, 1000 ml
  available in packs of 10 × 500 ml, 10 × 1000 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Only to be used if solution is clear, colourless and the container and its closure do not show visible signs of damage.

Containers are for single-use. Discard container and any unused content after use.
Do not reconnect partially used containers.

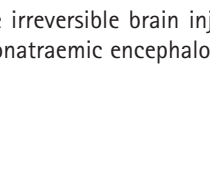
7. DATE OF REVISION OF THE TEXT

December 2019

Instructions for Handling the Ecoflac plus Container

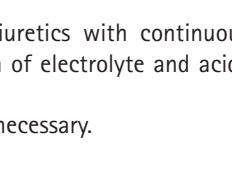
1. Gravity infusion

- Insert infusion set, fill half of drip chamber, fill infusion tube avoiding bubbles.
- Close air vent of infusion set.
- Connect infusion tube to cannula/catheter.
- Open clamp and start infusion with air vent closed

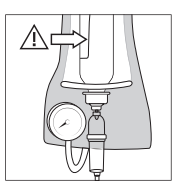


2. Pressure infusion

- Insert infusion set.
- Hold container upright.
- Leave clamp open, expel air from container and fill half of drip chamber.
- Turn container and expel air from infusion device.
- Close clamp.



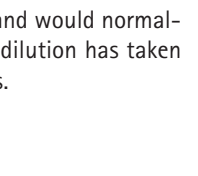
- Place container turned at 90° in pressure cuff (pressure is applied on the side of the container).
- Build up pressure.
- Open clamp and start infusion.



3. Admixture of additives

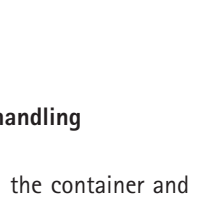
Addition via cannula

- Insert cannula vertically.



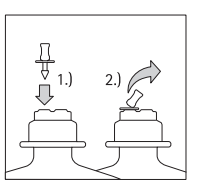
Addition using the transfer cap (Ecoflac® Mix)

1.) Attach transfer cap to the container.
2.) Attach vial to the other end (click!).
3.) Transfer solution into the vial containing the additive by pressing the Ecoflac® plus container. Dissolve additive completely. Turn Ecoflac® plus container with attached vial upside down. Press air into the vial until all solution has been transferred into the Ecoflac® plus container.



Documentation of addition and re-sealing the injection port with Ecopin®

1.) Insert Ecopin® into injection port
2.) Break off handle



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