# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Compound Sodium Lactate Intravenous Infusion BP, Ecobag (Hartmann's Solution)

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution contain

Sodium Chloride 6.00 g
Sodium Lactate Solution (50% w/w) 6.24 g
(equivalent to sodium lactate, 3.12 g)
Potassium Chloride 0.40 g
Calcium Chloride Dihydrate 0.27 g

*Electrolyte concentrations:*

Sodium 131 mmol/l
Potassium 5 mmol/l
Calcium 2 mmol/l
Chloride 111 mmol/l
Lactate 29 mmol/l

*Excipients*

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for infusion
A clear, colourless, aqueous solution.

Theoretical osmolarity: 278 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

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.

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).

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 0.08 – 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 infants1
4– 6 ml per kg BW per hour for toddlers[1]
2-4 ml per kg BW per hour for school children2
1 infants and toddlers: age range 28 days to 23 months
2 school children: 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 Intravenous Infusion BP is administered in an amount of 4 ml/kg BW/%burn.

*Children*
During the first 24h Compound Sodium Lactate Intravenous Infusion BP is administered in an amount of 3 ml/kgBW/% 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/kgBW/h;
- for children weighing more than 20 kg, the amount is 60 ml/h +1 ml/kgBW/h.

***Use as vehicle solution***
If Compound Sodium Lactate Intravenous Infusion BP 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.

**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
• Concomitant use of ceftriaxone and intravenous calcium-containing products is contraindicated in premature neonates and neonates (≤ 28 days of age).
• Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

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

**4.4 Special warnings and precautions for use**

Compound Sodium Lactate Intravenous Infusion BP should only be administered with particular caution in the following conditions:
- Hypertonic dehydration,
- Hyperkalaemia,
- Hyperchloraemia,
- Hypernatraemia,
- 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.

Patients receiving ceftriaxone
In patients of any age ceftriaxone must not be mixed or administered simultaneously with any calcium-containing intravenous solutions even via different infusion lines or different infusion sites (see section 6.2).
Cases of fatal reactions with calcium-ceftriaxone precipitates in lungs and kidneys in premature and full-term new borns aged less than 1 month have been described.
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.

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

Compound Sodium Lactate Intravenous Infusion BP 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 hyperhydration,

- hypertension, impaired renal function,present or imminent pre-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 extra vasation 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 ofserum 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, allair must be removed from the plastic container and the infusion set before the solution is administered as otherwise there is a risk of producing air embolism during infusion.

**4.5 Interaction with other medicinal products and other forms of interactions**

Administration of Compound Sodium Lactate Intravenous Infusion BP 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-sparingdiuretics (amiloride, spironolactone, triamterene, 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
- *Digitalisglycosides* (cardiac glycosides) may undergo enhancement of their effects during hypercalcaemia and lead to serious or fatal cardiac arrhythmia.
- Thiazide-diuretics and Vitamin D administered simultaneously with calcium may induce hypercalcaemia.

• If bisphosphonates, fluorides, several fluoroquinolones and tetracyclines are administered simultaneously with calcium containing solutions the bioavailablility (reduced absorption) of above named medicinal products may be reduced.
• 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.dexamphetamine sulphate, 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.

• Interaction with ceftriaxone See sections 4.4 and 6.2

**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 Intravenous Infusion BP in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section5.3).
As all components of Compound Sodium Lactate Intravenous Infusion BP 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 present or imminent pre-eclampsia.

*Breast-feeding*
Calcium is excreted in human milk, but at therapeutic doses of Compound Sodium Lactate Intravenous Infusion BP no effects on the breastfed newborns/infants are anticipated. Therefore Compound Sodium Lactate Intravenous In fusion BP 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

Nervous system disorders:
Not known: Acute 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).

**Reporting ofsuspected adversereactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

**4.9 Overdose**

***Symptoms***

Overdose may result in overhydration 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 Intravenous Infusion BP 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 Intravenous Infusion BP is particularly indicated in patients with a tendency to acidosis.

**5.2 Pharmacokinetic properties**

*Absorption*

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

*Distribution*

Administration of Compound Sodium Lactate Intravenous Infusion BP 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 Lacctate 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 Intravenous Infusion BP.

Physical incompatibility has also been reported with amphotericin, cephalothin sodium, ceftriaxone (see section 4.4).

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*

2 years (as packed for sale).

- *after first opening*
Once opened: Use immediately. Discard any unused contents.- *after admixture of additives*
Chemical and physical in-use stability of any additive medication at the pH of "Compound Sodium Lactate Intravenous Infusion BP" in the container should be established prior to use.

From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

**6.4 Special precautions for storage**

Do not store above 25°C.
For storage conditions after admixture of additives to medicinal product, see section 6.3.

**6.5 Nature and contents of container**

Plastic bags (Ecobag) with butyl rubber stoppers and outer protective bags. The primary bag consists of a three layer plastic laminate with a polypropylene inner bag and a polyamide outer layer.

- 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 of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

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 MARKETING AUTHORISATION HOLDER**

B. Braun Medical Limited
3 Naas Road Industrial Park
Dublin 12
Ireland

**8 MARKETING AUTHORISATION NUMBER**

PA0179/004/008

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of First Authorisation: 30th March 2007

Date of Last Renewal: 30th March 2012

**10 DATE OF REVISION OF THE TEXT**

March 2018