Otsuka Otsuka Pharmaceutical India Private Limited

Artwork Code : XXXXXXXXXX-XX					**Artwork Req. No: -**		
Quality of Paper/Board : Super Sun Shine					**Size of Artwork (In mm) : 210x266**		
Quality of Gum :					**GSM of Paper/Board : 60 GSM**		
Colour Code :	**BLACK** ■	**Pantone** ☐	**Pantone** ☐	**Pantone** ☐	**Pantone** ☐	**Pantone** ☐	**Pantone** ☐	**Pantone** ☐
Barcode Information:							
Barcode Scan Report:							
Packing: 500 ml NH PLB, EH PLB, BAG					**Plant Location : MF 02**		
Country: Malaysia					**Language : English**		
Ref. Code Creation/Blockage Note:					**Artwork Control Key No.:**		
"Controlled Copy" Holder (1)		**(2)**		**(3)**	**(4)**	**(5)**	

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.

15. Preclinical safety data
Not applicable

16. Packaging Size
500 mL Nipple Head Plastic Bottle, Euro Head Plastic Bottle & Non PVC Bag.

17. Storage Condition
Store at temperature not exceeding 30°C.

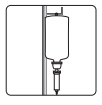
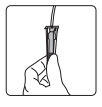
18. Instructions for Use & Handling

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.

Instructions for Handling
For Plastic bottle
Opening
- Remove the container from the overwrap pouch just before use.
- Check for minute leaks by squeezing bottle firmly. If leaks are found, discard Solution, as sterility may be impaired.
- Check solution for limpidity and absence of foreign matter. If solution is not clear or contains foreign matter, discard the solution.

Preparation for administration



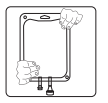
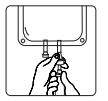
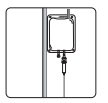
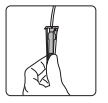
Use sterile material for preparation and administration.
- Hang container on IV bottle stand through hang hole support.
- Remove the aluminium foil from port of plastic bottle container.
- Use an aseptic method to set up the infusion.
- Attach administration set. Refer to directions of the accompanying set for connection, priming of the set and administration of the solution.

Techniques for injection of additive medications
Warning: Additives may be incompatible. Please check the package insert of the medication before adding it to solution.
To add medication before administration
- Using syringe with an appropriate needle, puncture resalable medication port and inject.
- Mix solution and medication thoroughly.

Caution: Do not store bottle containing added medications.

For Non PVC bag:
Opening
- Remove the container from the overwrap pouch just before use.
- Check for minute leaks by squeezing bag firmly. If leaks are found, discard Solution, as sterility may be impaired.
- Check solution for limpidity and absence of foreign matter. If solution is not clear or contains foreign matter, discard the solution.

Preparation for administration

Use sterile material for preparation and administration.
- Hang container on IV bag stand through hang hole support.
- Remove the flip off cap from bag container.
- Use an aseptic method to set up the infusion.
- Attach administration set. Refer to directions of the accompanying set for connection, priming of the set and administration of the solution.

Techniques for injection of additive medications
Warning: Additives may be incompatible. Please check the package insert of the medication before adding it to solution.
To add medication before administration
- Using syringe with an appropriate needle, puncture resalable medication port and inject.
- Mix solution and medication thoroughly.

Caution: Do not store bag containing added medications.

19. Manufacturer

Otsuka
Otsuka Pharmaceutical India Private Limited
Survey No.199 to 201, 208 To 210,
Village-Vasana-Chacharwadi, Tal: Sanand,
382213 District-Ahmedabad, India.

20. Product Registration Holder, Importer & Distributor
BioCare Pharmaceutical (M) Sdn. Bhd.
No.28G, 28-1 & 28-2, Pusat Dagangan PJCC
Jalan PJS 5/28 46150 Petaling Jaya,
Selangor, Malaysia.

Date of revision: 09-Dec-2024

MAL No.:-

XXXXXXXXXX
"Artwork number will be generated at the time of commercial process"

COMPOUND SODIUM LACTATE INTRAVENOUS INFUSION BP (Hartmann's Solution)

RL

For I.V. infusion use only

1. Composition
Active Ingredient:
Each 100 mL Solution contains:

Sodium Lactate Solution USP	
Equivalent to Sodium Lactate	0.320 g
Sodium Chloride BP	0.600 g
Potassium Chloride BP	0.040 g
Calcium Chloride Dihydrate BP	0.027 g

Excipients:
Water for Injections BP

2. Product Description
It is a clear and colourless solution essentially free from visible particles available in 500 mL Nipple Head Plastic Bottle, Euro Head Plastic Bottle & Euro head Non PVC Bag.

3. Indication
- 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. Dosage And Mode Of Administration
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 nonosmotic 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. Monitoring of serum sodium is particularly important for hypotonic fluids. Compound Sodium Lactate Intravenous Infusion B.P. 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 infants1
4 - 6 ml per kg BW per hour for toddlers1
2 - 4 ml per kg BW per hour for school children 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 Intravenous Infusion B.P. is administered in an amount of 4 ml/kg BW/%burn.
Children
During the first 24 h Compound Sodium Lactate Intravenous Infusion B.P. 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 Intravenous Infusion B.P. 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.

5. Contraindications
- Impairment of lactate utilisation with hyperlactataemia
- Hyperhydration

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

6. Warning and Precaution
This solution should only be administered with particular caution in the
following conditions:
- hypertonic dehydration
- hyperkalaemia
- hypernatraemia

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Font Type: Times New Roman

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- 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 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 utilization may be impaired in the presence of hypoxia or hepatic insufficiency.
Compound Sodium Lactate Intravenous Infusion B.P. 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.

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. [Only for polyethylene bottles]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.

7. Pregnant And Breast Feeding Woman
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 B.P. in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As all components of Compound Sodium Lactate Intravenous Infusion B.P. are naturally present in the body and their biochemical properties are well known the product can be used as indicated. Compound Sodium Lactate Intravenous Infusion B.P. should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin.
Caution should be exercised in toxaemia of pregnancy.

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

Fertility
No special precautions

8. Effects On Driving And Machine Operation
This medicinal product has no influence on the ability to drive and use machines.

9. Interactions with Other Medicaments
Administration of Compound Sodium Lactate Intravenous Infusion B.P. 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.

- 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.

- 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.

10. Incompatibilities:
Medicinal products containing oxalate, phosphate, or carbonate/bicarbonate may cause precipitation upon mixing with RL - Compound Sodium Lactate Intravenous Infusion BP.
No other medicinal product or substance should be added to the fluid unless known to be compatible and dilution took place under aseptic conditions.

11. Side Effect
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

12. Overdose: Symptom and Treatment
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.

13. 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 B.P. has a similar electrolyte composition as the extracellular fluid (neglecting some very minor differences). It is used for correction of serum electrolyte and acidbase 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 B.P. is particularly indicated in patients with a tendency to acidosis.

14. Pharmacokinetic Properties
Absorption
Since the ingredients of Compound Sodium Lactate Intravenous Infusion B.P. are infused intravenously their bioavailability is 100 %.

Distribution
Administration of Compound Sodium Lactate Intravenous Infusion B.P. directly results in replenishment of the interstitial space which amounts to about ⅔ of the extracellular space. Only ⅓ 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