SCHEDULING STATUS

S3

1. Name of the Medicinal Product

Ringer Lactate Infusion B. Braun, Solution for infusion

2. Qualitative and Quantitative Composition

Each 1000 mL of solution contains

Sodium chloride	6,00 g
Sodium lactate	3,2 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
Osmolarity	279 mOsmol/L

Excipients

For 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

Reduced plasma volume resulting from burns, trauma, severe diarrhoea and surgery.

Reduced blood volumes resulting from haemorrhage.

4.2 Posology and method of administration

Infuse as prescribed, taking into consideration central venous pressure and blood pressure.

4.3. Contraindications

- Renal insufficiency (see also section 4.4)
- The crush syndrome
- Severe hemolytoic reactions
- Adrenocortical insufficiency
- Hyperkalaemia (see also section 4.4)
- Early postoperative oliguria, except when gastrointestinal drainage is being done
- Hypernatraemia (see also section 4.4)

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.
Ringer Lactate Infusion B. Braun 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.

Only for polyethylene bottles and plastic bags:

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 Interaction with other medicinal products and other forms of interaction

Administration of **Ringer Lactate Infusion B. Braun** 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 (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.

4.9 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

Class of Medicine: A.24 Mineral substitutes, 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

Ringer Lactate Infusion B. Braun 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.

5.2 Pharmacokinetic properties

Absorption

Since the ingredients of **Ringer Lactate Infusion B. Braun** are infused intravenously their bioavailability is 100 %.

Distribution

Administration of **Ringer Lactate Infusion B. Braun** 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 **Ringer Lactate Infusion B. Braun** 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 **Ringer Lactate Infusion B. Braun**.

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

After first opening of the container: **Ringer lactate Infusion B. Braun must** be used immediately after first opening.

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

Store at or below 25 °C.

Keep in original container until required for use.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

A clear, colourless to slightly straw-coloured liquid.

A polyvinylchloride plastic bag in a polyethylene overwrap which is slightly opaque

presented in the following sizes:

200 mL and 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 HOLDER OF THE CERTIFICATE OF REGISTRATION:

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8. REGISTRATION NUMBER:

32/24/0130

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION:

21 January 2000

10. DATE OF REVISION OF THE TEXT

28 May 2021