DIRECTIONS FOR USE

B. Braun Melsungen AG - 34209 Melsungen, Germany

Ringer's Solution

1. NAME OF THE MEDICINAL PRODUCT

Ringer's Solution for Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution contains:

Sodium chloride	8.60 g
Potassium chloride	0.30 g
Calcium chloride dihydrate	0.33 g

Electrolyte concentrations:

Sodium	147	mmol/l
Potassium	4.0	mmol/l
Calcium	2.2	mmol/l
Chloride	156	mmol/l

Excipient(s) with known effect:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion
Clear, colourless aqueous solution

Theoretical osmolarity:	309 mOsm/l
Acidity (titration to pH 7.4):	< 0.3 mmol/l
pH:	5.0 - 7.0

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

- Fluid and electrolyte substitution in the condition of hypochloraemic alkalosis;
- Chloride losses;
- Isotonic or hypotonic dehydration;
- Short-term intravascular volume replacement;
- Vehicle solution for compatible medicinal products.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Recommended dosage schedule

Fluid and electrolyte substitution and treatment of dehydration:

The dosage of Ringer's Solution for Infusion depends on the patient's fluid and electrolyte balance, age, weight, clinical condition and physiological (acid-base) status of the patient.

Adults

Maximum daily dose

For routine maintenance, the daily dose should not exceed 40 ml per kg body weight per day.

Any additional losses (due to e.g. fever, diarrhoea, vomiting) should be substituted according to the volume and composition of the lost fluids.

In case of dehydration the dose of 40 ml/kg body weight (BW) per day might need to be exceeded. The dose should be calculated based on the severity of the dehydration and the clinical condition of the patient.

Maximum infusion rate

The maximum infusion rate should not exceed 5 ml per kg body weight per hour, corresponding to 1.7 drops per kg body weight per min.

For short term intravascular volume replacement the maximum infusion rate depends on the individual clinical situation of the patient but as a general recommendation a bolus of 500ml over less than 15 minutes might be applied, e.g. by pressure infusion.

Elderly population

See section 4.4

Paediatric population

Maximum daily dose

For routine maintenance the following daily doses should not be exceeded.

Age	Doses (ml/kg b.w./d)
1st day of life *	120
2nd day of life *	120
3rd day of life *	130
4th day of life *	150
5th day of life *	160
6th day of life *	180
1st month of life	160
from 2nd month of life	150
1-2 years	120
3-5 years	100
6-12 years	80
13-18 years	70

* for term neonates

Any additional losses (due to e.g. fever, diarrhoea, vomiting, etc.) should be substituted according to the volume and composition of the lost fluids.
In case of dehydration the above stated dose might need to be exceeded. The dose should be calculated based on the severity of the dehydration and the clinical condition of the patient.

Maximum infusion rate for routine maintenence

Body Weight	ml/ hour
0-10 kg	4 ml/kg b.w./h
10-20 kg	40 ml/h + 2 ml/kg b.w./h above 10 kg
>20 kg	60 ml/h + 1 ml/kg b.w./h above 20 kg

Short-term intravascular volume replacement

The dosage has to be calculated based on the individual clinical situation of the patient. Thus, a maximum daily dose can not be given.

Use as vehicle solution

If Ringer's Solution for Infusion is used as vehicle solution, the dosage and duration of use depend on the instructions given for the medicinal products to be dissolved or diluted.

Method of administration

Intravenous infusion

4.3 CONTRAINDICATIONS

Ringer's Solution for Infusion must not be administered in the following conditions:

- States of hyperhydration
- Acute congestive heart failure
- Severe renal insufficiency with oligo- or anuria
- Severe hypernatraemia
- Severe hyperchloraemia

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Ringer's Solution for Infusion should only be administered with particular caution in the following conditions:

- Hypertonic dehydration,
- Hypernatraemia,
- Hyperchloraemia,
- Disorders that are frequently associated with hyperkalaemia e.g. Addison's disease or sickle cell anaemia.Disorders where restriction of sodium and fluid intake are indicated, such as cardiac insufficiency, generalised oedema, pulmonary oedema, hypertension, pre-eclampsia, renal insufficiency or aldosteronism.
- Concomitant use of medicinal products that increase the serum potassium level (see section 4.5)
- Disorders where restriction of calcium intake is indicated, such as sarcoidosis

Clinical monitoring should include checks of the serum electrolyte concentration, the acid-base balance and the fluid balance. In addition, adequate urine flow must be ensured.

In cases of pre-existing hyponatraemia, to prevent development of the osmotic demyelination syndrome the increase of the serum sodium level should not exceed 9 mmol/l/day. As a general recommendation a correction rate of 4 to 6 mmol/l /day is reasonable in most cases, depending on patient condition and concomitant risk factors.
Care should be taken to prevent extravasation during intravenous infusion since calcium in the extravascular space may cause local reactions up to necrosis.
Emergency situations:
If in the management of acute hypovolaemia the solution must be administered rapidly by pressure infusion, care must be taken to expel all air from the container and the giving set prior to infusion (see section 6.6), as otherwise there is a risk of producing air embolism during infusion.

Paediatric population

Intravenous fluid therapy should be closely monitored in the paediatric population as they may have impaired ability to regulate fluids and electrolytes. Adequate urine flow must be ensured and careful monitoring of fluid balance, plasma and urinary electrolyte concentrations are essential.

Elderly patients

Elderly patients, who are more likely to suffer from cardiac insufficiency and renal impairment, should be closely monitored during treatment, and the dosage should be carefully adjusted, in order to avoid cardiocirculatory and renal complications resulting from hypervolaemia.

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.

4.5 INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Medicinal products interacting with sodium

The concomitant use of sodium-retaining drugs (e.g. corticosteroids, non-steroidal anti-inflammatory agents) may lead to oedema.

Medicinal products interacting with potassium

Potassium-sparing diuretics, ACE inhibitors, Angiotensin II receptor antagonists, non-steroidal anti-inflammatory agents, ciclosporine, tacrolimus or suxamethonium can increase the serum potassium level. The concomitant administration of potassium-containing solutions and those drugs may lead to severe hyperkalaemia, which may in turn lead to cardiac arrhythmia.
Administration of potassium can reduce the therapeutic effect of cardiac glycosides.
ACTH, corticosteroids and loop diuretics can increase the renal elimination of potassium.

Medicinal products interacting with calcium

Administration of calcium can intensify the inotropic and toxic effect of cardiac glycosides. Especially after IV administration, calcium can cause cardiac arrhythmia in digitalis-treated patients.
Thiazide-diuretics and Vitamin D increase the renal absorption of calcium.
Calcium complexes tetracycline antibiotics rendering them inactive.

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy

There are limited data (less than 300 pregnancy outcomes) regarding the use of sodium chloride, potassium chloride and calcium chloride in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).

As all components of the product are naturally present in the body the product can be used if indicated.
Nevertheless, caution should be exercised when this medicine is used during pregnancy especially in case of pre-eclampsia (see section 4.4).

Breast-feeding

As all active ingredients are present in human body, no negative effects are anticipated if used during lactation. Therefore, the solution can be used if indicated.

Fertility

No data available, however no negative effects are expected.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Ringer's Solution for Infusion has no or negligible influence on the ability to drive and use machines.

4.8 UNDESIRABLE EFFECTS

None known if used according to the directions given.

4.9 OVERDOSE

Symptoms

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

Treatment

Cessation of infusion, administration of diuretics with continuous monitoring of serum electrolytes, correction of electrolyte and acid-base imbalances.

5. PHARAMCOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Solutions affecting the electrolyte balance
ATC Code: B05B B01 (Electrolytes)
Ringer's Solution for Infusion has a similar electrolyte composition as the extracellular fluid.

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 relatively high chloride content the solution has a mild acidifying effect

5.2 PHARMACOKINETIC PROPERTIES

Absorption

As the solution is administered by intravenous infusion the bioavailabilty of its constituents is 100%.

Distribution

Administration of Ringer's Solution for Infusion 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.

The electrolytes are transferred to their respective electrolyte pools in the body. Sodium and chloride are mainly distributed in the extracellular space, whereas potassium and calcium are mainly distributed in the intracellular spare.

Biotransformation

Sodium, potassium, calcium and chloride are not metabolised in the strict sense.

Elimination

The electrolytes are mainly excreted in urine but small amounts are also excreted via the skin and the intestinal tract.

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5.3 PRECLINICAL SAFETY DATA

Non-clinical studies have not been performed with Ringer's Solution. Since the components of Ringer's Solution are physiologically present in human body, toxic effects of the single components are not expected when the product is used according to the instructions.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Water for injections

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
Calcium cations can form complexes with many substances and this may result in precipitation

6.3 SHELF LIFE

Unopened:

- Polyethylene bottles 3 years

After first opening:
Not applicable, see section 6.6

After addition of additives:
From a 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

Bottles:
Do not store above 30 °C

For storage conditions of the medicinal product after addition of additives, see section 6.3.

6.5 NATURE AND CONTENTS OF CONTAINER

- Polyethylene bottles,
  contents: 500 ml, 1000 ml
  available in packs of
  1 × 500 ml, 10 × 500 ml
  1 × 1000 ml, 10 × 1000 ml

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Any unused product or waste material should be disposed of in accordance with local requirements.
Containers are for single use only. Discard container and any unused content after use.
Only to be used if the solution is clear and colourless and the container and its closure are undamaged.

In the case of a rapid infusion under pressure, using plastic container with air space inside, the container and infusion set must be emptied of air before the infusion is started (see section 4.4).

Before using this product together with other solutions via e.g. a Y connector, the compatibility of these fluids should be checked.

7. DATE OF REVISION OF THE TEXT

March 2016

B. Braun Melsungen AG
34209 Melsungen, Germany