PRODUCT INFORMATION
RINGER’S SOLUTION FOR INTRAVENOUS INFUSION

NAME OF THE MEDICINE

Composition: the ingredients in Ringer’s Solution for Intravenous Infusion (Ringer’s Solution) comprise sodium chloride (8.6 g/L), potassium chloride (0.3 g/L) and calcium chloride dihydrate (0.33 g/L) in Water for Injections. Hydrochloric acid and/or sodium hydroxide may be added for pH adjustment.

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Molecular structure</th>
<th>Molecular mass</th>
<th>CAS number</th>
</tr>
</thead>
<tbody>
<tr>
<td>sodium chloride</td>
<td>NaCl</td>
<td>58.44</td>
<td>7647-14-5</td>
</tr>
<tr>
<td>potassium chloride</td>
<td>KCl</td>
<td>74.6</td>
<td>7447-40-7</td>
</tr>
<tr>
<td>calcium chloride (dihydrate)</td>
<td>CaCl₂·2H₂O</td>
<td>147</td>
<td>10035-04-8</td>
</tr>
</tbody>
</table>

DESCRIPTION

Potassium chloride and sodium chloride occur as a colourless or white crystal and are freely soluble in water. Calcium chloride is a white, crystalline powder, hygroscopic and freely soluble in water.

Ringer’s Solution is sterile and non-pyrogenic. There is no antimicrobial agent or buffer added. They are isotonic intravenous solutions with pH of 5.0 – 7.5 and an osmolarity of 308 mOsmol/L.

PHARMACOLOGY

Pharmacodynamics:
Ringer’s Solution is an isotonic solution of electrolytes. The constituents of Ringer’s Solution and their concentrations are designed to match those of plasma.

The pharmacodynamic properties of this solution are those of its components (water, sodium, potassium, calcium, and chloride). The main effect of Ringer’s Solution for is the expansion of the extracellular compartment including both the interstitial and intravascular fluids.

Ions, such as sodium, circulate through the cell membrane using various mechanisms of transport among which is the sodium pump (Na-K-ATPase). Sodium plays an important role in neurotransmission and cardiac electrophysiology, and also in its renal metabolism.

Potassium is essential for numerous metabolic and physiological processes including nerve conduction, muscle contraction, and acid-base regulation. A normal concentration of potassium in plasma is about 3.5 to 5.0 mmoles per litre. Potassium is predominantly an intracellular cation, primarily found in muscle; only about 2% is present in the extracellular...
The passage of potassium into the cells and retention against the concentration gradient requires active transport via the Na+/K+ ATPase enzyme.

Approximately 99% of calcium is incorporated into the skeleton. The remaining 1% is found in body tissues and fluids, and is essential for normal nerve conduction, muscle activity, and blood coagulation.

Chloride is mainly an extracellular anion found in low concentration in bone and in high concentration in some components of connective tissue such as collagen. Intracellular chloride is in high concentration in red blood cells and gastric mucosa. The balance of anions and cations are regulated by the kidneys. Reabsorption of chloride generally follows reabsorption of sodium.

**Pharmacokinetics**

The pharmacokinetic properties of this solution are those of its components (sodium chloride, potassium chloride, and calcium chloride).

The volume and the ionic composition of the extracellular and the intracellular compartments are as follows:

**Extracellular fluid:** approximately 19 litres

<table>
<thead>
<tr>
<th>Component</th>
<th>Concentration (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>142</td>
</tr>
<tr>
<td>Potassium</td>
<td>5</td>
</tr>
<tr>
<td>Calcium</td>
<td>2.5</td>
</tr>
<tr>
<td>Chloride</td>
<td>103</td>
</tr>
</tbody>
</table>

**Intracellular fluid:** approximately 23 litres

<table>
<thead>
<tr>
<th>Component</th>
<th>Concentration (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>15</td>
</tr>
<tr>
<td>Potassium</td>
<td>150</td>
</tr>
<tr>
<td>Calcium</td>
<td>1</td>
</tr>
<tr>
<td>Chloride</td>
<td>1</td>
</tr>
</tbody>
</table>

After injection of radiosodium (24Na), the half life is 11 to 13 days for 99% of the injected Na and one year for the remaining 1%. The distribution varies according to tissues: it is fast in muscles, liver, kidney, cartilage and skin; it is slow in erythrocytes and neurones; it is very slow in the bone. Sodium is predominantly excreted by the kidney, but there is extensive renal reabsorption. Small amounts of sodium are lost in the faeces and sweat.

Factors influencing potassium transfer between intracellular and extracellular fluid such as acid-base disturbances can distort the relationship between plasma concentrations and total body stores. Potassium is excreted mainly by the kidneys; it is secreted in the distal tubules in exchange of sodium or hydrogen ions. The capacity of the kidneys to conserve potassium is poor and some urinary excretion of potassium continues even when there is severe depletion. Some potassium is excreted in the faeces and small amounts may also be excreted in sweat.

The concentration of calcium in plasma is regulated by parathyroid hormone, calcitonin, and vitamin D. About 47% of calcium in plasma is in the ionised physiologically active form, about 6% is complexed with anions such as phosphate or citrate, and the remainder is bound to proteins, principally albumin. If the plasma-albumin concentration is raised (as in dehydration) or reduced (as is common in malignancy) it will affect the proportion of ionised calcium. Thus, the total plasma-calcium concentration is commonly adjusted for plasma albumin. Excess of calcium is predominantly excreted renally. Unabsorbed calcium is eliminated in the faeces, together with that secreted in the bile and pancreatic juice. Minor
amounts are lost in the sweat, skin, hair, and nails. Calcium crosses the placenta and is distributed into breast milk.

INDICATIONS

Ringer’s Solution is indicated for restoring the loss of water and electrolytes as required by the clinical condition of the patient.

CONTRAINDICATIONS

Ringer’s Solution is contraindicated in patients with:
- Extracellular hyperhydration or hypervolaemia
- Hypertonic dehydration
- Hyperkalaemia
- Hypernatraemia
- Hypercalcaemia
- Hyperchloreaemia.
- Severe renal insufficiency (with oliguria/anuria).
- Uncompensated cardiac failure
- Severe hypertension
- General oedema and ascitic cirrhosis
- Concomitant digitalis therapy (see Interactions with other Medicines).

As for other calcium-containing infusion solutions, concomitant treatment with ceftriaxone and Ringer’s Solution is contraindicated in newborns (≤28 days of age), even if separate infusion lines are used (risk of fatal ceftriaxone calcium salt precipitation in the neonate’s bloodstream).

PRECAUTIONS

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure.

Solutions containing sodium chloride should be administered with caution to patients with hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function, pre-eclampsia, aldosteronism or other conditions or treatment (e.g. corticoids/steroids) associated with sodium retention (see Interactions with other Medicines).

Solutions containing potassium salts should be administered with caution to patients with cardiac disease, or 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
- in case of concomitant blood transfusion, the solution must not be administered via the same infusion set because of the risk of coagulation.
Ringer’s Solution contains insufficient concentration of potassium and calcium to be used for maintenance of these ions or to correct their deficits. Hence, after dehydration is treated, the IV fluid has to be changed to a maintenance fluid that will provide these ions.

During long-term parenteral treatment, a convenient nutritive supply must be given to the patient.

**Ceftriaxone Interaction**
In patients older than 28 days (including adults), ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including Ringer’s Solution, through the same infusion line (e.g., via a Y-connector). If the same infusion line is used for sequential administration, the line must be thoroughly flushed between infusions with a compatible fluid.

**Use in pregnancy**
Ringer’s Solution may be used during pregnancy as long as the electrolyte and fluid balance is controlled. However, the potential risks and benefits for each specific patient should be carefully considered before using Ringer’s Solution in pregnant women. When a medicinal product is added to Ringer’s Solution, the nature of the drug and its use during pregnancy have to be considered separately.

**Use in lactation**
Ringer’s Solution may be used during lactation as long as the electrolyte and fluid balance is controlled. However, the potential risks and benefits for each specific patient should be carefully considered before using Ringer’s Solution in lactating women. When a medicinal product is added to Ringer’s Solution, the nature of the drug and its use during lactation have to be considered separately.

**Paediatric Use**
The use of Ringer’s Solution in paediatric patients should be based on clinical practice.

**Geriatric Use**
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

**Genotoxicity/ Carcinogenicity**
The active ingredients potassium chloride, sodium chloride and calcium chloride are neither carcinogenic nor mutagenic at physiological concentrations.

**INTERACTIONS WITH OTHER MEDICINES**
Interaction related to the presence of sodium:
- Corticoids/steroids and carbenoxolone which are associated with the retention of sodium and water (with oedema and hypertension).

Interaction related to the presence of potassium:
- Potassium-sparing diuretics (amiloride, spironolactone, triamterene, alone or in association)
- Angiotensin converting enzyme (ACE) inhibitors and, by extrapolation, angiotensin II receptor antagonists (ARAs)
- Tacrolimus, cyclosporine.
They increase concentration of potassium in the plasma and may lead to potentially fatal hyperkalaemia notably in case of a renal failure increasing the hyperkalaemic effect.

Interaction related to the presence of calcium:
- Digitalis glycosides (digitalis cardiotonics) whose effects are enhanced by the presence of calcium and may lead to serious or fatal cardiac arrhythmia
- Thiazide diuretics or vitamin D which can lead to hypercalcaemia when co-administered with calcium.

ADVERSE EFFECTS

During the administration of Ringer’s Solution, the following adverse reactions have been reported as very common (≥ 10%):

- Hyperhydration and heart failure in patients with cardiac disorder or pulmonary oedema
- Electrolytes disturbances

Adverse reactions may be associated to the technique of administration including febrile response, infection at the site of injection, local pain or reaction, vein irritation, venous thrombosis or phlebitis extending from the site of injection and extravasation.

Adverse reactions may be associated to the medicinal product added to the solution; the nature of the additive will determine the likelihood of any other undesirable effects.

In case of undesirable effect(s), the infusion must be discontinued.

DOSAGE AND ADMINISTRATION

To be used as directed by the physician. The dosage of Ringer’s Solution is dependent upon the age, weight, clinical conditions of the patient, and concomitant therapy.

Fluid balance and plasma electrolyte concentrations (sodium, potassium, calcium and chlorides) must be monitored during administration.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit, as only sterile and nonpyrogenic equipment must be used for intravenous administration. As with all parenteral solutions, compatibility of the additives with the solution must be assessed before addition, by checking for a possible colour change and/or the appearance of precipitates, insoluble complexes or crystals.

Before adding a substance or medication, verify that it is soluble and/or stable in water and that the pH range of Ringer’s Solution is appropriate. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. If in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Refer to instructions below. Solutions containing additives should be used immediately, and not stored. Do not reconnect any partially used containers.

The product should be used for one patient on one occasion only. Any unused portion should be discarded.
Direction for use of Viaflex plastic container

Do not use plastic containers in series connections. Such use could result in embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed. Vented intravenous administration sets with the vent open, or pressurising intravenous solutions contained in flexible plastic containers to increase flow rate can also result in air embolism if the residual air in the container is not fully evacuated prior to administration.

To open:
Tear over wrap down side at slit and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilisation process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution as sterility may be impaired. If supplemental medication is desired, follow directions below.

Preparation for Administration:
(1) Suspend container from eyelet support. (2) Remove plastic protector from outlet port at the bottom of container. (3) Attach administration set.

To Add Medication:
Additives may be incompatible

To add medication before solution administration:
Prepare medication site. Using syringe with 19 to 22-gauge needle, puncture resealable medication port and inject. Mix solution and medication thoroughly. For high-density medication such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

To add medication during solution administration:
Close clamp on the set. Prepare medication site. Using syringe with 19 to 22-gauge needle, puncture resealable medication port and inject. Remove container from IV pole and/or turn to upright position. Evaluate both ports by squeezing them while container is in the upright position. Mix solution and medication thoroughly. Return container to in use position, re-open the clamp and continue administration.

OVERDOSAGE

Overdose or too fast administration may lead to water and sodium overload with a risk of oedema, particularly when there is a defective renal sodium excretion. In such cases extra renal dialysis may be necessary.

Excessive administration of potassium may lead to the development of hyperkalaemia, especially in patients with renal impairment. Symptoms include paresthesia of the extremities, muscle weakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest, and mental confusion. Treatment of hyperkalaemia involves the administration of calcium, insulin (with glucose), sodium bicarbonate, exchange resins or dialysis.

Excessive administration of calcium salts may lead to hypercalcemia. Symptoms of hypercalcemia may include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi, and, in severe cases, cardiac arrhythmias and coma. Too rapid intravenous injection of calcium salts may also lead to many of the symptoms of hypercalcemia as well as to a chalky taste, hot flushes, and peripheral vasodilatation. Mild asymptomatic hypercalcemia
will usually resolve on stopping administration of calcium and other contributory drugs such as vitamin D. If hypercalcaemia is severe, urgent treatment (such as loop diuretics, haemodialysis, calcitonin, bisphosphonates, trisodium edetate) is required.

Excessive administration of chloride salts may cause a loss of bicarbonate with an acidifying effect.

When overdose is related to medicinal products added to the solution infused, the signs and symptoms of over infusion will be related to the nature of the additive being used.

In the event of accidental over infusion, treatment should be discontinued and the patient should be observed for the appropriate signs and symptoms related to the drug administered. The relevant symptomatic and supportive measures should be provided as necessary.

**PRESENTATION AND STORAGE CONDITIONS**

The Ringer’s Solution is supplied in VIAFLEX plastic containers as a single unit dose as shown in the following table:

<table>
<thead>
<tr>
<th>Code No</th>
<th>Name of the active components [Concentrations (%, mmol/1000mL)]</th>
<th>Osmolarity (mOsmol/L)</th>
<th>ARTG/AUSTR</th>
<th>Pack size (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHB2304</td>
<td>Potassium Chloride (0.03%, 4), Sodium Chloride (0.86%, 147), Calcium Chloride (0.033%, 2.2).</td>
<td>308</td>
<td>19443</td>
<td>1000</td>
</tr>
</tbody>
</table>

*Note:* Osmolarity is a calculated figure; in a dilute condition, osmolarity/L is approximately equivalent to Osmolality (mOsmol/kg).

*Storage:* Exposure of pharmaceutical products to heat should be minimised. Avoid excessive heat. It is recommended that the product be stored below 30°C.

**NAME AND ADDRESS OF THE SPONSOR**

Baxter Healthcare Pty Ltd  
1 Baxter Drive  
Old Toongabbie NSW 2146

**POISON SCHEDULE OF THE MEDICINE**

Unscheduled

**DATE OF FIRST INCLUSION IN THE AUSTRALIA REGISTER OF THERAPEUTIC GOODS (ARTG)**

30 September 1991
DATE OF MOST RECENT AMENDMENT
26 March 2015

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