POTASSIUM 10MMOL

Potassium Chloride 10mmol (7.5g/L) and Sodium Chloride (2.9g/L) infusion solution, BP in 100mL

POTASSIUM CHLORIDE 20MMOL IN 0.9% SODIUM CHLORIDE

Potassium Chloride 20mmol (0.15%) and 0.9% Sodium Chloride infusion solution, BP in 1000mL

POTASSIUM CHLORIDE 30MMOL IN 0.9% SODIUM CHLORIDE

Potassium Chloride 30mmol (0.224%) and 0.9% Sodium Chloride infusion solution, BP in 1000mL

POTASSIUM CHLORIDE 40MMOL IN 0.9% SODIUM CHLORIDE

Potassium Chloride 40mmol (29.8g/L) and 0.9% (9g/L) Sodium Chloride infusion solution, BP in 100mL

POTASSIUM 40MMOL

Potassium Chloride 40mmol (2.98g/L) and 0.9% (9g/L) Sodium Chloride infusion solution, BP in 1000mL

Composition

The active ingredients are potassium chloride and sodium chloride.
Chemical Structure/Molecular Formulae

The chemical names are potassium chloride and sodium chloride with chemical formulae as KCl and NaCl, respectively.

The CAS numbers are Potassium Chloride 7447-40-7 and Sodium Chloride 7647-14-5.

Molecular formulae of potassium chloride and sodium chloride are KCl and NaCl, respectively.

DESCRIPTION

Potassium chloride and sodium chloride occur as colourless or white crystals and are freely soluble in water.

Potassium Chloride and Sodium Chloride intravenous infusions are sterile, non-pyrogenic solutions. The concentrations of the active ingredients, dissolved in Water for Injection, are shown in Table 1 (see PRESENTATION AND STORAGE CONDITIONS). Hydrochloric acid may be added for pH adjustment. They do not contain an antimicrobial agent or an added buffer and have a pH of 4.0 – 7.0.

The following products are isotonic solutions (see Table 1 PRESENTATION AND STORAGE CONDITIONS):

- Potassium Chloride 10mmol and 0.29% Sodium Chloride in 100mL
- Potassium Chloride 20mmol and 0.9% Sodium Chloride in 1000mL

Potassium Chloride 30mmol and 0.9% Sodium Chloride in 1000mL, Potassium Chloride 40mmol and 0.9% Sodium Chloride in 1000mL and Potassium Chloride 40mmol and 0.9% Sodium Chloride in 100mL are hypertonic solutions (see Table 1 PRESENTATION AND STORAGE CONDITIONS and PRECAUTIONS).

PHARMACOLOGY

Mechanism of Action

Potassium Chloride and Sodium Chloride intravenous infusion is mainly intended for the treatment of potassium depletion. Thus the mode of action of these formulations should be looked at from that viewpoint.

Potassium is the major cation of intracellular fluid (approximately 160mmol/L of intracellular water) found primarily in muscle cells. It functions principally in the maintenance of acid-base balance; isotonicity and electrodynamic characteristics of the cells. Potassium
participates in carbohydrate utilisation, protein synthesis, and is critical in the regulation of nerve conduction and muscle contraction, particularly in the cardiac muscle.

In contrast, sodium is the major cation of the extracellular fluid (135 – 145mmol/L) and functions principally in the control of water distribution, fluid and electrolyte balance and osmotic pressure of body fluids. Sodium is also associated with chloride and bicarbonate in the regulation of acid-base balance. A membrane bound enzyme, sodium-potassium activated ATPase (Na/K-ATPase) regulates the passage of potassium against a higher potassium concentration in the cells. It actively pumps sodium ions out of the cells into extracellular compartments, whilst the potassium ions are pumped into the cells through a gate-mechanism against concentration gradients in order to maintain homeostasis of cell electrolytes.

Chloride, the major extracellular anion, closely follows the physiological disposition of sodium cation in maintenance of acid-base balance, isotonicity and electrodynamic characteristics of the cells. An increase of chloride concentration may result in a decrease of bicarbonate level, which leads to plasma acidosis, as shown by the electroneutrality of the cells by the following equation:

That is: \[ \text{Na}^+ = \text{Cl}^- + \text{HCO}_3^- + \text{[anion gap]}^- \]

where pH is related to equation: \[ \text{pH} = \text{pK}_{\text{H}_2\text{CO}_3} + \log \left[ \text{HCO}_3^- \right]/\left[\text{H}_2\text{CO}_3\right] \]

The anion gap is called "unmeasured anion", thus, Potassium Chloride and Sodium Chloride intravenous infusion has value as a source of water, and electrolytes where the kidney may excrete potassium up to 80 – 90mmol daily (see Table 1, for PRESENTATION OF THE PRODUCTS).

Daily requirements of potassium are between 800mg to 1.2g.

**Pharmacokinetics**

As the Potassium Chloride and Sodium Chloride intravenous infusion solution is directly administered to the systemic circulation by infusion, the bioavailability (absorption) of the active components is complete (100%).

After its distribution into extracellular compartments, these ions follow the physiological pathways of the individual ion. That is, potassium ions and sodium ions are pumped into and out of the cells, respectively; by the action of Na/K-ATPase.

The level of potassium in the body is regulated by glomerular filtration and distal tubular secretion. Potassium excretion is accompanied by sodium and water reabsorption back into systemic circulation. Thus, the kidney constantly adjusts the sodium and potassium level through this mechanism. The loss of sodium can be reduced to zero by increasing potassium and hydrogen ion excretion. Hormones, ADH (antidiuretic hormone) and
aldosterone control the kidney function in reabsorption of water and excretion of potassium, respectively.

The capacity of the kidney to conserve potassium ions 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 be excreted in sweat.

**INDICATIONS**

Potassium Chloride and Sodium Chloride intravenous infusion is indicated as a source of water and to restore electrolyte balance as required by the patient’s clinical condition, such as hypokalaemia.

**CONTRAINDICATIONS**

The Potassium Chloride and Sodium Chloride intravenous infusion is contraindicated in patients with:

- know hypersensitivity to the product
- documented hyperkalaemia, hyperchloraemia or hypernatraemia
- potassium retention
- congestive heart failure
- severe impairment of renal function
- acidosis
- haemolysis
- Addison’s disease
- in conjunction with potassium sparing diuretics
- clinical states in which the administration of sodium and chloride is detrimental.

**PRECAUTIONS**

The 40mmol Potassium Chloride and Sodium Chloride (100mL) infusion is hypertonic. This solution must only be administered:

- to patients in high dependency units e.g. Intensive Care Units or Coronary Care Units under constant ECG monitoring
- via the lumen of a central venous catheter where the primary solution is typically 0.9% sodium chloride or 5% glucose in water.

**Monitoring**

Adequate urine flow must be ensured and careful monitoring of plasma potassium and other electrolyte concentrations is essential. High dose or high speed infusion must be performed under continuous ECG monitoring.
**Special warnings**

To avoid potassium intoxication, Potassium Chloride and Sodium Chloride intravenous infusion must not be infused rapidly. Administration should be carried out under regular and careful surveillance. Regular monitoring of clinical status, plasma electrolyte concentrations, plasma creatinine levels, BUN level, acid-base balance and ECG is essential in patients receiving potassium therapy, particularly those with cardiac or renal impairment. Adequate urine flow should be ensured and fluid balance should be monitored.

Potassium salts should be administered with considerable care to patients with cardiac disease or conditions predisposing to hyperkalaemia and/or associated with increased sensitivity to potassium such as patients with:
- renal impairment or adrenocorticol insufficiency
- acute dehydration
- extensive tissue destruction such as occurs with severe burns
- in patients under digitalis therapy, regular monitoring of the plasma potassium level is mandatory
- potassium-aggravated skeletal muscle channelopathies (e.g., hyperkalaemic periodic paralysis, paramyotonia congenita, and potassium-aggravated myotonia/paramyotonia).

Potassium Chloride and Sodium Chloride intravenous infusion should be administered with caution to patients who are at risk of experiencing hyperosmolality or undergo correction of alkalosis (conditions associated with a shift of potassium from intracellular to extracellular space) and patients treated concurrently or recently with agents or products that can cause hyperkalaemia (see **INTERACTIONS WITH OTHER MEDICINES**). Close monitoring, careful dose selection and adjustment is required particularly in high risk patients.

Administration of Potassium Chloride and Sodium Chloride intravenous infusion can cause cardiac conduction disorders (including complete heart block) and other cardiac arrhythmias at any time during infusion. Continuous ECG monitoring is performed to aid in the detection of cardiac arrhythmias due to a sudden increase in serum potassium concentration (e.g. when potassium infusion is started) or transient or sustained hyperkalaemia (see **ADVERSE REACTIONS** and **OVERDOSAGE**).

Frequently, mild or moderate hyperkalaemia is asymptomatic and may be manifested only by increased serum potassium concentrations and possibly characteristic ECG changes. However, fatal arrhythmias can develop at any time during hyperkalaemia. Serum potassium levels are not necessarily indicative of tissue potassium levels.

When infusing Potassium Chloride and Sodium Chloride intravenous infusion; care must be taken to prevent paravenous administration or extravasation because such solutions may be associated with tissue damage, which may be severe and include vascular, nerve and tendon damage, leading to surgical intervention, including amputation. Secondary complications including pulmonary embolism from thrombophlebitis have been reported as a consequence of tissue damage from potassium chloride.
Sodium salts should be administered with caution to patients with hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function, pre-eclampsia, or other conditions associated with sodium retention (see also INTERACTIONS WITH OTHER MEDICINES).

In order to reduce risks of thrombophlebitis, it is recommended to change the injection site every 24hrs.

Under a dilute condition, osmolarity/L is approximately the same as osmolality/kg. The addition of potassium chloride into an isotonic sodium chloride renders the Potassium Chloride and Sodium Chloride intravenous infusion to be hypertonic. Administration of substantially hypertonic solutions may lead to a wide variety of complications, such as crenation (shrinkage) of red blood cells and general cellular dehydration.

The administration of the Potassium Chloride and Sodium Chloride intravenous infusion can cause fluid and/or solute overloading resulting in dilution of the serum electrolyte concentrations, over-hydration, congested states, or pulmonary oedema. The risk of dilution states is inversely proportional to the electrolyte concentrations of the injections. Whilst the risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations of the injections.

In patients with diminished renal function, administration of Potassium Chloride and Sodium Chloride intravenous infusion may result in sodium or potassium retention. Prolonged therapy should be monitored for changes in fluid balance, electrolyte concentration and acid-base balance.

**Carcinogenicity/Mutagenicity**

The active ingredients, potassium chloride and sodium chloride are not carcinogenic or mutagenic. They are basic nutrients in all living cells.

**Use in Pregnancy**

Category C

Animal reproduction studies have not been conducted with Potassium Chloride and Sodium Chloride intravenous infusion. Given it is not known whether this product can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity, administration to pregnant women should be based on whether the potential benefits outweigh the risks.

**Use in Lactation**

Safety in lactation has not been established. Use this product in a nursing woman only when it is clearly needed and the potential benefits outweigh the potential risks to the baby.
Paediatric Use

These solutions have not been developed for use in children, and age specific paediatric protocols must be consulted.

Paediatric use requires the application of specific institutional protocols to calculate appropriate dose rates for individual patients.

Use in the Elderly

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

INTERACTIONS WITH OTHER MEDICINES

Solutions containing potassium should be used with caution in patients treated concurrently or recently with agents or products that can cause hyperkalaemia or increase the risk of hyperkalaemia (e.g. potassium sparing diuretics including amiloride, spironolactone and triamterene, ACE inhibitors, angiotensin 2 receptor antagonists, cyclosporin, tacrolimus and medicines that contain potassium such as potassium salts of penicillin). Administration of potassium in patients treated with such agents is associated with an increased risk of severe and potentially fatal hyperkalaemia particularly in the presence of other risk factors for hyperkalaemia.

Caution must be exercised in the administration of these products to patients receiving corticosteroids or corticotropin, as it may lead to sodium and water retention, oedema and hypertension.

Potassium Chloride is not compatible with Mannitol 20%, Sodium Bicarbonate and Colloidal Solutions.

Potassium Chloride in Sodium Chloride infusion solution is available in Viaflex bags. The safety of the Viaflex plastic bag has been confirmed in tests with animals according to the USP biological tests for plastic containers, as well as by tissue culture toxicity studies. Nevertheless, care should be exercised regarding a possible incompatibility outcomes resulting either from the interaction between the plastic container or active ingredients and the added therapeutic substances (if used as a vehicle of drug delivery) (see also DOSAGE AND ADMINISTRATION).

Only the volume in the 1000mL bags will accommodate additives. The introduction of additives to any solution, regardless of type of container, requires special attention to ensure that no incompatibilities result. While some incompatibilities are readily observed, one must be aware that subtle physical, chemical and pharmacological incompatibilities can occur. The medical literature, data sheet, package insert and other available sources of
information should be thoroughly reviewed, prior to use, to ensure compatibility with Potassium Chloride and Sodium Chloride intravenous infusion.

**ADVERSE EFFECTS**

Adverse reactions to potassium containing solutions include hyperkalaemia, paraesthesia of the extremities, flaccid paralysis, mental confusion, hypotension, cardiac arrhythmias, heart block, ECG abnormalities and cardiac arrest.

Adverse reactions which may occur because of the solution or the technique of administration, including fever response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation and hypervolemia. If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary.

**Post-Marketing Adverse Reactions**

The following adverse reactions have been reported in the post-marketing experience listed by MedDRA System Organ Class (SOC).

**IMMUNE SYSTEM DISORDERS:** Hypersensitivity, as manifested by rash and angioedema

**METABOLISM AND NUTRITION DISORDER:** Hyperkalaemia

**CARDIAC DISORDERS:** Cardiac arrest*, asystole*, ventricular fibrillation*, bradycardia (*as manifestation of rapid intravenous administration and/or of hyperkalaemia)

**RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS:** Dyspnoea

**GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:** Chest pain, infusion site pain, infusion site irritation, burning sensation.

Other adverse reaction associated with administration of Potassium Chloride and Sodium Chloride intravenous infusion include:
- in association with extravasation: skin necrosis, skin ulcer, soft tissue necrosis, muscle necrosis, nerve injury, tendon injury and vascular injury
- infusion site thrombosis, infusion site phlebitis, infusion site swelling and infusion site erythema.
DOSAGE AND ADMINISTRATION

To be used as directed by the physician for intravenous use only. The dosage of Potassium Chloride and Sodium Chloride intravenous infusions is dependent upon the age, weight, concomitant treatments, and clinical & biological (acid-base balance) condition of the patient as well as laboratory determinations. A rate-limiting device such as a rate-controlled infusion pump should be used to prevent unintentional bolus doses of solutions containing potassium chloride. Institutional guidelines for administration of intravenous potassium should be followed.

Potassium Chloride 40mmol and 0.9% Sodium Chloride in 100mL must be administered via a central vein to diminish the risk of causing sclerosis. Be sure the catheter is not in the atrium or ventricle to avoid localised hyperkalaemia.

The following intravenous potassium infusion solutions should be administered in a large peripheral or central vein to diminish the risk of causing sclerosis. If infused through a central vein, be sure the catheter is not in the atrium or ventricle to avoid localised hyperkalaemia.

- Potassium Chloride 10mmol and 0.29% Sodium Chloride in 100mL
- Potassium Chloride 20mmol and 0.9% Sodium Chloride in 1000mL
- Potassium Chloride 30mmol and 0.9% Sodium Chloride in 1000mL
- Potassium Chloride 40mmol and 0.9% Sodium Chloride in 1000mL

Solutions containing potassium should be administered under the following conditions:
- The 100mL presentation must be infused over at least 1 hr.
- Potassium Chloride 40mmol and 0.9% Sodium Chloride in 100mL must be administered via a central line (see PRECAUTIONS)
- The maximum time over which infusion may occur is 12 hours for the 100mL product, and 24 hours for the 1000mL presentations.

The recommended administration rate should not exceed 20mmol/hour and not exceed 80mmol for a 24-hour period (= 6g KCl/24hr).

Paediatric use requires the application of specific institutional protocols to calculate appropriate dose rates for individual patients. Do not exceed 3mmol/kg/day.

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container.

Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution, as sterility may be impaired.

Potassium Chloride and Sodium Chloride intravenous infusion is intended for intravenous administration using sterile, non-pyrogenic equipment and strict aseptic technique. Parenteral drug products should be inspected visually for particulate matter and
discolouration prior to administration wherever solution and container permit (see PRECAUTIONS). Do not administer unless solution is clear and seal is intact.

The solutions do not contain an antimicrobial agent, and are for single use in only one patient. Unused portions must be discarded.

The volume in the 1000mL bags will accommodate additives.

The volume in the 100mL bags, will NOT accommodate additives. Do not add supplementary medication.

Additives may be incompatible. Complete information is not available. Only those additives known to be compatible can be added to these infusions. Consult with pharmacist, if available. If in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Add additives to inverted container (ports uppermost) with a 0.63 – 0.80mm needle. Squeeze ports and mix thoroughly and carefully when additives have been introduced. Do not store solutions containing additives.

Monitoring

Adequate urine flow must be ensured and careful monitoring of electrolyte concentrations and ECG is essential (see PRECAUTIONS).

OVERDOSAGE

Potassium overdose can cause potentially fatal hyperkalaemia. The clinical signs and symptoms of hyperkalaemia include:

- disturbances in cardiac conduction and arrhythmias, including bradycardia, heart block, asystole, ventricular tachycardia, ventricular fibrillation
- hypotension, cold skin, grey pallor and peripheral collapse with fall in blood pressure
- muscle weakness up to and including muscular and respiratory paralysis, paraesthesia
- gastrointestinal symptoms (ilues, nausea, vomiting, abdominal pain)
- mental confusion.

Extremely high serum potassium concentrations (8 – 11mmol/L) may cause death from cardiac depression, arrhythmias or arrest.

Frequently, mild or moderate hyperkalemia is asymptomatic and may be manifested only by increased serum potassium concentrations and, possibly, characteristic electrocardiographic changes. However, fatal arrhythmias can develop at any time.

In addition to arrhythmias and conduction disorders, the ECG shows progressive changes that occur with increasing potassium levels. Possible changes include: peaking of T waves, loss of P waves and QRS widening.
The presence of any ECG findings that are suspected to be caused by hyperkalaemia should be considered a medical emergency.

No specific antidotes to this preparation are known. Should overdose occur, treatment should discontinue and the patient should be observed for symptoms of the infusion including any additives, with appropriate supportive measures instituted as required. If hyperkalaemia is present or suspected, discontinue the infusion immediately and institute close ECG, laboratory and other monitoring and, as necessary, corrective therapy to reduce serum potassium levels.

Lowering of the potassium level should be approached with thorough consideration on adverse effects that may occur, in particular with digitalised patients.

A state of hypokalaemia increases the risk of digitalis toxicity. Plasma electrolyte abnormalities (hypomagnesemia, hypokalaemia and metabolic alkalosis) also contribute to the clinical toxicity even at normal digoxin plasma level. Thus, caution should be exercised when lowering the potassium level in a digitalised patient.

In the event of overdosage, in New Zealand please contact the National Poisons Information Centre (telephone 0800 POISON or 0800 764 766), or in Australia the Poison Information Centre (telephone 13 11 26).

**PRESENTATION AND STORAGE CONDITIONS**

Potassium Chloride and Sodium Chloride intravenous infusion is supplied in Viaflex plastic containers as a single unit dose. They are available in several strengths, and the attributes are shown in the following table.
Table 1: Potassium Chloride and Sodium Chloride intravenous infusion solutions

<table>
<thead>
<tr>
<th>Code No.*</th>
<th>Name of the active components [concentrations (%, mmol/container)]</th>
<th>Osmolarity Φ (mOsmol/L)</th>
<th>TT50-</th>
<th>Pack Size (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHB6008</td>
<td>Potassium Chloride (0.75%, 10) &amp; Sodium Chloride (0.29%, 5)</td>
<td>300.0 (300)</td>
<td>7541</td>
<td>100</td>
</tr>
<tr>
<td>AHB1764</td>
<td>Potassium Chloride (0.15%, 20) &amp; Sodium Chloride (0.9%, 154)</td>
<td>348.0 (340)</td>
<td>2184/18</td>
<td>1000</td>
</tr>
<tr>
<td>AHB1274</td>
<td>Potassium Chloride (0.224%, 30) &amp; Sodium Chloride (0.9%, 154)</td>
<td>368.0 (360)</td>
<td>5538</td>
<td>1000</td>
</tr>
<tr>
<td>AHB6034</td>
<td>Potassium Chloride (0.298%, 40) &amp; Sodium Chloride (0.9%, 154)</td>
<td>388.0 (388)</td>
<td>7542</td>
<td>1000</td>
</tr>
<tr>
<td>AHB6053</td>
<td>Potassium Chloride (0.298%, 40) &amp; Sodium Chloride (0.9%, 154)</td>
<td>1100.0 (1100)</td>
<td>7542/1</td>
<td>100</td>
</tr>
</tbody>
</table>

Note:
Osmolarity Φ is a calculated figure. In dilute conditions osmolarity/L is approximately the same as osmolality/kg as shown by the figures in the brackets (mOsmol/kg). AHB6053 (40mmol/100mL) is significantly hypertonic.

*Not all packs may be marketed.

Storage

Exposure of pharmaceutical products to heat should be minimised. Avoid excessive heat. It is recommended that the product should be stored below 30°C. Do not freeze.

MEDICINE CLASSIFICATION

General Sale Medicine.
NAME AND ADDRESS

NZ Distributor

Baxter Healthcare Ltd
PO Box 14 062
Panmure
Auckland 1741.

Australian Distributor

Baxter Healthcare Pty Ltd
1 Baxter Drive
Toongabbie, NSW 2146.

DATE OF PREPARATION

30 June 2015.

Based on Australian PI amended 6 December 2013 and RSI2013 0103.

Please refer to the Medsafe website (www.medsafe.govt.nz) for most recent data sheet.

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