Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion 10 mmol/100 mL, 20 mmol/1000 mL, 30 mmol/1000 mL, 40 mmol/1000 mL

Name of the Medicine

Potassium Chloride and Sodium Chloride

Composition: the active ingredients are: potassium chloride and sodium chloride. 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.

Chemical structure: KCl and NaCl

Description

Potassium chloride and sodium chloride occur as colourless or white crystals and are freely soluble in water. **The Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion** is a sterile, non-pyrogenic solution. The amounts of potassium chloride and sodium chloride dissolved in Water for Injections are shown in Table 1 (see *Presentation*). Hydrochloric acid may be added for pH adjustment. They do not contain an antimicrobial agent or added buffer and have a pH of 4.0 - 7.0. The products are isotonic solutions except for Potassium chloride 30mmol and 0.9% Sodium chloride and Potassium chloride 40mmol and 0.9% Sodium chloride, these are hypertonic solutions (see Table 1 and *Precautions*).

Pharmacology

Mechanism of Action:

The Baxter 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 a major cation of the intracellular fluid (160mmol/litre 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. In contrast, sodium is the major cation of the extracellular fluid (135 to 145mmol/litre) and functions principally in the control of water distribution, fluid and electrolyte balance and osmotic pressure of body fluids.

Na-K-ATPase membrane bound enzymes regulate the passage of potassium against a higher potassium concentration in 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.

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 charge-neutrality of the cells by the following equation. That is, $Na+ = Cl^- + HCO_3^- + [\text{anion gap}]^-$, where pH is related to equation, $pH = pK_{H2C03} + \log [HCO_3]/[H_2CO_3]$. The anion gap is called "unmeasured anion", thus, Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion has a value as a source of water, and electrolytes where kidney may excrete potassium up to (80 - 90)mmol daily (see Table 1, for Presentation of the products).

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

Pharmacokinetics

As Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion is directly administered to the systemic circulation, the bioavailability (absorption) of the active components is complete (100 per cent). From vascular system potassium ions first enter the extracellular/interstitial fluid, which then are pumped into the cells against concentration gradient by the Na-K-ATPase active transport mechanism.

The level of potassium in the body is regulated by glomerular filtration and distal tubular secretion. Potassium excretion site is accompanied by sodium and water reabsorption back into systemic circulation. Thus, 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 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

The Baxter 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 Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion is contra-indicated 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

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, Baxter 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 muscule channelopathies (e.g., hyperkalaemic periodic paralysis, paramyotonia congenita, and potassium-aggravated myotonia/paramyotonia).

Baxter 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 Baxter 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 Baxter 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.

In a dilute condition, osmolarity/L is approximately the same with osmolality/kg.

The addition of potassium chloride into an isotonic sodium chloride renders the Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion to be hypertonic (see **Presentation and Storage Conditions,** Table 1, for osmolarity of solutions). Administration of substantially hypertonic solution may lead to a wide variety of complications, such as crenation (shrinkage) of red blood cells and general cellular dehydration.

The administration of the Baxter 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. 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 Baxter 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 neither carcinogenic nor mutagenic.

Use in pregnancy (Category C)
Animal reproduction studies have not been conducted with the Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion. It is also not known whether these dosage forms can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. The Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion should be given to pregnant women only if clearly needed.

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

Use in children

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.

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 (eg potassium sparing diuretics including amiloride, spironolactone and triamterene, ACE inhibitors, angiontensin II receptor antagonists, cyclosporin, tacrolimus and drugs 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.

Corticosteroids and corticotropin are associated with the retention of sodium and water, with oedema and hypertension. Potassium Chloride is not compatible with Mannitol 20%, Sodium Bicarbonate and

Colloidal Solutions.

The safety of the Viaflex plastic container used to contain the Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion has been confirmed in tests in animals according to the USP biological tests for plastic container, as well as by tissue culture toxicity studies. Nevertheless, care should be exercised regarding a possible incompatibility outcome resulting either from the interaction between the plastic container or active ingredients and the added therapeutic substances. (*See also Dosage and Administration).*

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, the package insert and other available sources of information should be reviewed for thorough understanding of possible incompatibility problems.

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, include 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 Baxter 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 the Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion is dependent upon the age, weight, clinical and 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.**

Intravenous potassium 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. Solutions containing potassium should be administered under the following conditions:

The 100mL presentation must be infused over at least 1 hr.

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.

The Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion is intended for intravenous administration using sterile 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. Do not administer unless solution is clear and seal is intact.

The solutions contain no antimicrobial agents, and are for single use in only one patient. Unused portions must be discarded.

The volume in the 1000mL bags, but not the 100mL bags, will accommodate additives**.** Do not add supplementary medication.

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

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 to 0.80mm needle. Squeeze ports and mix thoroughly. 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 (8-11 mmol/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, treat the symptoms and institute appropriate supportive measures 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.

Presentation and storage conditions

Baxter Potassium Chloride and Sodium Chloride Intravenous Infusion is supplied in Viaflex plastic containers as *a* single unit dose shown in the following Table.

Table 1: Baxter Potassium Chloride and Sodium Chloride I.V. infusions

Code No*	Name of the active components [concentrations (%, mmol/container)]	Osmolarity$^{\Phi}$ (mOsmol/L)	ARTG/ AUSTR	Pack Size (mL)
AHB6008	Potassium Chloride (0.75%,10) & Sodium Chloride (0.29%, 5)	300.0 (300)	159379	100
AHB1764	Potassium Chloride (0.15%, 20) & Sodium Chloride (0.9%, 154)	348.0 (340)	19466	1000
AHB1274	Potassium Chloride (0.224%, 30) & Sodium Chloride (0.9%, 154)	368.0 (360)	19470	1000
AHB6011	Potassium Chloride (0.298%,40) & Sodium Chloride (0.584%, 100)	280.0 (280)	159381	1000
AHB6034	Potassium Chloride (0.298%,40) & Sodium Chloride (0.9%, 154)	388.0(388)	225806	1000

Note: Osmolarity$^{\Phi}$ is a calculated figure; in dilute condition, osmolarity/L is approximately the same as osmolality/kg. The figures in the brackets are osmolality (mOsmol/kg).

***** Not all codes are marketed.

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

Name and address of the sponsor

Baxter Healthcare Pty Limited
1 Baxter Drive
Toongabbie NSW 2146
Sydney, Australia.

Poison schedule of the medicine

Unscheduled

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG)

30 September 1991 – AUST R 19466 and 19470

13 April 2011 – AUST R 159379 and 159381

30 September 2015 – AUST R 225806