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 (IVI)** 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 (IVI) 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 IVIhas 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 IIVI 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 IVI 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 IVI 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.

Hypersensitivity reactions
Hypersensitivity / infusion reactions including anaphylaxis have been reported with other products containing potassium chloride and sodium chloride. Stop the infusion immediately if signs or symptoms of hypersensitivity / infusion reactions develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Special warnings

To avoid potassium intoxication, Baxter Potassium Chloride and Sodium Chloride IVI 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.

When infusing Baxter Potassium Chloride and Sodium Chloride IVI; 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).

Rapid correction of hypernatraemia and hyponatraemia is potentially dangerous (risk of serious neurologic complications).
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 IVI 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.

Risk of Hyperkalaemia
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 injury or burns
- certain cardiac disorders such as congestive heart failure or AV block (especially if they receive digitalis). 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).

Baxter Potassium Chloride and Sodium Chloride IVI should be administered with caution to patients who are at risk of experiencing hyperosmolality, acidosis, 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.

Hyperkalaemia 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.

Use in patients at risk of sodium retention, fluid overload and oedema
Baxter Potassium Chloride and Sodium Chloride IVI should be used with particular caution, in patients with or at risk for:

- Hypernatraemia,
- Hyperchloremia,
- Metabolic acidosis,
- Hypervolemia,
- Conditions that may cause sodium retention, fluid overload and oedema (central and pheripheral)

Risk of serum electrolytes and water imbalance
Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition, the intravenous administration of the Baxter Potassium Chloride and Sodium Chloride IVI can cause:

- fluid and/or solute overloading resulting in dilution of the serum electrolyte concentrations,
- electrolyte disturbances such as:
  - hypernatraemia
  - hyponatraemia
- acid-base imbalance
- overhydration / hypervolemia, congested states, including central (e.g., pulmonary congestion) and peripheral 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.

Regarding medications that increase the risk of hyponatraemia or sodium and fluid retention, see **Interactions with Other Medicines.**

In patients with diminished renal function, administration of Baxter Potassium Chloride and Sodium Chloride IVI may result in sodium or potassium retention. Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentration and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

Hyponatraemia
Baxter Potassium Chloride and Sodium Chloride IVI should be used with particular caution in patients with or at risk of hyponatraemia, for example:

- In children
- In elderly patients
- In women,
- Postoperatively
- In persons with psychogenic polydipsia,
- In patients treated with medications that increase the risk of hyponatraemia (such as certain antiepileptic and psychotropic medications).

The risk for developing hyponatraemic encelopathy is increased, for example:

- In paediatric patients (≤16 years of age)
- In women (in particular, premenopausal women)
- In patients with hypoxemia
- In patients with underlying central nervous system disease

Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema, and death. Acute symptomatic hyponatraemic encelopathy is considered a medical emergency.

Use in patients at risk of several renal impairment
Baxter Potassium Chloride and Sodium Chloride IVI should be administered with particular caution to patients at risk of severe renal impairment. In such patients, administration of Baxter Potassium Chloride and Sodium Chloride IVI may result in sodium retention, fluid overload, and/or may predispose to hyperkalaemia.

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

Pressurising intravenous solutions contained in flexible containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

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 IVI. It is also not known whether these dosage forms can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. There are no adequate data from the use of Baxter Potassium Chloride and Sodium Chloride IVI in pregnant women. Physicians should carefully consider the potential risks and benefits for each specific patient before administering Baxter Potassium Chloride and Sodium Chloride IVI.

Use in lactation
Safety in lactation has not been established. There are no adequate data from the use of Baxter Potassium Chloride and Sodium Chloride IVI in lactating women. Physicians should carefully consider the potential risks and benefits for each specific patient before administering Baxter Potassium Chloride and Sodium Chloride IVI.

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

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy, and should be determined by a physician experienced in paediatric intravenous fluid therapy. Paediatric use requires the application of specific institutional protocols to calculate appropriate dose rates for individual patients.

Children (including neonates and older children) are at increased risk of developing hyponatraemia as well as for developing hyponatraemic encephalopathy. The infusion of Baxter Potassium Chloride and Sodium Chloride IVI together with the non-osmotic secretion of ADH may result in hyponatraemia.

Plasma electrolyte concentrations should be closely monitored in the paediatric population.

Use in the elderly
When selecting the type of infusion solution and the volume/rate of infusion for a geriatric patient, consider that geriatric patients are generally more likely to have cardiac, renal, hepatic, and other diseases and/or concomitant drug therapy.

Interactions with other Medicines

Caution is advised in patients treated with lithium. Renal sodium and lithium clearance may be increased during administration of Baxter Potassium Chloride and Sodium Chloride IVI and this can result in decreased lithium levels.
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.

Baxter Potassium Chloride and Sodium Chloride IVI should be used with particular caution in patients on concomitant medications that may increase the risk of sodium and fluid retention, such as corticosteroids. 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.

Baxter Potassium Chloride and Sodium Chloride IVI should be administered with caution in patients on concomitant medications that increase the risk of hyponatraemia such as certain antiepileptic and psychotropic medications.

The safety of the Viaflex plastic container used to contain the Baxter Potassium Chloride and Sodium Chloride IVI 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. Additives known or determined to be incompatible should not be used.

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, Hyponatraemia, Hypernatraemia, acidosis hyperchloremic, fluid overload

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, chills, infusion site pain, infusion site irritation, burning sensation.

Other adverse reaction associated with administration of Baxter Potassium Chloride and Sodium Chloride IVI 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 choice of the specific Baxter Potassium Chloride and Sodium Chloride IVI formulation, dosage, volume, rate and duration of administration is dependent upon the age, weight, clinical and biological (acid-base balance) condition of the patient, concomitant therapy and laboratory determinations. Additional electrolyte supplementation may be indicated according to the clinical needs of the patient. Administration should be determined by a physician experienced in intravenous fluid therapy. 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. The Baxter Potassium Chloride and Sodium Chloride IVI range have a pH of 4.0 - 7.0 and their osmolarity are shown in Table 1 (see Presentation and Storage Conditions). The osmolarity of a final admixed infusion solution must be taken into account when peripheral administration is considered. Hyperosmolar solutions may cause venous irritation and phlebitis. Thus, clinically significant hyperosmolar solutions are recommended to be administered through a large central vein, for rapid dilution of the hyperosmolar solution.

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 IVI 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. When introducing additives to Baxter Potassium Chloride and Sodium Chloride IVI, the instructions for use of the medication to be added and other relevant literature must be consulted. Before adding a substance or medication, verify that it is soluble and stable in Potassium Chloride and Sodium Chloride IVI, and that the pH range of the solution is appropriate. 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. After addition, if there is a discoloration and/or the appearance of precipitates, insoluble complexes or crystals, do not use.

In case of damage, the container should be discarded. Do not store solutions containing additives.

Discard any unused portion. For single use only.

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

Overdosage

Excess administration of Potassium Chloride and Sodium Chloride IVI can cause:

- Hyponatraemia (which can lead to CNS manifestations including seizures, coma, cerebral edema and death)
- Hypernatraemia, especially in patients with severe renal impairment
- Hyperkalaemia. 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 of extremities
  - gastrointestinal symptoms (ileus, nausea, vomiting, abdominal pain)
  - mental confusion
  - fluid overload (which can lead to central and/or peripheral oedema).

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

Frequently, mild or moderate hyperkalaemia 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.

When assessing an overdose, any additives in the solution must also be considered. The effects of an overdose may require immediate medical attention and treatment. Interventions include discontinuation of Potassium Chloride and Sodium Chloride IVI administration, dose reduction, and other measures as indicated for the specific clinical constellation.

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 IVI is supplied in Viaflex plastic containers as *a* single unit dose shown in the following Table.

Table 1: Baxter Potassium Chloride and Sodium Chloride IVI

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
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
30 September 2015 – AUST R 225806

Date of most recent amendment
23 August 2017