1 POTASSIUM CHLORIDE, GLUCOSE & SODIUM CHLORIDE (solution for infusion)

Potassium Chloride 20mmol (0.15%) in 4% Glucose and 0.18% Sodium Chloride (BP)
Potassium Chloride 30mmol (0.224%) in 4% Glucose and 0.18% Sodium Chloride (BP)
Potassium Chloride 20mmol (0.15%) in 5% Glucose and 0.45% Sodium Chloride (BP)
Potassium Chloride 20mmol (0.15%) in 5% Glucose and 0.9% Sodium Chloride (BP).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The active ingredients are potassium chloride, glucose (anhydrous) and sodium chloride.

The concentrations of the active ingredients in Water for Injections are shown in the following table:

Potassium Chloride, Glucose and Sodium Chloride infusion solutions			
Product*	Potassium Chloride	Sodium Chloride	Glucose
0.15% Potassium chloride, 0.18% Sodium Chloride and 4% Glucose infusion solution, 1000mL (AHB1704)	20mmol/L	30mmol/L	222mmol/L
0.224% Potassium chloride, 0.18% Sodium Chloride and 4% Glucose infusion solution, 1000mL (AHB1224)	30mmol/L	30mmol/L	222mmol/L
0.149% Potassium chloride, 0.45% Sodium Chloride and 5% Glucose infusion solution, 1000mL (AHB6024)	20mmol/L	77mmol/L	278mmol/L
0.149% Potassium chloride, 0.9% Sodium Chloride and 5% Glucose infusion solution, 1000mL (AHB6066)	20mmol/L	154mmol/L	278mmol/L
**Not all products listed in the table are marketed*			

Potassium Chloride, Glucose and Sodium Chloride infusion solutions do not contain an antimicrobial agent or an added buffer.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

Potassium Chloride, Glucose and Sodium Chloride infusion solution for intravenous infusion are sterile, non-pyrogenic solutions and are for single use in one patient on one occasion only.

Appearance

The solutions are sterile, clear, colourless to faintly straw-coloured, practically free from visible particles.

Potassium Chloride, Glucose and Sodium Chloride infusion solutions can be isotonic or hypertonic as reflected by their osmolarities (calculated) listed in the following table.

Potassium Chloride, Glucose and Sodium Chloride infusion solution preparations		
Product	Osmolarity$^{\Phi}$ (mOsmol/L) [Osmolality, mOsmol/kg]	Energy (kJ/L)
0.15% Potassium chloride, 0.18% Sodium Chloride and 4% Glucose infusion solution, 1000mL (AHB1704)	324 [322]	668
0.224% Potassium chloride, 0.18% Sodium Chloride and 4% Glucose infusion solution, 1000mL (AHB1224)	344 [342]	668
0.149% Potassium chloride, 0.45% Sodium Chloride and 5% Glucose infusion solution, 1000mL (AHB6024)	472 [472]	835
0.149% Potassium chloride, 0.9% Sodium Chloride and 5% Glucose infusion solution, 1000mL (AHB6066)	626 [626]	835
Note: Osmolarity Φ is a calculated figure. In dilute conditions osmolarity is approximately the same as osmolality. 1 gram of glucose provides 16.7 kiloJoules (kJ) of energy.		

Potassium Chloride, Glucose and Sodium Chloride infusion solutions have a pH of 3.5 - 6.5.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Potassium Chloride, Glucose and Sodium Chloride infusion solution is indicated for replenishing fluid losses, as an energy source and for restoration or maintenance of sodium, potassium and chloride ions in the body fluids.

It may be used as a vehicle of drug delivery where intravenous delivery is appropriate and the medicine is compatible with this solution.

4.2 Dose and method of administration

To be used as directed by the physician. The choice of the specific **Potassium Chloride, Glucose and Sodium Chloride** concentrations, dosage, volume, rate and duration of administration depend on the age, weight and clinical condition of the patient and concomitant therapy as well as laboratory determinations; administration should be determined by a physician. For patients with electrolyte and glucose abnormalities and for paediatric patients, consult a physician with experience in intravenous fluid therapy.

Hyperosmolar solutions may cause venous irritation and phlebitis. Thus, any hyperosmolar solutions are recommended to be administered through a large central vein, for thorough and rapid dilution of the hyperosmolar solution. For information on the products' osmolarity, see table in section 2.

Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit (see section 4.4). Do not administer unless solution is clear and seal is intact. Only sterile and nonpyrogenic equipment must be used for intravenous administration.

A gradual increase of flow rate should be considered when starting administration of glucose-containing products.

Electrolyte supplementation may be indicated according to the clinical needs of the patient.

The **Potassium Chloride, Glucose and Sodium Chloride** infusion solution filled in Viaflex containers is intended for intravenous administration using sterile equipment.

The equipment should be primed with the solution in order to prevent air embolism due to residual air in the system. Additives may be introduced before infusion or during infusion through the injection site. Additives may be incompatible. Check additive compatibility with both the solution and container prior to use. Complete information is not available. Those additives known to be incompatible should not be used. Consult with a pharmacist, if available.

If in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly and carefully when additives have been introduced. Do not store solutions containing additives.

The product should be used once only. Any unused portion should be discarded. Do not reconnect partially used bags.

Direction for use of VIAFLEX plastic container

Warning: Do not remove unit from over-wrap until ready for use. The inner bag maintains the sterility of the product. 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 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. Check solution for limpidity and absence of foreign matter. If solution is not clear or contains foreign matter, discard the solution. 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

Potassium Chloride, Glucose and Sodium Chloride infusion solution is a sterile preparation. Thus, aseptic technique must be applied throughout the administration.

(1) Suspend container from eyelet support.

(2) Remove plastic protector from outlet port at the bottom of container.

(3) Attach administration set; use an aseptic method to set up the infusion.

To add medication

Warning: Additives may be incompatible. Before adding a substance or medication, verify that it is soluble and/or stable in **Potassium Chloride, Glucose and Sodium Chloride** infusion solution and that the pH range is appropriate. Check the product information document(s) of the medication(s), the instructions for use of the medication to be added and other relevant literature must be

consulted prior to their addition to **Potassium Chloride, Glucose and Sodium Chloride** infusion solution.

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 medications, such as potassium chloride, squeeze ports while ports are upright and mix thoroughly. After addition, if there is a colour change and/or the appearance of precipitates, insoluble complexes or crystals, do not use.

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. Evacuate 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. Do not store solutions containing additives.

4.3 Contraindications

The levels of sodium and potassium in **Potassium Chloride, Glucose and Sodium Chloride** infusion solution are relatively low. Nevertheless it is contraindicated:

- in patients who have known hypersensitivity to the product,
- in patients suffering from conditions in which administration of either sodium chloride or potassium chloride alone is contraindicated,
- in patients with hypernatraemia, hyperchloraemia and/or hyperkalaemia that are not related to the concentration effect associated to a volume depletion, severe renal insufficiency (with oliguria/anuria), uncompensated cardiac failure, Addison's disease and patients who have had a head trauma with 24 hours (with blood glucose concentrations being closely monitored during episodes of intracranial hypertension).

The solution is also contraindicated in patients with uncompensated diabetes, other known glucose intolerances (such as metabolic stress situations), hyperosmolar coma, hyperglycaemia and hyperlactatemia.

Cornstarch is the raw material for the production of glucose. For patients known to have allergy to corn or corn products, this product is contraindicated.

4.4 Special warnings and precautions for use

General
Potassium Chloride, Glucose and Sodium Chloride infusion solution is available in a VIAFLEX bag. 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 possible incompatibility outcomes resulted either from the interaction between the plastic container or active ingredients and any added therapeutic substances (if used as a vehicle of drug delivery) (see also Section 4.2).

The introduction of additives to any solution, regardless of the type of container, requires special attention to assure 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, the package insert and other available sources of information should be reviewed for thorough understanding of possible incompatibility problems with this product. The product information documents of added medications should be checked

prior to use, to ensure compatibility with **Potassium Chloride, Glucose and Sodium Chloride** infusion solution.

Do not administer **Potassium Chloride, Glucose and Sodium Chloride** infusion solution unless clear, colourless and free of particles (see Section 4.2), and the seals are intact.

Under a dilute condition, osmolarity/L is approximately the same as osmolality/kg. The osmolarity and osmolality values for the **Potassium Chloride, Glucose and Sodium Chloride** infusion solutions are listed in the table in section 3. Administration of a substantially hypertonic solution may lead to a wide variety of complications, such as crenation (shrinkage) of red blood cells and general cellular dehydration. The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema and death, therefore acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

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

Administration should be carried out under regular and careful surveillance. Regular monitoring of clinical status, blood glucose level, 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 must be ensured and fluid balance should be monitored.

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

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including anaphylaxis, have been reported with **Potassium Chloride, Glucose and Sodium Chloride** infusion solution (see section 4.8). Stop the infusion immediately if signs or symptoms of hypersensitivity/infusion reactions develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Risk of hyperkalaemia

Hyperkalaemia is the most common and serious hazard of potassium treatments. Since an exact measurement of potassium deficiency is not usually possible, potassium supplements should be administered slowly and with caution.

Potassium Chloride, Glucose and Sodium Chloride infusion solution should be administered with caution, to patients with conditions predisposing to hyperkalaemia and/or associated with increased sensitivity to potassium, such as patients with potassium-aggravated skeletal muscle channelopathies (e.g. hyperkalaemic periodic paralysis, paramyotonia congenital, and potassium-aggravated myotonia/patamyotonia).

Those solutions containing sodium should be used with great care, if at all, in patients with cardiac disease including congestive heart failure, or AV block (especially if they receive digitalis), conditions predisposing to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration or extensive tissue destruction as occurs with severe burns.

Sodium salts should be administered with considerable care to patients with hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function, pre-eclampsia or clinical states in which there exists oedema with sodium retention.

Similarly, 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.

The administration of **Potassium Chloride, Glucose and Sodium Chloride** infusion solution can cause fluid and/or solute overloading resulting in dilution of the serum electrolyte concentrations, overhydration, 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.

Potassium Chloride, Glucose and Sodium Chloride infusion solution should be used with care in patients with subclinical diabetes mellitus (see section 4.5), hyperkalaemia, severe renal failure, and in conditions in which potassium retention is present. Careful monitoring of plasma levels is recommended in these clinical situations.

Administration of glucose containing solutions may lead to hyperglycaemia, therefore it is not recommended to use this solution after acute ischemic strokes as hyperglycaemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery. If hyperglycaemia occurs, rate of infusion should be adjusted or insulin administered (see section 4.5).

Potassium Chloride, Glucose and Sodium Chloride infusion solution should be administered with caution to patients who are at risk of experiencing hyperosmolarity, acidosis, or undergoing 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.

Other groups of patients in whom **Potassium Chloride, Glucose and Sodium Chloride** infusion solution should be used with caution include patients with cardiac arrhythmia. Arrhythmias can develop at any time during hyperkalaemia. Frequently, mild or moderate hyperkalaemia is asymptomatic and may be manifested only by increased serum potassium concentrations and, possibly, characteristic ECG changes.

Hyponatraemia

Potassium Chloride, Glucose and Sodium Chloride infusion solution should be used with particular caution, in patients with or at risk of hyponatraemia.

Glucose intravenous infusions are usually isotonic solutions. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolization. Monitoring of serum sodium is particularly important for hypotonic fluids. Depending on the tonicity of the solution, the volume and rate of infusion, and depending on a patient's underlying clinical condition and capability to metabolize glucose, intravenous administration of glucose can cause electrolyte disturbances, most importantly hypo- or hyperosmotic hyponatraemia.

The infusion of solutions with sodium concentrations < 0.9% may result in hyponatraemia. Close clinical monitoring may be warranted. Hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterised by headache, nausea, seizures, lethargy and vomiting which can lead to coma and death. Patients with brain oedema are at particular risk of severe, irreversible and life-threatening brain injury. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia.

The risk for hyponatraemia is increased, 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, see section 4.5).

The risk for developing hyponatraemic encephalopathy is increased, for example:
- in pediatric patients (≤ 16 years of age)
- in women (in particular, premenopausal women)
- in patients with hypoxemia
- in patients with underlying central nervous system disease.

Use in patients at risk of sodium retention, fluid overload and oedema

Potassium Chloride, Glucose and Sodium Chloride infusion solution should be used with particular caution, in patients with or at risk of:
- hypervolemia
- conditions that may cause sodium retention, fluid overload and oedema (central and peripheral)
- medications that may increase the risk of sodium and fluid retention, such as corticosteroids.

Potassium Chloride, Glucose and Sodium Chloride infusion solution should be used with particular caution, in patients at risk of the above conditions, hypernatraemia, hyperchloraemia and metabolic acidosis.

Risk of hypo and hyperosmolality, serum electrolytes and water imbalance

Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolize glucose, intravenous administration of **Potassium Chloride, Glucose and Sodium Chloride** infusion solution can cause:
- hypoosmolality
- hyperosmolality, osmotic diuresis and dehydration
- electrolyte disturbances such as:
    - hyponatraemia
    - hypophosphatemia
    - hypomagnesemia
- overhydration/hypervolemia and, for example, congested states, including central (e.g. pulmonary congestion) and peripheral oedema.

Potassium Chloride, Glucose and Sodium Chloride infusion solution can also cause:
- acid-base imbalance
- an increase in serum glucose concentration is associated with an increase in serum osmolality. Osmotic diuresis associated with hyperglycaemia can result in or contribute to the development of dehydration and electrolyte losses.

Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

Risk of hyperglycaemia

Rapid administration of glucose solutions may produce substantial hyperglycaemia and hyperosmolar syndrome. In order to avoid hyperglycemia the infusion rate should not exceed the patient's ability to utilize glucose. To reduce the risk of hyperglycaemia-associated complications, the infusion rate must be adjusted and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient. Intravenous glucose should be administered with caution in patients with, for example:

- impaired glucose tolerance (such as in diabetes mellitus, renal impairment, or in the presence of sepsis, trauma, or shock)
- severe malnutrition (risk of precipitating a refeeding syndrome)
- thiamine deficiency, e.g., in patients with chronic alcoholism (risk of severe lactic acidosis due to impaired oxidative metabolism of pyruvate)
- water and electrolyte disturbances that could be aggravated by increased glucose and/or free water load.

Other groups of patients in whom **Potassium Chloride, Glucose and Sodium Chloride** infusion solution should be used with caution include:

- patients with ischemic stroke. Hyperglycaemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after acute ischemic strokes
- patients with severe traumatic brain injury. Early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury
- newborns.

Prolonged intravenous administration of glucose and associated hyperglycaemia may result in decreased rates of glucose-stimulated insulin secretion.

Refeeding syndrome

Refeeding severely undernourishered patients may result in the refeeding syndrome that is characterized by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intake while avoiding overfeeding can prevent these complications.

Use in patients at risk of severe renal impairment

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

Blood

Potassium Chloride, Glucose and Sodium Chloride infusion solution should not be administered simultaneously with blood through the same administration set because of the possibility of haemolysis and pseudoagglutination.

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.

Use in the elderly

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

Paediatric use

Neonates, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycaemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycaemic control in order to avoid potential long term adverse effects. Hypoglycaemia in the neonate can cause prolonged seizures, coma and brain damage. Hyperglycaemia has been associated with cerebral injury, including intraventricular haemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotizing enterocolitits, bronchopulmonary dysplasia, increased oxygen requirements, prolonged length of hospital stay, and death.

Infants and children may have an impaired ability to regulate fluid and electrolytes. Fluid replacement therapy should be closely monitored in these populations as fluid and electrolyte disturbances (such as hyponatraemia and hypokalaemia) may occur. Children (including neonates and older children) are at increased risk of developing hyponatraemia as well as developing hyponatraemic encephalopathy. The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterised by headache, nausea, seizures, lethargy, and vomiting which may lead to coma and death. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening cerebral injury.

Plasma electrolyte concentrations should be closely monitored in the paediatric population. Rapid correction of hyponatraemia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in paediatric intravenous fluid therapy.

Effects on laboratory tests

The effect of this medicine on laboratory tests has not been established.

4.5 Interaction with other medicines and other forms of interaction

Potassium Chloride, Glucose and Sodium Chloride infusion solution should not be administered simultaneously with blood preparations through the same administration set, because of the possibility of pseudo-agglutination or haemolysis.

If using this solution as a vehicle of drug delivery, the product information document(s) of the medicine(s) must be reviewed to ensure compatibility with the solution.

Potassium Chloride, Glucose and Sodium Chloride infusion solution 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, such as potassium sparing diuretics. These products should not be administered concomitantly with potassium sparing diuretics (such as amiloride, spironolactone, triamterene), angiotensin converting enzyme (ACE) inhibitors or angiotensin 2 receptor antagonists (A2RAs) as simultaneous administration of these medicines can result in increased risk of severe and potentially fatal hyperkalaemia, in particular in the presence of other risk factors for hyperkalaemia.

Potassium Chloride, Glucose and Sodium Chloride infusion solution should also be used with caution in concomitant cyclosporine, tacrolimus and medicines that contain potassium.

Caution is advised when administering **Potassium Chloride, Glucose and Sodium Chloride** infusion solution to patients treated with medicines leading to an increased vasopressin effect. The below listed medicines increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hyponatraemia following treatment with IV fluids (see sections 4.4 and 4.8):

- medicines stimulating vasopressin release such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, opioids
- medicines potentiating vasopressin action such as chlorpropamide, non-steroidal antiinflammatories (NSAIDS), cyclophosphamide
- Vasopressin analogues such as desmopressin, oxytocin, vasopressin, terlipressin.

Caution is advised when administering **Potassium Chloride, Glucose and Sodium Chloride** infusion solution to patients treated with medicines that may increase the risk of hyponatraemia, such as diuretics and antiepileptics. Regarding medications that increase the risk of hyponatraemia or sodium and fluid retention, see section 4.4.

Concurrent use of these products with insulin will decrease serum potassium. Use of these infusions may necessitate review of a patient's oral hypoglycaemic or insulin requirements, so close monitoring of serum glucose levels is also required. Both the glycaemic effects of **Potassium Chloride, Glucose and Sodium Chloride** infusion solutions and its effects on water and electrolyte balance should be taken into account when using these products in patients treated with other substances that affect glycaemic control, or fluid and/or electrolyte balance.

Caution is advised in patients treated with lithium. Renal sodium and lithium clearance may be increased during administration of **Potassium Chloride, Glucose and Sodium Chloride** infusion solutions and can result in decreased lithium levels.

Beta-adrenergic agents

Beta adrenoceptor blockade increases both peak serum potassium concentration and the time required for serum potassium to return to basal levels in subjects receiving an acute intravenous potassium load.

Non-steroidal anti-inflammatory drugs

These may cause hyperkalaemia by inducing secondary hypoaldosteronism following inhibition of renal prostaglandin synthesis.

Heparin

Heparin reduces the synthesis of aldosterone, which may result in hyperkalaemia, especially in patients with underlying renal insufficiency or other problems that impair potassium excretion.

Digitalis glycosides

Potassium supplementation is not recommended with concurrent digitalis in those patients with severe or complete heart block. Careful monitoring is necessary if potassium chloride is used to correct hypokalaemia in such patients.

Sodium bicarbonate

Concurrent use will decrease serum potassium.

See also section 6.2.

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy (Category C)

Animal reproduction studies have not been conducted with **Potassium Chloride, Glucose and Sodium Chloride** infusion solution. There have been reports that use in the mother during labor may lead to foetal hyperglycaemia, hyperinsulinaemia and metabolic acidosis, with subsequent neonatal hypoglycaemia due to foetal insulin production and jaundice. Given it is not known whether these dosage forms can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity, administration in pregnant women should be based on whether the potential benefits outweigh the risks.

Breast-feeding

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.

4.7 Effects on ability to drive and use machines

There is no information on the effects of **Potassium Chloride, Glucose and Sodium Chloride** infusion solution on the ability to operate an automobile or other heavy machinery.

4.8 Undesirable effects

Adverse reactions 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.

Prolonged administration or rapid infusion of large volumes of glucose-containing solutions may lead to hyperosmolarity, dehydration, hyperglycaemia, hyperglucosuria and osmotic diuresis (due to hyperglycaemia).

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.

Retention of excess sodium, when there is defective renal sodium excretion, may result in pulmonary and peripheral oedema. Hyponatraemia has also been reported for similar solutions containing low concentrations of sodium chloride (< 0.9%).

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

An excessive administration of any of these preparations may result in symptoms of hyperkalaemia. This is particularly manifested in patients with impaired renal function. Infusion of a potassium chloride preparation may also lead to a dangerous level of hyperkalaemia if it is administered at a rate of, or more than, 20mmol/hour. The shift of potassium ions from extracellular fluid into intracellular fluid occurs at a slow rate, therefore, in the interim, a rapid infusion may manifest as hyperkalaemia.

Symptoms and signs of potassium intoxication include:

- *Cardiovascular*. Fall in blood pressure, cardiac depression, arrhythmias, heart block and cardiac arrest. Hyperkalaemia is usually asymptomatic but may exhibit the following ECG abnormalities: disappearance of the P wave, prolongation of the QT interval, widening and slurring of the QRS complex, changes of the ST segment and tall peaked T waves.
- *Gastrointestinal*. Nausea, vomiting and diarrhoea may occur.
- *Other*. Listlessness, mental confusion, paraesthesia of the extremities, muscle weakness, heaviness of the legs, paralysis.

Post-marketing

The following adverse reactions have been reported in the post-marketing experience:

- *Immune System Disorders:* analphylactic reaction, hypersensitivity
- *Metabolism and Nutrition Disorders:* hyponatraemia, hyperglycaemia
- *Vascular Disorders:* phlebitis
- *Skin and Subcutaneous Tissue Disorders:* rash, pruritus
- *General Disorders and Administration Site Conditions:* injection site reactions including, infusion site pain, injection site vesicles, chills, pyrexia.

Other reactions (Class reactions)

Other adverse reactions reported with other potassium chloride, sodium chloride and glucose intravenous infusions include:

- hyperkalaemia
- cardiac arrest
- hyponatraemia, which may be symptomatic
- hyponatraemic encephalopathy
- hyperchloraemic acidosis.

Anaphylactic reactions, hypersensitivity, pyrexia and chills have also been reported for similar solutions containing glucose.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Symptoms

There is no overdose experience with **Potassium Chloride, Glucose and Sodium Chloride** infusion solution preparations. However, excessive administration or impaired excretion of potassium may lead to:

- hyperglycaemia, adverse effects on water and electrolyte balance, and corresponding complications. For example, severe hyperglycaemia and severe dilutional hyponatraemia and their complications, can be fatal
- hyponatraemia (which can lead to CNS manifestations including seizures, coma, cerebral oedema and death)
- hypernatraemia, especially in patients with severe renal impairment
- fluid overload (which can lead to central and/or peripheral oedema)
- development of potentially fatal hyperkalaemia (see section 4.8). 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. Manifestations of hyperkalaemia may include:

  - disturbances in cardiac conduction and arrhythimias, including bradycardia, heart block, asystole, ventricular tachycardia, ventricular fibrillation
  - hypotension
  - muscle weakness up to and including muscular and respiratory paralysis, paresthesia of extremities
  - gastrointestinal symptoms (ileus, nausea, vomiting, abdominal pain).
- arrhythmias and conduction disorders, 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
  - QRS widening.

However, the correlation between potassium levels and ECG changes is not precise, and whether, or at which, potassium level certain ECG signs develop depends on factors such as patient sensitivity, the presence of other electrolytes disorders, and the rapidity of the development of hyperkalaemia. 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. Clinically significant overdose of **Potassium Chloride, Glucose and Sodium Chloride** infusion solution may, therefore, constitute a medical emergency.

Overdose is usually asymptomatic and may be manifested only by increased serum potassium levels and characteristic ECG features (see sections 4.4 and 4.8).

Treatment

No specific antidotes to this preparation are known, interventions include discontinuation of **Potassium Chloride, Glucose and Sodium Chloride** infusion solution administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

Should overdose occur, treatment should be discontinued and the patient should be observed for symptoms of the infusion including any additives, with appropriate supportive measures instituted as required. The use of potassium containing foods or medications causing potassium retention must also be discontinued.

Treatment of hyperkalaemia depends on its severity. 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. It must be kept in mind that rapid lowering of serum potassium concentrations in digitalised patients can cause cardiac toxicity.

Clinically, only the intravascular potassium concentration causes the cardiac disorders. Therefore, infusion of the potassium chloride solution and other exogenous sources of potassium, such as potassium-rich containing foods or medications causing potassium retention (potassium-sparing diuretic) must be discontinued immediately. In patients with severe hyperkalaemia, measures which facilitate the shift of potassium ions from the vascular to the intracellular space, should be initiated. It can be achieved by administration of sodium bicarbonate, glucose/insulin, or calcium gluconate infusions.

In patients with serum potassium concentrations greater than 6.5mmol/L, intravenous infusion of 40 – 160mmol of sodium bicarbonate over a 5 minute period has been recommended. This dose

may be repeated every 15 minutes if ECG abnormalities persist. This treatment results in a temporary alkalosis and lowers serum potassium levels by 0.6mmol/L for every 0.1 increase of pH.

Glucose/insulin infusion is another treatment for an overdose episode with potassium chloride medication. It consists of 300 – 500mL of 10 – 25% Glucose Intravenous Infusion containing 5 – 10IU Insulin per 20g of glucose infused over a 1 hour period.

Patients whose ECGs show the absence of P waves or a broad QRS complex and who are not receiving cardiac glucosides should immediately be given intravenously 0.5 – 1.0g (5 – 10mL of a 10% solution) of calcium gluconate or another calcium salt over a 2-minute period (with continuous ECG monitoring) to antagonize the cardiac toxic effects of potassium. If ECG abnormalities persist, repeated doses of calcium salt may be given, allowing 1 – 2 minutes between doses.

When the ECG approaches normal, efforts should be directed toward removal of excess potassium from the body. This is a choice of treatment, when the removal of the potassium should be initiated as soon as possible. This is accomplished by administration of sodium polystyrene sulphonate resin orally or rectally, where sodium is exchanged with potassium in the gastrointestinal tract. One gram of resin will remove 1mmol of potassium, but at the same time it will add 2 – 3mmol of sodium, which may lead to a sodium overload. To overcome the constipating effect by the resin, it is formulated in sorbitol solution (20%). The initial dose of 30 – 60g of resin in 120 – 240mL of 20% sorbitol has been recommended. It can be repeated every 1 – 2 hours.

As a last resort, haemodialysis or peritoneal dialysis can be used to remove potassium from the body, in particular, patients with renal impairment. The infusion of furosemide (high ceiling diuretics) with a substantial amount of sodium chloride and bland solution will excrete potassium at the distal tubules of the renal system by sodium exchange mechanism into the urine.

For advice on the management of overdose please contact the National Poisons Centre on phone number: 0800 764 766 [0800 POISON] in New Zealand (or 131126 in Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

Electrolytes with Carbohydrates.

ATC code

B05BB02.

Mechanism of action

Glucose is readily metabolised into carbon dioxide and water with a release of energy. Thus, administration of a glucose solution either by oral or parenteral route will provide water for body hydration as well as energy. In addition, it may reduce catabolic loss of nitrogen from the body and aid in prevention of depletion of liver glycogen. That is, in the absence of glucose, amino acids undergo deamination followed by oxidation in order to release energy.

Potassium is the major cation of intracellular fluid (160mEq/L of intracellular water) and functions principally in the control of body fluid composition and electrolyte balance. Potassium participates in carbohydrate utilisation, protein synthesis, and is critical in the regulation of nerve conduction and muscle contraction, particularly in the heart.

In contrast, sodium is a major cation of the extracellular fluid and functions principally in the control of water distribution, fluid and electrolyte balance, and osmotic pressure of the body fluids. Sodium is also associated with chloride and bicarbonate in the regulation of acid-base balance. A membrane bound enzyme, sodium-potassium activated ATP-ase (Na/K-ATPase), actively pumps sodium ions out of the cells into extracellular compartments, whilst the potassium ions are pumped into the cells 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 eletroneutrality of the cells by the following equation.

That is: $Na^+ = Cl^- + HCO_3^- + [\text{anion gap}]^-$

where pH is related to equation: $pH = pK_{H2CO3} + \log [HCO_3^-]/[H_2CO_3]$

The anion gap is called "unmeasured anion".

Physiochemical properties

Potassium chloride

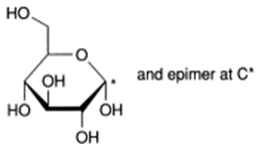
Molecular formula:	KCl
Molecular Weight:	74.55
Appearance:	colourless or white crystal
Solubility:	freely soluble in water
CAS:	7447-40-7

Sodium chloride

Molecular formula:	NaCl
Molecular Weight:	58.44
Appearance:	colourless or white crystal
Solubility:	freely soluble in water and practically insoluble in anhydrous ethanol
CAS:	7647-14-5

Glucose (D-(+)glucopyranose)

Chemical structure:



Molecular formula:	$C_6H_{12}O_6$
Molecular Weight:	180.2
Appearance:	a white or almost white, crystalline powder
Solubility:	freely soluble in water, sparingly soluble in ethanol (96%)
CAS:	50-99-7

5.2 Pharmacokinetic properties

Absorption

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

Distribution
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.

Excretion
Sodium and potassium ions are principally excreted by the kidneys.

5.3 Preclinical safety data
Genotoxicity
The active ingredients, glucose, sodium chloride and potassium chloride are not mutagenic. They are the basic constituents in all living cells.

Carcinogenicity
The active ingredients, glucose, sodium chloride and potassium chloride are not carcinogenic. They are the basic constituents in all living cells.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Water for injections.

6.2 Incompatibilities
Additives may be incompatible. Check additive compatibility with both the solution and container prior to use. Those additives known to be incompatible should not be used. Consult with pharmacist, if available.

6.3 Shelf life
24 months from date of manufacture. The expiry date can be found on the packaging.

6.4 Special precautions for storage
Store at or below 30°C. Do not freeze.

6.5 Nature and contents of container
Potassium Chloride, Glucose and Sodium Chloride infusion solution preparations are supplied in VIAFLEX plastic bags as a 500mL or 1000mL single unit dose*:

- **Potassium Chloride 20mmol (0.15%) in 4% Glucose and 0.18% Sodium Chloride** infusion solution 1000mL bag (12's) (AHB1704) TT50-5540
- **Potassium Chloride 20mmol (0.15%) in 4% Glucose and 0.18% Sodium Chloride** infusion solution 500mL bag (18's) (AHB1703) TT50-5540
- **Potassium Chloride 30mmol (0.224%) in 4% Glucose and 0.18% Sodium Chloride** infusion solution 1000mL bag (AHB1224) TT50-5540/1
- **Potassium Chloride 20mmol (0.15%) in 5% Glucose and 0.45% Sodium Chloride** infusion solution 1000mL bag (AHB6024) TT50-9818
- **Potassium Chloride 20mmol (0.15%) in 5% Glucose and 0.9% Sodium Chloride** infusion solution 1000mL bag (AHB6066) TT50-9819

*Not all products may be marketed.

6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

Potassium Chloride, Glucose and Sodium Chloride infusion solutions are distributed in New Zealand by:

Baxter Healthcare Ltd
33 Vestey Drive
Mt Wellington
Auckland 1060

Baxter Healthcare Ltd
PO Box 14 062
Panmure
Auckland 1741

Phone (09) 574 2400.

Potassium Chloride, Glucose and Sodium Chloride infusion solutions are distributed in Australia by:
Baxter Healthcare Pty Ltd
1 Baxter Drive
Old Toongabbie, NSW 2146.

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:

Potassium Chloride 20mmol (0.15%) in 4% Glucose and 0.18% Sodium Chloride infusion solution:
29 September 1980.

Potassium Chloride 30mmol (0.224%) in 4% Glucose and 0.18% Sodium Chloride infusion solution:
29 September 1980.

Potassium Chloride 20mmol (0.15%) in 5% Glucose and 0.45% Sodium Chloride infusion solution:
9 June 2016.

Potassium Chloride 20mmol (0.15%) in 5% Glucose and 0.9% Sodium Chloride infusion solution:
9 June 2016.

10 DATE OF REVISION OF THE TEXT

23 May 2019.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
ALL	Consistent use of headings, trade name, formatting.
2	Information tabulated and reference to section 6.1 included.
3	Information rearranged and osmolarity and energy tabulated.
4.2	Added information about electrolyte and glucose abnormalities.
4.4	Added hyponatraemia information.
4.5	Added caution related to interactions with other medicines.
4.9	Added information about overdose symptoms.
5.1	Physiochemical properties updated.
6.5	Product information consolidated, removed osmolarity and energy information.

Based on Australian PI amended 20 May 2019 and CCSI 441/442 2018 0628.

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