1 POTASSIUM CHLORIDE AND GLUCOSE (solution for infusion)

Potassium Chloride 20mmol in 5% Glucose
Potassium Chloride 30mmol in 5% Glucose

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients
Potassium chloride and Glucose.

The concentrations of the active ingredients are as follows:
Potassium Chloride 20mmol (0.15%) in 5% Glucose infusion solution, BP
Potassium Chloride 30mmol (0.224%) in 5% Glucose infusion solution, BP.

Potassium Chloride and Glucose 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 and Glucose infusions are sterile, non-pyrogenic solutions. They are clear, colourless solutions for intravenous infusion. They have a pH of 3.5 - 6.5

Their osmolarities are in the upper level of the isotonic range as listed in the following table.

Potassium Chloride and Glucose infusion solution preparations	
Product name and quantity of the active components	**Osmolarity$^{\Phi}$ (mOsmol/L)**
Potassium Chloride 0.15% (20mmol/L) and Glucose 5% (278mmol/L)	317.0 (318.0)
Potassium Chloride 0.224% (30mmol/L) and Glucose 5% (278mmol/L)	340.0 (338.0)
Note: Osmolarity Φ is a calculated figure, whilst figures in the bracket are approximately Osmolality (mOsmol/kg).	

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Potassium Chloride and Glucose infusion solution is indicated for replenishing fluid losses, as an energy source and for restoration or maintenance of potassium and chloride ion concentrations. This is also an alternative route of administration for the patients who are unable to take potassium orally or if hypokalaemia is severe.

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

4.2 Dose and method of administration

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

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, colourless and free of particles and the seals are intact.

Electrolyte supplementation may be indicated according to the clinical needs of the patient. A gradual increase of flow rate should be considered when starting administration of glucose-containing products.

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. See section 3 for information on the products' osmolality.

Except in the presence of severe renal impairment, hyperkalaemia is not likely to occur from slow intravenous administration of a dilute solution of potassium chloride. However, hyperkalaemia may result from rapid intravenous administration of potassium chloride. Generally, the concentration of potassium in an intravenous fluid should not exceed 40mmol/L and the rate of administration should not exceed potassium 20mmol/hour (see table in section 6.5 for comparison).

Potassium Chloride and Glucose infusion solutions are intended for intravenous administration using sterile and non-pyrogenic equipment. They are a pre-mixed potassium chloride in isotonic glucose solution, which are readily available for restoration of potassium, such as in the treatment of hypokalaemia.

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.

The introduction of additives to any parenteral solution, regardless of the type of container, requires special attention so that it will not be adversely affected by an incompatibility problem. While some incompatibilities are readily observed, one must be aware that subtle physical, chemical and pharmacological incompatibilities can occur.

Before adding a substance or medication, verify that it is soluble and/or stable in **Potassium Chloride and Glucose** infusion solutions and that the pH range of **Potassium Chloride and Glucose** infusion solutions are appropriate. The Product Information Document(s) of the medication(s), the instructions for use of the medication(s) to be added and other relevant literature must be consulted prior to their addition to **Potassium Chloride and Glucose** infusion solutions.

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. After addition, if there is a colour change and/or the appearance of precipitates, insoluble complexes or crystals, do not use. 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
Do not remove unit from over-wrap until ready for use. The inner bag maintains the sterility of the product.

Do not connect 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. 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. 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.

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

If supplemental medication is desired, follow directions below.

Preparation for administration
Potassium Chloride and Glucose infusion solutions are sterile preparations. Thus aseptic technique must be applied throughout administration.
(1) Suspend container from eyelet support.
(2) Remove plastic protector from outlet port at the bottom of container.
(3) Attach administration set.

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

To add medication during solution administration
Close clamp on the set. Prepare medication site. Using syringe with 19 to 22-gauge needle, puncture resealable medication port and inject. Remove container from IV pole and/or turn to upright position. 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.

After addition, if there is a color change and/or the appearance of precipitates, insoluble complexes or crystals, do not use. Do not store solutions containing additives.

4.3 Contraindications
Although the level of potassium ions in **Potassium Chloride and Glucose** infusion solution is relatively low, administration of this product is contraindicated:
- In patients who have known hypersensitivity to the product.
- In patients suffering from renal impairment with oliguria, anuria or azotemia; untreated chronic adrenocortical insufficiency (Addison's disease); hyperadrenalism associated with adrenogenital syndrome; extensive tissue breakdown such as in severe burns; hyperkalaemia of any form; clinically significant hyperglycaemia.

Potassium is contraindicated in patients having a disease associated with abnormality of AV conduction in the heart, because an increased potassium level (hyperkalaemia) may worsen the degree of this heart block syndrome.

Corn starch is the raw material for the production of glucose. Therefore, for patients known to have an allergy to corn, or corn products, **Potassium Chloride and Glucose** infusion solution is contraindicated.

4.4 Special warnings and precautions for use

Potassium Chloride and Glucose intravenous infusion solutions are available in Viaflex bags. The safety of the Viaflex plastic bag has been confirmed in tests with animals according to the USP biological tests for plastic containers, as well as by tissue culture toxicity studies. Nevertheless, care should be exercised regarding possible incompatibility outcomes resulting either from the interaction between the plastic container or active ingredients and the added therapeutic substances (see also section 4.2).

Do not administer **Potassium Chloride and Glucose** 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 of **Potassium Chloride and Glucose** infusion solution is listed in section 3. Administration of substantially hypertonic solutions may lead to a wide variety of complications, such as crenation (shrinkage) of red blood cells and general cellular dehydration.

Administration should be carried out under regular and careful surveillance. Regular monitoring of clinical status, plasma electrolyte concentrations, and ECG is essential in patients receiving potassium therapy, particularly those with pre-existing imbalances and those with hepatic, cardiac or renal impairment. Plasma potassium levels may not be directly related to tissue levels.

Due to the risk of pseudo-agglutination precipitated by its glucose content, **Potassium Chloride and Glucose** infusion solution must not be added to, or administered simultaneously through, the same tubing with citrate anticoagulated/preserved blood (see section 4.5).

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

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including anaphylaxis, have been reported with other **Potassium Chloride and Glucose** infusion solutions (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, especially in patients with cardiac disease including congestive heart failure, conditions predisposing to hyperkalaemia such as renal dysfunction, hepatic insufficiency and those that are digitalised.

Potassium Chloride and Glucose infusion solution should be administered with caution, if at all, to patients with conditions predisposing to hyperkalaemia and/or associated with increased sensitivity to potassium, such as patients with:

- Severe renal impairment.
- Acute dehydration.
- Extensive tissue injury or burns.
- Certain cardiac disorders such as congestive heart failure or atrioventricular (AV) block (especially if they receive digitalis).
- Potassium-aggravated skeletal muscle channelopathies (e.g., hyperkalaemic periodic paralysis, paramyotonia congenita, and potassium-aggravated myotonia/paramyotonia).

Thus, the presence of adequate renal function must be confirmed and frequent observation of clinical status of the patient and periodic ECGs and/or determinations of serum concentrations should be made.

Potassium Chloride and Glucose infusion solution should be administered with caution to patients who are at risk of experiencing hyperosmolality, 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 or increase the risk of hyperkalaemia (see section 4.5).

Other groups of patients in whom **Potassium Chloride and Glucose** 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.

Use in patients at risk of severe renal impairment

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

Hyperglycaemia

Potassium Chloride and Glucose infusion solution should be used with caution in patients with overt or subclinical diabetes mellitus (see section 4.5) as they contain glucose.

Rapid administration of glucose solutions may produce substantial hyperglycaemia and hyperosmolar syndrome. In order to avoid hyperglycaemia, the infusion rate should not exceed the patient's ability to utilise 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 and Glucose** infusion solution should be used with caution include:

- Patients with ischaemic stroke. Hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and impairing recovery after acute ischaemic strokes.
- Patients with severe traumatic brain injury (in particular during the first 24 hours following the trauma). Early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury.
- Newborns (see *Paediatric use*, below).

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

Risk of hypo- and hyper-osmolality, 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 metabolise glucose, intravenous administration of glucose can cause:

- Hypoosmolality.
- Hyperosmolality, osmotic diuresis and dehydration.
- Electrolyte disturbances such as:
  - hyponatraemia,
  - hypophosphataemia,
  - hypomagnesaemia.
- Acid-base imbalance.
- Overhydration/hypervolaemia and, for example, congested states, including central (e.g., pulmonary congestion) and peripheral oedema. Particular caution should be taken in patients with conditions that may cause sodium retention, fluid overload, and oedema (central and peripheral).
- Hyponatraemia and a decrease in extracellular sodium concentrations related to hyperglycaemia causing a transcellular shift of water. Infusion of **Potassium Chloride and Glucose** infusion solution corresponds to the increasing body's load of free water, possibly leading to hypoosmotic hyponatraemia.

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.

Particular caution is advised in patients at increased risk of and from water and electrolyte disturbances that could be aggravated by increased free water load.

Hyponatraemia

The use of **Potassium Chloride and Glucose** infusion solution may result in hyponatraemia. Close clinical monitoring may be warranted.

Glucose intravenous infusions are usually isotonic solutions. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolism. 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 metabolise glucose, intravenous administration of glucose can cause electrolyte disturbances, most importantly hypo- or hyperosmotic hyponatraemia.

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 hyponatremia.

Hyponatraemia can lead to acute hyponatraemic encephalopathy (brain 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.

The risk of 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).

The risk for developing hyponatraemic encephalopathy 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.

Hypokalaemia
The infusion of solutions with potassium chloride and glucose may result in hypokalaemia. Hypokalaemia can lead to arrhythmias, muscle weakness, paralysis, heart block, and rhabdomyolysis.

Potassium Chloride and Glucose infusion solution should be used with particular caution, warranting close clinical monitoring, for example:
- In patients with metabolic alkalosis.
- In patients with thyrotoxic or hypokalaemic periodic paralysis.
- In patients with increased gastrointestinal losses (e.g. diarrhoea, vomiting).
- In patients on prolonged low potassium diet (e.g. undernourished or cachectic patients).
- In patients with primary hyperaldosteronism.
- In patients treated with medications that increase the risk of hypokalaemia (e.g. hydrochlorothiazide, loop diuretics, beta-2 agonists, or insulin).

Refeeding syndrome
Refeeding severely undernourished patients may result in the refeeding syndrome that is characterised 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.

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

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

Paediatric use
Neonates, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycaemia. Close monitoring during treatment with intravenous glucose solutions is needed to ensure adequate glycaemic control, in order to avoid potential long-term adverse effects (see section 4.6). 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, necrotising enterocolitits, bronchopulmonary dysplasia, increased oxygen requirements, prolonged length of hospital stay, and death.

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. Hyponatraemia can lead to acute hyponatraemic encephalopathy (brain 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 sever, irreversible and life-threatening brain injury. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

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, volume 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 20mmol (0.15%) in 5% Glucose infusion solution or
Potassium Chloride 30mmol (0.224%) in 5% Glucose infusion solution [**Potassium Chloride and Glucose** intravenous infusion] should not be administered simultaneously with blood preparations through the same administration set, because of the possibility of pseudo-agglutination or haemolysis.

Potassium Chloride and Glucose 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. Administration of potassium in patients treated with such agents is associated with an increased risk of severe and potentially fatal hyperkalaemia, in particular in the presence of other risk factors for hyperkalaemia. 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). Simultaneous administration of either of these medicines or potassium supplements with **Potassium Chloride and Glucose** infusion solution can result in severe hyperkalaemia.

Potassium Chloride and Glucose infusion solution should also be used with caution in patients treated with corticosteroids, cyclosporin, tacrolimus and medicines that contain potassium.

Caution is advised when administering **Potassium Chloride and Glucose** infusion solutions to patients treated with medications leading to an increased vasopressin effect. The below listed medications 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):

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

Caution is advised when administering **Potassium Chloride and Glucose** infusion solutions to patients treated with medications that may increase the risk of hyponatraemia, such as diuretics and antiepileptics (e.g., oxcarbazepine).

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 and Glucose** infusion solution 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.

Potassium Chloride and Glucose infusion solution should be used with caution in patients treated with medications that can increase the risk of hyponatraemia, or sodium and fluid retention, such as corticosteroids. See 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 and Glucose** infusion solution. It is also not known whether these products can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity.

Intrapartum maternal intravenous glucose infusion may result in foetal hyperglycaemia and metabolic acidosis as well as rebound neonatal hypoglycaemia due to foetal insulin production (see section 4.4/*Paediatric use*). **Potassium Chloride and Glucose** infusion solution should be given to pregnant women only if clearly needed after careful consideration of the potential risks and benefits.

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 and Glucose** 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. 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.

Physiologically, an excessive administration of any potassium preparation may result in symptoms of hyperkalaemia. This is particularly manifested in patients with renal impairment. The clinical signs and symptoms of potassium intoxication include paresthesia of the extremities, weakness or heaviness of the legs, cardiac arrhythmias, heart block, cardiac arrest and mental confusion. Intravenous infusion of potassium at rates exceeding 20mmol/hour, or concentrations of potassium exceeding 40mmol/L or less in the case of renal impairment, may lead to a dangerous level of hyperkalaemia. Potassium serum levels of greater than 6mmol/L commonly manifest cardiac arrhythmias.

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.
Other: Listlessness, mental confusion, paraesthesia of the extremities, muscle weakness, heaviness of the legs, paralysis.

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

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

- GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site rash, Infusion site pain.

Other reactions (Class reactions)
Other adverse reactions reported with other similar products include:

- IMMUNE SYSTEM DISORDERS: anaphylactic reaction/hypersensitivity.
- METABOLISM AND NUTRITION DISORDERS: hyperkalaemia, hypokalaemia, hyponatraemia.
- GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: infusion site reactions, including infusion site vesicles, infusion site pruritus, infusion site phlebitis, chills, pyrexia.
- NERVOUS SYSTEM DISORDERS: hyponatraemic encephalopathy.
- CARDIAC DISORDERS: cardiac arrest (as a manifestation of hyperkalaemia).

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

There is no overdose experience with **Potassium Chloride and Glucose** 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, severe dilutional hyponatraemia,

hyponatraemia (which can lead to CNS manifestations including seizures, coma, cerebral oedema) and their complications, can be fatal (see section 4.4).
- Fluid overload (which can lead to central and/or peripheral oedema) (see section 4.4).
- Development of potentially fatal hyperkalaemia. It is usually asymptomatic and may be manifested only by an increased serum potassium concentration and characteristic ECG changes (peaking of T waves, depression of the ST segment, disappearance of P wave, prolongation of the QT interval, and widened QRS complex). Extremely high serum potassium concentrations (8 – 11mmol/L) may cause death from cardiac depression, arrhythmia or arrest (see section 4.8).

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. Manifestations of hyperkalaemia may also 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).

When assessing an overdose, any additives in the solution must also be considered. Clinically significant overdose of **Potassium Chloride and Glucose** infusion solution may, therefore, constitute a medical emergency.

Treatment
No specific antidotes to this preparation are known. Should overdose occur, interventions include discontinuation of solution administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

If hyperkalemia 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. Treatment of hyperkalaemia depends on its severity. 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 the pH.

Glucose/insulin infusion is another treatment for an overdose episode with potassium chloride medications. 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 substantial amounts 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	*ATC code*
Other IV Solution Additives.	B05XX.

Mechanism of action

Glucose is readily metabolised into carbon dioxide and water, with a release of energy. As such, an administration of a glucose solution either by oral or parenteral route provides water for body hydration as well as energy (for conversion to kJ units, see table in section 6.5). 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 (approximately 160mmol/L of intracellular water) and it controls the body fluid composition and electrolyte balance; 98% of the total body potassium is intracellular. In the extracellular fluids (interstitial and vascular compartments) sodium ions predominate whilst potassium ions are generally low ranging from 3.5 to 5.0mmol/L. A membrane bound enzyme, sodium-potassium activated ATPase (Na/K-ATPase), actively pumps sodium ions out of the cells and potassium ions into the cells through a gate-mechanism against a concentration gradient in order to maintain a homeostasis of electrolytes of the cells. Potassium participates in carbohydrate utilization, protein synthesis, and is critical in the regulation of nerve conduction and muscle contraction, particularly in the heart.

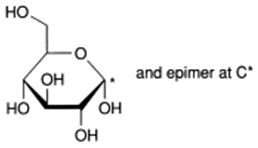
Chloride, the major extracellular anion, closely follows the physiological disposition of sodium cation in maintenance of acid-base balance, isotonicity and electrodynamic characteristics of the cells. Thus, **Potassium Chloride and Glucose** infusion solution has value as a source of water, electrolytes and energy (835kJ/L); see table in section 6.5 for the strength of the solution.

Clinical trials
No data available.

Physiochemical properties potassium chloride

Molecular formula	KCl
Molecular weight	74.55
Appearance	Colorless or white crystal
Solubility	Freely soluble in water
CAS No.	7447-40-7

Physiochemical properties glucose

Chemical name	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 No.	50-99-7

5.2 Pharmacokinetic properties

Potassium Chloride and Glucose infusion solution is directly administered to the systemic circulation by infusion; the bioavailability (absorption) of the active components is complete (100%). After its distribution into extracellular compartments, these ions are actively pumped into the cells by action of Na/K-ATPase. Glucose, insulin and oxygen facilitate the movement of potassium into the cells. Thus, in insulin-deficient diabetic patients, the tolerance of potassium load is impaired.

Under normal conditions, the kidney primarily excretes the excess of potassium, if any, with only a small amount appearing in the faeces. The capacity of the kidney to conserve potassium ions is poor, and a deficiency of these ions will develop rapidly if intake drops significantly. In the kidney, it is secreted in the distal tubules, where the sodium-potassium exchange takes place. A small amount of potassium is lost in sweat.

5.3 Preclinical safety data

Genotoxicity
The active ingredients glucose and potassium chloride are not mutagenic. They are basic nutrients in all living cells.

Carcinogenicity
The active ingredients glucose and potassium chloride are not carcinogenic. They are basic nutrients in all living cells.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections
Hydrochloric acid (for pH adjustment).

6.2 Incompatibilities

Additives may be incompatible. Consult with a pharmacist, if available. Check additive compatibility with both the solution and container prior to use. Those additives known to be incompatible should not be used (see section 4.2).

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

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.

Exposure of the products to heat should be minimised. Avoid excessive heat.

6.5 Nature and contents of container

Potassium Chloride and Glucose infusion solutions are supplied in Viaflex plastic bags as a single unit dose. They are available in the strengths shown in the following table:

Potassium Chloride and Glucose infusion solution preparations			
Code No.	Product name and quantity of the active components [energy (kJ/L)]	TT50-	Pack Size* (mL)
AHB1134	Potassium Chloride 0.15% (20mmol/L) and Glucose 5% (278mmol/L) [835 kJ/L]	5539	1000 (x12)
AHB1174	Potassium Chloride 0.224% (30mmol/L) and Glucose 5% (278mmol/L) [835 kJ/L]	5539/1	1000 (x12)
1 gram of glucose provides 16.7 kiloJoules (kJ) of energy. * Not all packs may be marketed.			

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

Potassium Chloride and Glucose 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 and Glucose 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 in 5% Glucose infusion solution: 29 September 1980.
Potassium Chloride 30mmol in 5% Glucose infusion solution: 29 September 1980.

10 DATE OF REVISION OF THE TEXT

13 November 2019.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Editorial changes: formatting, spacing, capitalisation, bullet points, headings, made consistent throughout, and consistent with other Data Sheets in the Baxter product range. Information relocated throughout to more appropriate locations, repeated information deleted.
4.2	Warning added to consult physician. Safety information relating to introduction of additives moved from 6.2. Safety information added to use aseptic technique.
4.4	Safety information added relating to hyponatraemia.
4.5	Safety information added relating to vasopressin effect.
5.1	Physiochemical properties included.
6.1	Section updated.

Based on Australian PI amended 9 August 2019; and CCSI44820180725.

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