Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 1.50 mg Potassium Chloride and 50.0 mg Glucose
Each 500 ml bottle contains 0.75 g Potassium Chloride and 25 g Glucose
Each 1000 ml bottle contains 1.50 g Potassium Chloride and 50 g Glucose

mmol/l: K^+: 20 Cl^-: 20

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
Clear solution, free from visible particles.

pH 3.5 – 6.0
Osmolarity 318 mOsm/l

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prevention and treatment of potassium depletion and/or hypokalaemia in cases where supply of water and carbohydrates is required due to either restriction of the intake of fluids and electrolytes or depletion by normal routes.

4.2 Posology and method of administration

Posology
Doses may be expressed in terms of mEq or mmol of potassium, mass of potassium, or mass of potassium salt:
1 g KCl = 525 mg of K^+ or 13.4 mEq or 13.4 mmol of K^+ and Cl^-
1 mmol K^+ = 39.1 mg K^+.

The dosage of this solution depends on the age, weight, clinical and biological (acid-base balance) conditions of the patient, concomitant therapy and in particular the patient's hydration state.

General posology
The recommended dosage for the treatment of carbohydrates and fluid depletion is
- for adults: 500 ml to 3 litres/24 h

- for babies and children:
0 - 10 kg body weight: 100 ml/kg/24 h
10 - 20 kg body weight: 1000 ml + (50 ml/kg over 10 kg) /24 h
> 20 kg body weight: 1500 ml + (20 ml/kg over 20 kg)/24 h

The infusion rate should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycaemia. Therefore the maximum dose ranges from 5 mg/kg/min for adults to 10 - 18 mg/kg/min for babies and children depending on the age and the total body mass.

Posology for prevention and treatment of potassium depletion

Adults, Older people and Adolescents

A typical dose of potassium for the prevention of hypokalaemia may be up to 50 mmol daily and similar doses may be adequate in mild potassium deficiency. The maximal recommended dose of potassium is 2 to 3 mmol/kg/24 h.

When used for the treatment of hypokalaemia, the recommended dosage is 20 mmol of potassium over 2 to 3 hours (i.e. 7-10 mmol/h) under ECG control.

The maximum recommended administration rate should not exceed 15-20 mmol/h.

Patients with renal impairment should receive lower doses.

In any case, the dosage given under "General Posology" should not be exceeded.

Use in Paediatric Population

When used in the treatment of hypokalaemia the recommended dosage is 0.3 – 0.5 mmol/kg/b.w./h. The dose has to be adjusted on frequently obtained lab values.

The maximum recommended dose of potassium is 2 to 3 mmol/kg/b.w./day.

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy and should be determined by the consulting physician experienced in paediatric intravenous fluid therapy (see Section 4.4).

Method of administration

Route of administration

The administration is performed by intravenous route using sterile and non-pyrogenic equipment.

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

Solutions containing potassium should be administered slowly.

Rate of administration

As administered intravenously, potassium should not be given faster than 15 to 20 mmol/h to avoid dangerous hyperkalaemia.

Monitoring

Adequate urine flow must be ensured and careful monitoring of plasma-potassium and other electrolyte concentrations is essential. Higher dosage or high speed infusion must be performed under ECG control.

Fluid balance, serum glucose, serum sodium and other electrolytes may need to be monitored before and during administration, especially in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonist drugs due to the risk of hyponatraemia.

Monitoring of serum sodium is particularly important for products with lower sodium concentration compared to serum sodium concentration. After infusion of Potassium Chloride 0.15% w/v & Glucose 5% w/v a rapid active glucose transport into the body cells occurs. This condition promotes an effect which can be considered as supply of free water and can lead to severe hyponatraemia.(see sections 4.4, 4.5 and 4.8).

4.3 Contraindications

- Hyperchloremia and hyperkalaemia
- Severe renal insufficiency (with oliguria/anuria)
- Uncompensated cardiac failure
- Addison's disease

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

4.4 Special warnings and precautions for use

Intravenous 5% glucose-infusions are isotonic. Glucose solutions with higher glucose concentration are hypertonic. In the body, however, glucose containing fluids can lead to an effect which can be considered as supply of free water due to a rapid active glucose transport into the body cells. This condition can lead to severe hyponatraemia (see section 4.2).

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.

Hyponatraemia:
Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, burns, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of physiologically hypotonic fluids.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (brain oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Children, women in the fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, and cerebral contusion) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure.

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.

Potassium salts should be administered with considerable care to patients with cardiac disease (e.g. myocardial infarction, cardiac arrhythmias) or conditions predisposing to hyperkalemia such as renal or adrenocortical insufficiency, acute dehydration, or extensive tissue destruction as occurs with severe burns.
In patients under digitalis therapy regular monitoring of the plasma potassium level is mandatory.

Infusion of solutions containing glucose could be contraindicated in the first 24 hours following head trauma and blood glucose concentration should be closely monitored during intracranial hypertension episodes.

Administration of glucose containing solutions may lead to hyperglycaemia. In this case, it is recommended not 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.

In diabetic patients, the amount of infused glucose has to be taken into account and insulin requirements may be modified.

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

Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion contains glucose derived from corn. It should be used with caution in patients with known corn allergies (see section 4.8).

Paediatric Population
Newborns – 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 newborn can cause prolonged seizures, coma and brain damage. Hyperglycaemia has been associated with intraventricular haemorrhage, late onset bacterial

and fungal infection, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stay, and death.

In order to avoid potentially fatal over infusion of intravenous fluids to the neonate, special attention needs to be paid to the method of administration. When using a syringe pump to administer intravenous fluids or medicines to neonates, a bottle of fluid should not be left connected to the syringe.

When using an infusion pump all clamps on the intravenous administration set must be closed before removing the administration set from the pump, or switching the pump off. This is required regardless of whether the administration set has an anti-free flow device.

The intravenous infusion device and administration equipment must be frequently monitored.

Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes. 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.

4.5 Interaction with other medicinal products and other forms of interactions

Drugs leading to an increased vasopressin effect
The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i.v. fluids (see sections 4.2, 4.4 and 4.8).

- Drugs stimulating vasopressin release, e.g.: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics
- Drugs potentiating vasopressin action, e.g.: Chlorpropamide, NSAIDs, cyclophosphamide
- Vasopressin analogues, e.g.: Desmopressin, oxytocin, vasopressin, terlipressin

Other medicinal products increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

Solutions containing potassium should be used with caution, in patients receiving drugs that increase plasma-potassium concentrations (e.g. potassium-sparing diuretics, ACE inhibitors, Angiotensin II receptors antagonists, ciclosporin, tacrolimus and drugs that contain potassium).
The pharmacological effect of digitalis glycosides (digoxin and methyldigoxin) and antiarrhythmic agents (such as quinidine, hydroquinidine, procainamide) can be altered as a function of blood potassium levels:

- Digitalis: hyperkalaemia reduces the therapeutic action of these drugs whereas hypokalaemia can cause digitalis toxicity.
- Antiarrhythmic agents: hyperkalaemia increases their antiarrhythmic effects and hypokalaemia reduces their efficacy.

Glucose should not be administered through the same infusion equipment as whole blood, as haemolysis and clumping can occur.

4.6 Fertility, pregnancy and lactation

Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion should be administrated with special caution for pregnant women during labour particularly if administered in combination with oxytocin due to the risk of hyponatraemia (see section 4.4, 4.5 and 4.8).
Hyperkalaemic and hypokalaemic serum levels lead to impaired cardiac function of the maternal and foetal hearts. Therefore, maternal electrolyte levels must be controlled regularly.
As long as the maternal electrolyte serum levels are kept within the physiological range, there are no potential concerns regarding administration of Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Adverse reactions may be associated to the technique of administration, including febrile response, infection at the site of injection, local pain or reaction, vein irritation, venous thrombosis or phlebitis extending from the site of injection, extravasation, and hypervolemia.
In case of undesirable effect(s), the infusion must be discontinued.
Anaphylactic reaction, hypersensitivity, and chills have also been reported.[1]
[1]Reported for similar solutions containing dextrose.

Table 1

System Organ Class	Symptoms (LLT terms MedDRA)	Frequency
Immune system disorders	Allergic reaction, Anaphylactic reaction**, Hypersensitivity**	Not known (*)
Metabolism and nutrition disorders	Hypervolaemia, Hospital acquired hyponatraemia***	
Nervous system disorders	Hyponatraemic encephalopathy***	
Skin and subcutaneous tissue disorders	Sweating	
General disorders and administration site conditions	Chills**, Shivering Febrile reaction, Fever Infection at site of injection Thrombophlebitis	

Tabulated list of adverse reactions
(*) cannot be estimated from the available data
(**) Potential manifestation in patients with allergy to corn, see section 4.4.
(***) Hospital acquired hyponatraemia may cause irreversible brain injury and death, due to development of acute hyponatraemic encephalopathy (see sections 4.2. 4.4, 4.5).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: + 353 1 6764971; Fax: + 353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie

4.9 Overdose

Excessive administration of potassium may lead to the development of hyperkalaemia, especially in patients with renal impairment. Symptoms include paresthesia of the extremities, muscle weakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest, and mental confusion.

One of the important indicators of potassium toxicity is ECG changes including tall, peaked T-waves, depression of S-T segment, disappearance of the P-wave, prolongation of the Q-T interval, and widening and slurring of the QRS complex.

Treatment of hyperkalaemia involves the administration of calcium, insulin or sodium bicarbonate, and exchange resins or dialysis.

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

In the event of accidental over infusion, treatment should be discontinued and the patient should be observed for the appropriate signs and symptoms related to the drug administered. The relevant symptomatic and supportive measures should be provided as necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Blood substitutes and perfusion solutions; electrolytes with carbohydrates, ATC code: B05BB02

Potassium Chloride 0.15% w/v & Glucose 5% w/v is a hypertonic solution of electrolytes and glucose, with an approximate osmolarity of 318 mOsm/l.

The pharmacodynamic properties of this solution are those of its components (potassium, chloride and glucose).

Potassium is predominantly an intracellular cation, primarily found in muscle; only about 2% is present in the extracellular fluid. It is essential for numerous metabolic and physiological processes including nerve conduction, muscle contraction, and acid-base regulation.

Chloride is mainly an extracellular anion. Intracellular chloride is in high concentration in red blood cells and gastric mucosa.

Glucose is the principal source of energy in cellular metabolism.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of Potassium Chloride 0.15% w/v & Glucose 5% w/v are those of its components (potassium, chloride and glucose).

Intravenous administration of this solution provides an immediate supply of electrolytes and glucose to blood.

Factors influencing potassium transfer between intracellular and extracellular fluid such as acid-base disturbances can distort the relationship between plasma concentrations and total body stores. Potassium is excreted mainly by the kidneys; it is secreted in the distal tubules in exchange for sodium or hydrogen ions.
The capacity of the kidneys to conserve potassium is poor and some urinary excretion of potassium continues even when there is severe depletion. Some potassium is excreted in the faeces and small amounts may also be excreted in sweat.

The two main metabolic pathways of glucose are gluconeogenesis (energy storage) and glycogenolysis (energy release). Glucose metabolism is regulated by insulin.

5.3 Preclinical safety data

Preclinical safety data of Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion in animals are not relevant since potassium chloride and glucose are physiological components of the body.

Toxic effects are not to be expected if serum electrolytes are kept within physiological range.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities

Incompatibility of the medicinal product to be added to Potassium Chloride 0.15% w/v & Glucose 5% w/v must be assessed before addition.
In the absence of compatibility studies, this solution must not be mixed with other medicinal products.
It is the responsibility of the physician to judge the incompatibility of an additive medication with the Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion by checking for eventual colour change and/or eventual precipitate, insoluble complexes or the appearance of crystals. The Instructions for Use of the medication to be added must be consulted.

Before adding a drug, verify that it is soluble and/or stable in water at the pH of Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion (pH: 3.5 to 6.0).

As a guidance, the following medications are incompatible with the Potassium Chloride 0.15% w/v & Glucose 5% solution (non-exhaustive listing):
- Amphotericin B
- Dobutamine.

Glucose should not be administered through the same infusion equipment as whole blood, as haemolysis and clumping can occur.

Those additives known to be incompatible should not be used.

6.3 Shelf life

24 months

Shelf life after first opening:
Stability of the product after first opening has not been tested, therefore, the product has to be used immediately after first opening.

In-use shelf life (additives):
Chemical and physical stability of any additive medication at the pH of the Potassium Chloride 0.15% w/v & Glucose 5% w/v Solution for Infusion should be established prior to use.

From a microbiological point of view, the mixtures of this medicinal product with other medicinal products must be used immediately unless the mixture has taken place under controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Potassium Chloride 0.15% w/v & Glucose 5% w/v is available in 500 ml and 1000 ml low-density polyethylene bottles as primary packaging closed with a polyolefin cap containing a polyisoprene rubber stopper. It is supplied in packs of 10 bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Potassium Chloride 0.15% w/v & Glucose 5% w/vis a ready to use solution.
It is for single use only. Any unused solution should be discarded.

Use only if the solution is clear, without visible particles and if the container is undamaged.

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

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/053/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 22nd April 2020

10 DATE OF REVISION OF THE TEXT

November 2019