SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Potassium Chloride 0.15% w/v, Sodium Chloride 0.18% w/v, and Glucose 4% w/v Intravenous Infusion BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Potassium Chloride 0.15 % w/v, Sodium Chloride 0.18 % w/v, and Glucose 4 % w/v Intravenous Infusion BP (in the following referred to as "0.15% KCl, 0.18% NaCl, and 4% Glucose") contains:

	1,000 ml	*mg/ml*
Potassium chloride	1.50 g	1.50
Sodium chloride	1.80 g	1.80
Anhydrous glucose (as glucose monohydrate)	40.00 g	40.00
Electrolyte concentrations:		
Potassium	20 mmol/l	
Sodium	30 mmol/l	
Chloride	50 mmol/l	

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
Clear colourless aqueous solution

Caloric value (approx.)	160 kcal
Theoretical osmolarity (approx.)	322 mOsm/l
pH (approx.)	4.5

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For correction or maintenance of potassium, sodium, chloride and fluid balance in cases where a supply of energy is required.

4.2 Posology and method of administration

The dosage is dependent on age, weight and clinical condition of the patient, especially those with renal or cardiac insufficiency. 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 physiologically hypotonic fluids. "0.15% KCl, 0.18% NaCl, and 4% Glucose" may become hypotonic after administration due to glucose metabolisation in the body (see sections 4.4, 4.5 and 4.8).

Dosage and rate of infusion should be determined by ECG and serum electrolyte monitoring.

Adults:

Potassium Dosage/Rate of Infusion Guidelines

Serum K+	Maximum infusion rate	Maximum concentration
> 2.5 mmol/l	10 mmol/h	40 mmol/l
< 2 mmol/l	40 mmol/h	80 mmol/l

The maximum recommended dose of potassium is 2 – 3 mmol/kg b.w./24 h

The administered amount of glucose should not exceed 3-4 g/kg b.w. in 24 h. Generally, not more than 40 ml fluid/kg b.w./d should be supplied.

Children:

The volume and rate of infusion will depend upon the requirements of the individual patient. Reduced volumes and rates of infusion will be required.

Rate of Infusion :

The rate of infusion should be guided by ECG and serum electrolyte monitoring. Adequate urine flow must be ensured.

The maximum rate of infusion should not exceed 10 mmol potassium/h when serum potassium levels are above 2.5 mmol/l and 40 mmol/h if serum potassium levels are below 2 mmol/l.

Duration of use

"0.15% KCl, 0.18% NaCl, and 4% Glucose" may be administered as long as there is an indication for energy, electrolyte and fluid administration.

Method and route of administration

Intravenous infusion via a large peripheral or central vein to avoid the risk of sclerosing. If infused through a central vein, to avoid localised hyperkalaemia the catheter must not be in the atrium or ventricle.

This container contains a significant volume of air. To avoid risk of air embolism, this product must not be administered by pressure infusion.

4.3 Contraindications

- Hyperkalaemia,
- Severe renal impairment with oliguria, anuria, or azotaemia,
- Hyperchloraemia,
- Acute ischaemic stroke,
- Head trauma (first 24 hours),
- Hyperhydration.

4.4 Special warnings and precautions for use

- Solutions with low salt, especially sodium, should only be administered with special caution to children and close monitoring of electrolyte and fluid balance should be performed.
- Solutions containing potassium should be administered slowly and only after renal function has been established and proved adequate. In patients with renal impairment, its use must be carefully controlled by frequent determinations of plasma potassium concentrations and periodic ECGs. The infusion must be discontinued if signs of renal insufficiency develop during infusion.
- Solutions containing sodium chloride must be used with caution in patients who have an impaired ability to handle sodium and fluid such as heart disease especially with a history of congestive heart failure, patients with renal insufficiency, cirrhosis of the liver, cardio-pulmonary disease, or patients receiving salt-retaining steroids.
- Potassium supplements should be administered with caution in patients with cardiac disease particularly in digitalised patients. Rapid lowering of plasma potassium concentrations (e.g. when discontinuing the infusion) in digitalised patients can cause cardiac glycoside toxicity.
- “0.15% KCl, 0.18% NaCl, and 4% Glucose” is a slightly hypertonic solution. In the body, however, the solution can become physiologically hypotonic due to rapid glucose metabolisation (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 metabolise glucose, intravenous administration of these solutions 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 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.

- Care must be exercised in the administration of large volume infusion of hypotonic fluids to patients with congested states or pulmonary oedema.
- As a hypotonic solution containing only 30 mmol sodium/l, the infusion should also be administered with care in patients with hypotonic dehydration and in cases of hyponatraemia.
- Caution should be exercised when the solution is administered to patients with diabetes, especially those with insulin-refractory hyperglycaemia and in patients with glucose intolerance for any other reason (see also section 4.5). Blood glucose monitoring will be required.
- Solutions containing glucose should not be administered simultaneously with, before or after an administration of blood through the same infusion equipment because of the possibility of pseudoagglutination.
- It is recommended that all intravenous apparatus be replaced at least once every 24 h.

Clinical supervision should include ECGs, regular checks of fluid balance and serum electrolytes.

4.5 Interaction with other medicinal products and other forms of interaction

“0.15% KCl, 0.18% NaCl, and 4% Glucose” as a glucose containing solution should not be administered simultaneously with, before or after an administration of blood through the same infusion equipment because of the possibility of pseudoagglutination.

Corticosteroids or corticotropins may lead to reduced glucose tolerance and corticosteroids are associated with the retention of sodium and water

Care should be taken in the concurrent use of drugs containing potassium and drugs with the potential to induce hyperkalaemia, such as:

- potassium-sparing diuretics e.g. spironolactone, triamterene
- ACE inhibitors

- cyclosporine.
- Suxamethonium

- Medicinal products 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.

- In patients on digoxin, hypokalaemia may result in digoxin toxicity. Potassium administration must be very carefully discontinued in these patients.

Contamitant application of suxamethonium and potassium may lead to a considerable increase in serum potassium level (hyperkalaemia).

Other clinically relevant pharmacological drug interactions are not known.

4.6 Pregnancy and lactation

For “0.15% KCl, 0.18% NaCl, and 4% Glucose” no controlled clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

It has been suggested that if used during labour, the glucose load on the mother may lead to foetal hyperglycaemia, hyperinsulinaemia and acidosis, with subsequent neonatal hypoglycaemia. Others have found no evidence of such an effect.

“0.15% KCl, 0.18% NaCl, and 4% Glucose” 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).

Caution should be exercised when prescribing to pregnant or nursing women.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Listing of undesirable effects

Undesirable effects are listed according to their frequencies as follows:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (frequency cannot be estimated from the available data)

General disorders and administration site conditions

Not known: Local pain and phlebitis may occur during administration of solutions containing 40 mmol or more potassium per litre.

Metabolism and nutrition disorders:

Not known: Hospital Acquired Hyponatraemia

Neurological disorders:

Not known: Hyponatraemic encephalopathy

Hospital acquired hyponatraemia may cause irreversible brain injury and death due to development of acute hyponatraemic encephalopathy (see sections 4.2 and 4.4).

In patients with severe renal or metabolic impairment or when the infusion is either carried out too rapidly or to excess, it is possible that overhydration, hyperglycaemia or potassium intoxication results. Symptoms of hyperkalaemia include paresthesias of extremities, muscle or respiratory paralysis, areflexia, weakness, listlessness, cold skin, gray pallor, mental confusion, weakness and heaviness of legs, hypotension, cardiac arrhythmia, heart block, ECG abnormalities with development of biphasic curves and cardiac arrest.

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 teh Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms

If excretory mechanisms are impaired or the infusion is either carried out too rapidly or to excess, hyperkalaemia, hyperhydration, metabolic and electrolyte

disorders can result. Especially the potassium homeostasis will be affected in case of overdose. The possible symptoms of potassium intoxication are described in section 4.8.

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

Excessive or rapid administration of sodium chloride solution may lead to hypervolaemic haemodilution with hypertension, tachycardia and oedema.

Emergency treatment, antidotes

Immediate interruption of the infusion, ECG monitoring, if necessary enhancement of urine flow and thus fluid and electrolyte excretion, administration of sodium bicarbonate. If insulin is given to increase cellular uptake of potassium, glucose should be given to avoid hypoglycaemia. In patients with persistent ECG abnormalities e.g. calcium gluconate may be administered to antagonise the cardiotoxic effects of potassium. Caution should be exercised if the patient is on cardiac glycosides as rapid lowering of the potassium levels may enhance cardiac glycoside toxicity. Haemodialysis or peritoneal dialysis may be required in patients with renal insufficiency.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group (ATC code): B05B B

“0.15% KCl, 0.18% NaCl, and 4% Glucose” contains glucose and the electrolytes potassium, sodium, and chloride in water.

Potassium is the major cation of intracellular fluid and is essential for maintenance of acid-base balance, isotonicity, and electrodynamic characteristics of the cell. The electrolyte is an important activator in many enzymatic reactions and is essential to a number of physiologic processes including transmission of nerve impulses, contraction of cardiac, smooth, and skeletal muscles, gastric secretion, renal function, tissue synthesis, carbohydrate utilisation and protein synthesis.

Sodium is the major cation of the extracellular fluid and is principally responsible for the control of water distribution, fluid and electrolyte balance, and osmotic pressure of body fluids. Together with chloride and bicarbonate, sodium plays also an important role in the regulation of acid-base balance. Chloride, the major extracellular anion, closely follows the physiologic disposition of sodium, and changes in the acid-base balance of the body are reflected by changes in serum chloride concentration.

Glucose is the main carbohydrate in the body and is essential to some organs. In the body glucose itself and derivates of glucose metabolism are used for energy supply, modification of proteins and lipids, formation of

mucopolysaccarides and lactose, as components of nucleic acids, and conjugates for the excretion of various substances.

In postoperative, posttraumatic and other clinical instances severe fluid and electrolyte losses and catabolic situations are frequently observed and the above named physiologic functions are impaired. In these patients the application of the components contained in “0.15% KCl, 0.18% NaCl, and 4% Glucose” is indicated to restore fluid and electrolyte levels, supply energy and thus prevent further damage to the body.

5.2 Pharmacokinetic properties

Since the ingredients of “0.15% KCl, 0.18% NaCl, and 4% Glucose” are infused intravenously their bioavailability is 100 %.

Infused potassium is actively transported into the cells, where its concentration is up to 40 times that outside the cell. Plasma potassium concentrations generally range from 3.5 – 5 mmol/l. Sodium and chloride mainly distribute in the extracellular space. Plasma sodium concentration is normally regulated at a concentration of 135 – 145 mmol/l and chloride at 95-107 mmol/l. The kidneys are the main route of excretion for potassium, sodium, and chloride but small amounts are lost via the skin and intestinal tract. Especially surgery results in increased urinary excretion of potassium while water and sodium is retained. For supplementation it is essential to take into consideration that the homeostasis of the single electrolytes is influenced by the others and their regulation is thus interdependent to some degree. For example, a deficiency of either potassium or chloride will lead to a deficit of the other and supplementation in this case has to provide both electrolytes to be effective.

Plasma glucose levels are most closely regulated mainly by the liver together with various hormones and skeletal muscle. Normally glucose is completely oxidised to CO_2 and water, but this metabolic pathway is limited. Excess glucose is stored as glycogen or converted to fat. In severe trauma and other clinical situations such as e.g. diabetes, glucose clearance, oxidation, and recycling are affected and administration must be careful as otherwise hyperglycaemia may result. Cautious administration of glucose can substantially reduce catabolism, help to cover increased energy needs and supply enough glucose for the glucose dependent tissues.

5.3 Preclinical safety data

No preclinical studies have been conducted with “0.15% KCl, 0.18% NaCl, and 4% Glucose”. However, if the dosage instructions are followed, administration of “0.15% KCl, 0.18% NaCl, and 4% Glucose” will only restore physiological electrolyte and fluid homeostasis and supply a fraction of the energy needed by the patient. All components of “0.15% KCl, 0.18% NaCl, and 4% Glucose” are naturally present in the body and their

biochemical properties are well known. Therefore, toxic effects are not to be expected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections.

6.2 Incompatibilities

Compatibilities should be checked when additives are used, as additives may be incompatible. Any questions on compatibility should be directed to the manufacturer, i.e. B. Braun Melsungen AG.

As with all parenteral solutions, before adding medications, compatibility of these additives with the solution in the container must be assessed.

It is the responsibility of the user to judge the incompatibility of an additive medication with the Potassium Chloride 0.15 % w/v, Sodium Chloride 0.18 % w/v and Glucose 4 % w/v Intravenous Infusion BP by checking for eventual colour change and/or eventual precipitate, insoluble complexes or crystals.

Before introducing an additive verify it is soluble and stable in water at the pH of Potassium Chloride 0.15 % w/v, Sodium Chloride 0.18 % w/v and Glucose 4% w/v Intravenous Infusion BP.

When a compatible medication is added to this formulation, the solution must be administered immediately, unless dilution has taken place in controlled and validated aseptic conditions.

Those additives known to be incompatible should not be used.

6.3 Shelf life

Unopened: 24 months.

In-use shelf-life (Additives)

Chemical and physical stability of any additive medication at the pH of the Potassium Chloride 0.15% w/v, Sodium Chloride 0.18 % w/v and Glucose 4 % w/v Intravenous Infusion BP in the container should be established prior to use.

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions are

the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions. .

6.4 Special precautions for storage

Unopened: Do not store above 25 °C.

6.5 Nature and contents of container

Polyethylene plastic containers, 500 ml and 1000 ml in packs of 10.

6.6 Instructions for use and handling

Use only if the solution is clear, without visible particles and if the container is undamaged. The solution should not be administered if the container or its closure show visible signs of damage.

For single use only. Discard unused contents. Do not reconnect partially used container.

Administer immediately following the insertion of infusion set.

The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

Thorough and careful aseptic mixing of any additive is mandatory. Solutions containing additives should be used immediately after preparation, unless preparation has taken place in controlled and validated aseptic conditions.

In case of an adverse reaction, infusion must be stopped immediately.

7 MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

PL 03551/0080

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28th August 2003

10 DATE OF REVISION OF THE TEXT

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