Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion contains:

In 1 000 ml

Potassium chloride	1.50 g
Sodium chloride	9.00 g

Electrolyte concentrations:

Potassium	20 mmol/l
Sodium	154 mmol/l
Chloride	174 mmol/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
A clear colourless aqueous solution

Theoretical osmolarity (approx.) 340 mOsmol/l
pH(approx.) 4.5 – 7.0

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Correction or maintenance of potassium, sodium, chloride and fluid balance, depending upon the clinical condition of the patient.
The solution is particularly indicated in the treatment of hypokalaemia, hypotonic and isotonic dehydration, and hypochloraemic alkalosis.

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

Adequate urine flow must be ensured.

Adults:
The following recommendations are general guidelines on potassium, however prescribing should follow local guidelines.

Potassium
The amount required for correction of moderate potassium deficiency and in maintenance may be calculated according to the following formula:

mmol K+required = (body weight [kg] × 0.2)* × 2 × (serum-K+target** – serum- K+actual [mmol/l])

*Term represents the extracellular fluid volume
** should be 4.5 mmol/l

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

Fluids
Generally, not more than 40 ml fluid/kg b.w./ day should be supplied. In cases where more potassium is needed, other strengths should be considered as well.

Paediatric population
The volume and rate of infusion will depend upon the requirements of the individual patient. Reduced volumes and rates of infusion may be required.Generally a substitution rate of 0.5 mmol/kg bw per hour should not be exceeded. Continuous ECG monitoring should be applied during infusion.

Maximum daily dose
The maximum recommended dose of potassium is 3 mmol/kg BW per 24 hours. In any case the limits for daily fluid intake must not be exceeded.

Elderly

Basically the same dosage as for adults applies, but caution should be exercised in patients suffering from further diseases like cardiac insufficiency or renal insufficiency that may frequently be associated with advanced age. See section 4.

Infusion rate
The infusion rate will depend on the conditions of the individual patient (see section 4.4)

In patients with chronic hyponatraemia the rate of infusion should be slow so that the resulting increase of the serum sodium level is limited to a maximum of 0.35 mmol/l/h.

Duration of use

This medicinal product may be administered as long as there is an indication for electrolyte and fluid administration.

Method and route of administration

Intravenous use.
The maximum rate of Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion administration via peripheral lines is 10 mmol potassium per hour. For greater infusion rates, the solutions should be infused via a central line.
As a matter of principle, infusion pumps should be used for the infusion of potassium in the setting of correction therapy.

4.3 Contraindications

- Hyperkalaemia,
- Severe renal impairment with oliguria, anuria or azotaemia,
- Hyperchloraemia and severe hypernatraemia,
- Hyperhydration.

4.4 Special warnings and precautions for use

Special warnings

Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion should only be administrated with caution in cases of:

- Hypernatraemia
- patients with oedematous states
- pulmonary oedema
- disorders where restriction of sodium intake is indicated, such as cardiac nsufficiency, generalised oedema, pulmonary oedema,hypertension, pre-eclampsia, severe renal insufficiency or liver cirrhosis.

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.

Potassium supplements should be administered with caution in patients with cardiac disease particularly in digitalised patients (see section 4.5).

Sodium chloride supplementation must be exercised slowly in patients with chronic hyponatraemia as too rapid correction of serum sodium levels may in rare cases lead to osmotic side effects.

As a slightly hypertonic solution the infusion should also be administered with care in patients with hypertonic dehydration.

Special caution must be exercised if the solution is administered to acidotic patients.

Caution should be exercised when the solution is administered to patients with Addison's disease as these patients are predisposed to hyperkalaemia.

Paediatric population:
Premature or term infants may retain an excess of sodium due to immature renal function. In premature or term infants, repeated infusion of sodium chloride should therefore only be given after determination of the serum sodium level.

Elderly patients:
Elderly patients, who are more likely to suffer from cardiac insufficiency and renal impairment, should be closely monitored during treatment, and the dosage should be carefully adjusted, in order to avoid cardio circulatory and renal complications resulting from fluid overload.

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

It is recommended that intravenous equipment is replaced at least once every 24 hours.

4.5 Interaction with other medicinal products and other forms of interactions

- **Digoxin, cardiac glycosides**

In patients under treatment with cardiac glycosides, care should be taken to keep the potassium concentration constant.

In case of **hyperkalaemia** - the effect of cardiac glycosides may be weakened, and in case of **hypokalaemia** it may result in cardiac glycoside toxicity. Interactions might occur in the concurrent administration of other antiarrytmics. Potassium administration must be very carefully discontinued in these patients.

- **Drugs with the potential to induce hyperkalaemia**

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

- spironolactone,
- triamterene,
- ACE inhibitors
- Angiotensin II receptor antagonists
- non-steroidal anti-inflammatory agents
- ciclosporin,
- tacrolimus
- suxamethonium

The concomitant administration of potassium-containing solutions and these drugs may lead to severe hyperkalaemia, which may in turn lead to cardiac arrhythmia.

The concomitant use of sodium-retaining drugs (e.g. corticosteroids, non-steroidal anti- inflammatory agents) may lead to oedema.

- **Drugs leading to a decrease of the serum potassium level**

ACTH, corticosteroids and loop diuretics can increase the renal elimination of potassium.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). However, as allcomponents of Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion are naturally present in the body and their biochemical properties are well known , no toxic effects in relation to pregnancy are to be expected.

Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion can be used during pregnancy if clinically needed.

Nevertheless, caution should be exercised in the presence of pre-eclampsia (see section 4.4).

Breast-feeding There are no or limited amount of data from the use of potassium chloride and sodium chloride in lactating women.

However, as all components of this medicinal product are naturally present in the body and their biochemical properties are well known, no toxic effects in relation to lactation are to be expected. Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion can be used during breastfeeding if clinically needed.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

When used accordingly no adverse drug reactions are to be expected.

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 reactions at the infusion site, including local pain, venous irritation and occasionally thrombophlebitis may occur.

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

Symptoms
In case of overdose hyperkalaemia, hyperhydration, acid-base imbalances, oedema, particularly hypernatraemia, hyperchloraemia or potassium intoxication and electrolyte disorders can result.

The symptoms of hyperkalaemia are primarily cardiovascular disorders and include hypotension, cardiac arrhythmia, heart block, ECG abnormalities with development of biphasic curves and cardiac arrest. Other symptoms include paresthesias of extremities, muscle or respiratory paralysis, areflexia, weakness and mental confusion

Rapid increase of the serum sodium level in patients with chronic hyponatraemia may lead to the osmotic demyelination syndrome (see section 4.4).

Treatment
Immediate interruption of the infusion, ECG monitoring, if necessary enhancement of urine flow and thus fluid and electrolyte excretion, administration of sodium bicarbonate and insulin.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.
Haemodialysis or peritoneal dialysis may be required in patients with renal insufficiency.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

Solutions affecting the electrolyte balance
ATC code: B05B B01

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.

<u>Pharmacodynamic effects</u>

In postoperative, posttraumatic and other clinical instances severe fluid and electrolyte losses are frequently observed and the above named physiologic functions are impaired. In these patients the application of the components contained in Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion is indicated to restore fluid and electrolyte levels and thus prevent further damage to the body.

5.2 Pharmacokinetic properties

Absorption

Since the ingredients of Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion are infused intravenously their bioavailability is 100%.

Distribution

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.

Biotransformation

Although sodium, potassium and chloride is absorbed, distributed and excreted, there is no metabolism in the strict sense.

The kidneys are the major regulator of the sodium and water balances. In co-operation with the hormonal control mechanisms (renin-angiotensin-aldosterone system, antidiuretic hormone) and the hypothetical natriuretic hormone they are primarily responsible for keeping the volume of the extracellular space constant and regulating its fluid composition. 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 Chloride is exchanged for hydrogen carbonate in the tubule system and is, thus, involved in the regulation of the acid base balance.

Elimination

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.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development. No preclinical studies have been conducted with Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion. However, if the dosage instructions are followed, administration of Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion will only restore physiological electrolyte and fluid homeostasis of the patient. All components of Potassium Chloride 0.15% w/v and Sodium Chloride 0.9% w/v Solution for Infusion 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

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened: 3 years

-after first opening the container
Not applicable. See 6.6.

-after addition of additives
From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Unopened: Do not store above 25 °C.

For storage conditions of the medicinal product after addition of an additive, see section 6.3.

6.5 Nature and contents of container

Bottles of colourless low-density polyethylene, contents: Polyethylene bottles containing 500 ml and 1,000 ml available in packs of 10.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Use only if the solution is clear, colourless and if the container is undamaged. The solution should be free of visible particles. The solution should not be administered if the container or its closure shows visible signs of damage.

Containers are for single use only. Discard container and any unused contents after use. Do not reconnect partially used containers.

Any unused product or waste material should be disposed of in accordance with local requirements.
The equipment to be primed with the solution in order to prevent air entering the system.

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

7 MARKETING AUTHORISATION HOLDER

B.BRAUN Melsungen AG
Carl-Braun-Straße. 1,
34212 Melsungen,
Germany

8 MARKETING AUTHORISATION NUMBER

PA0736/037/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24th August 2012
Date of last renwal: 29th April 2017

10 DATE OF REVISION OF THE TEXT

October 2018