VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

"KCl 0.15%/0.3% & Gluc 5%" is a solution for infusion, i.e. it is administered through a thin tube placed into a vein. Potassium and chloride ions are important for maintaining the correct fluid balance in and around the body's cells and tissues, and are involved in nerve signals and muscle contractions. Glucose is a simple sugar which provides a source of energy. This solution is given directly into the blood to restore the balance of potassium levels, and will also add water to tissues which are dehydrated and provide some energy.

Low potassium (hypokalaemia) refers to a lower than normal potassium level in your bloodstream. Potassium is a chemical (electrolyte) that is critical to the proper functioning of nerve and muscles cells, particularly heart muscle cells. Normally, your blood potassium level is 3.6 to 5.2 millimoles (measure of amount-of-potassium concentration in blood) per liter (mmol/L). The frequency of hypokalemia in the general population is difficult to estimate; however, probably fewer than 1% of people who are not taking medication have a serum potassium level lower than 3.5 mmol/L. Potassium intake – present in food and drinks – varies according to age, sex, ethnic background, and socioeconomic status. Whether these differences in intake produce different degrees of hypokalemia or different sensitivities to hypokalemic insults is not known. Up to 21% of hospitalized patients have serum potassium levels lower than 3.5 mmol/L, with 5% of patients exhibiting potassium levels lower than 3 mmol/L. Among elderly patients, 5% demonstrate potassium levels lower than 3 mmol/L. Of patients taking some kind of drugs to increase urine output (diuretics), 20-50% develop hypokalemia. In patients taking these drugs hypokalaemia may be enhanced by concomitant illness, such as heart failure or renal impairment.

"KCl 0.15%/0.3% & NaCl 0.9%" is a solution for infusion, i.e. it is administered through a thin tube placed into a vein. Most importantly it is used for the substitution of fluid and salts (electrolytes), especially in case of low potassium (hypokalemia) and chloride and some dehydration conditions. Potassium and chloride ions are important for maintaining the correct fluid balance in and around the body's cells and tissues, and are involved in nerve signals and muscle contractions. Body cells are bathed in a watery fluid that contains primary sodium and chloride ions. These molecules play a vital role in maintaining proper fluid balance and keeping tissues hydrated. Additionally, sodium is involved in many cell processes such as muscle contraction, transmission of nerve impulses, and kidney function. Chloride ions are responsible for maintaining the acid-base balance. To sustain life it's very important to maintain these ions within a narrow therapeutic range.

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effects in patients taking these drugs may be enhanced by concomitant illnesses, such as heart failure or renal impairment.

"KCl 0.15%/0.3% & NaCl 0.9%" may be also used in dehydration conditions (e.g. diarrhoea and vomiting). Especially in smaller children water loss, particularly due to inflammation of the stomach and small intestine, is a common emergency department complaint. Worldwide for children younger than 5 years, the annual incidence of diarrheal illness is approximately 1.5 billion. Infants and younger children are more susceptible to volume depletion than older children.

Additional to dehydration in children a bad hydration state is rather common in elderly populations. Especially in community dwelling adults and adults older than 70 years chronic dehydration can occur in 48% to 60% of the patients.

"KCl 0.15%/0.3% & NaCl 0.18% & Gluc 4%" is a solution for infusion, i.e. it is administered through a thin tube placed into a vein. Potassium and sodium are important for maintaining the correct fluid balance in and around the body's cells and tissues, and are involved in nerve signals and muscle contractions. Chloride ions are responsible for maintaining the acid-base balance. To sustain life it's very important to maintain these ions within a narrow therapeutic range. Glucose is a simple sugar which provides a source of energy. This solution is given directly into the blood to restore the balance of potassium, sodium and chloride levels, and will also add water to tissues which are dehydrated and provide some energy.

Low potassium (hypokalemia) refers to a lower than normal potassium level in your bloodstream. Potassium is a chemical (electrolyte) that is critical to the proper functioning of nerve and muscles cells, particularly heart muscle cells. Normally, your blood potassium level is 3.6 to 5.2 millimoles (measure of amount-of-potassium concentration in blood) per liter (mmol/L). The frequency of hypokalemia in the general population is difficult to estimate; however, probably fewer than 1% of people who are not taking medication have a serum potassium level lower than 3.5 mmol/L. Potassium intake varies according to age, sex, ethnic background, and socioeconomic status. Whether these differences in intake produce different degrees of hypokalemia or different sensitivities to hypokalemic insults is not known. Up to 21% of hospitalized patients have serum potassium levels lower than 3.5 mmol/L, with 5% of patients exhibiting potassium levels lower than 3 mmol/L. Among elderly patients, 5% demonstrate potassium levels lower than 3 mmol/L. Of patients taking some kind of drugs to increase urine output (diuretics), 20-50% develop hypokalemia Hypokalemia or its effects in patients taking these drugs may be enhanced by concomitant illnesses, such as heart failure or renal impairment.

VI.2.2 Summary of treatment benefits

"KCl 0.15%/0.3% & Gluc 5%", "KCl 0.15%/0.3% & NaCl 0.9%", and "KCl 0.15%/0.3% & NaCl 0.18% & Gluc 4%" have been used for several decades and have demonstrated their positive effect in correction of fluid and electrolyte (especially potassium) imbalances. Despite limited data about the efficacy of the individual components of this solution, data on similar medicinal products as well as years of experience on clinical "well established" use allow one to state that there is no doubt about the efficacious and safe application of i.v. solutions such as "KCl 0.15%/0.3% & Gluc 5%", "KCl 0.15%/0.3% & NaCl 0.9%", and "KCl 0.15%/0.3% & NaCl 0.18% & Gluc 4%" solution for infusion.

VI.2.3 Unknowns relating to treatment benefits

Since several decades "KCl 0.15%/0.3% & Gluc 5%", "KCl 0.15%/0.3% & NaCl 0.9%" is in use for

the preparation of parenteral solutions. There are no unknowns relating to treatment benefits.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Elevated potassium level in the blood (hyperkalaemia)	In hyperkalaemia serum potassium levels are elevated above the normal range. KCl 0.15%/0.3% & Gluc 5%", "KCl 0.15%/0.3% & NaCl 0.9%" contains potassium and could increase the serum potassium content and thus lead to the electrolyte imbalance.	The infusion rate should be appropriately dosed. KCl 0.15%/0.3% & Gluc 5%", "KCl 0.15%/0.3% & NaCl 0.9%" must not be used in patients with hyperkalaemia. Potassium supplements should be administered with caution in patients with heart disease particularly in patients taking a heart medicament called digitalis. Potassium supplements should be administered with caution in patients with disorders that are frequently associated with hyperkalaemia e.g. ADDISON's disease (a rare chronic endocrine system disorder in which the adrenal glands do not produce sufficient steroid hormones) or sickle cell anaemia (a disorder of red blood cells). Regular controls of the blood composition and ECG are necessary. Hereby imbalances could either be naturally compensated or detected.

Risk	What is known	Preventability
Elevated sodium level in the blood (hypernatraemia)	In hypernatraemia serum sodium levels are elevated above the normal range. • Potassium Chloride 1.5 mg/ml and Sodium Chloride 9 mg/ml Solution for Infusion and • Potassium Chloride 3 mg/ml and Sodium Chloride 9 mg/ml Solution for Infusion have a sodium concentration higher than the normal blood sodium concentration and could therefore increase the blood sodium concentration.	The infusion rate should be appropriately dosed. • Potassium Chloride 1.5 mg/ml and Sodium Chloride 9 mg/ml Solution for Infusion and • Potassium Chloride 3 mg/ml and Sodium Chloride 9 mg/ml Solution for Infusion must not be used in patients with severe hypernatraemia. Sodium containing drugs should be administered with caution in patients with impaired renal function or with a concomitant medication of sodium retaining drugs. Blood controls of serum sodium are inexpensive and represent a standard blood test almost availabe in any laboratory. Regular controls of the blood composition are necessary. Hereby imbalances could either be naturally compensated or detected.

Risk	What is known	Preventability
Elevated levels of glucose in the blood (hyperglycaemia)	Healthy individuals are able to maintain the blood glucose level in a normal range. These regulation mechanisms may be impaired under certain conditions (e.g. diabetes mellitus). The infusion of glucose containing drugs like • Potassium Chloride 1.5 mg/ml (0.15 % w/v) or 3 mg/ml (0.3 % w/v) and Glucose 50 mg/ml (5 % w/v) or • Potassium Chloride 1.5 mg/ml (0.15 % w/v) or 3 mg/ml (0.3 % w/v), Sodium Chloride 1.8 mg/ml (0.18% w/v) and Glucose 40 mg/ml (4 % w/v) in these patients may lead to an increase of blood glucose levels above normal values.	The infusion rate should be appropriately dosed. Caution should be exercised when the solution is administered to patients with diabetes, and in patients with impaired glucose tolerance for any other reason. Blood glucose monitoring will be required. Administration of glucose solutions is not recommended after acute ischaemic strokes as hyperglycaemia was reported to worsen ischaemic brain damage and impair recovery.

Important potential risks

None.

Important missing information

None

VI.2.5 Summary of additional risk minimisation measures by safety concern

Not applicable.

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Version	Date	Safety Concerns	Comment
1.0	See effective date in header	Identified Risks: • Hyperkalaemia	None
1.1	See effective date in header	Identified Risks: • Hypernatraemia • Hyperglycaemia	Additional risks requested by authority within assessment reports UK/H/4388/II/006/G UK/H/4390/II/006/G
1.2	See last page	Identified Risks: • Hyperkalaemia	No changes of the safety concerns. Only changes of the

Version	Date	Safety Concerns	Comment
		• Hypernatraemia • Hyperglycaemia	PI texts were requested by authority UK/H/4388/II/006/G UK/H/4390/II/006/G