Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ionolyte solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The solution for infusion contains:

	500 ml	1000 ml
Sodium acetate trihydrate	2.32 g	4.63 g
Sodium chloride	3.01 g	6.02 g
Potassium chloride	0.15 g	0.30 g
Magnesium chloride hexahydrate	0.15 g	0.30 g

Electrolytes:
Na+ 137.0 mmol/l
K+ 4.0 mmol/l
Mg++ 1.5 mmol/l
Cl- 110.0 mmol/l
CH_3COO^- 34.0 mmol/l

Theoretical osmolarity: 286.5 mOsm/l
Titrable acidity: < 2.5 mmol NaOH/l
pH: 6.9 – 7.9

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for infusion.

A clear and colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ionolyte is indicated for:

- Predominantly extracellular dehydration, regardless of cause (vomiting, diarrhea, fistulas, etc.)
- Hypovolemia regardless of cause (hemorrhagic shock, burns, peri-operative water and electrolyte loss)
- Mild metabolic acidosis

4.2 Posology and method of administration

Posology

Adults and paediatric patients
The dose and rate of administration depends on age, body weight, clinical and biological conditions of the patient (including acid-base balance) and the concomitant therapy.

Recommended dosage:
The maximum daily dose corresponds to the fluid and electrolyte needs of the patient. To temporary restore blood volume 3 to 5 times the volume of the lost blood is required.

Typical recommended dosages are:

For adults, the elderly and adolescents (age 12 years and above): 500 ml to 3 litres/24 hours.
For infants, toddlers and children (from 28 days to 11 years of age): 20 ml/kg to 100 ml/kg/24 hours.

Administration rate:
In continuous treatment outside acute fluid losses the infusion rate is usually 40 ml/kg/24 hours in adults.
In paediatric patients the infusion rate is 5 ml/kg/hour in average but the value varies with the age: 6-8 ml/kg/hour for infants, 4-6 ml/kg/hour for toddlers, and 2-4 ml/kg/hour for school children.

Method of administration
For intravenous use.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

This medicine is contraindicated in the following situations:
- Fluid overload (hyperhydration), especially in cases of pulmonary oedema and congestive cardiac failure
- Severe renal insufficiency
- Metabolic alkalosis and
- Hyperkalaemia

4.4 Special warnings and precautions for use

The patient's clinical status and laboratory parameters (fluid balance, blood and urine electrolytes as well as acid-base balance) must be monitored, especially during use of larger volumes of this solution.

Fluid overload caused by overdose should be avoided in general. Particularly for patients with cardiac insufficiency or severe kidney dysfunctions the increased risk of hyperhydration must be taken into consideration; posology must be adapted.

In metabolic alkalosis and clinical situations where alkalisation should be avoided, solutions like 0.9% sodium chloride solution should be preferred over alkalising solutions like Ionolyte.

Particular care must be taken in patients with severe electrolyte abnormalities, like hypernatraemia, hypermagnesaemia and hyperchloraemia.

Solutions containing sodium chloride should be administered with caution to patients with hypertension, heart failure, peripheral or pulmonary edema, impaired renal function, pre-eclampsia, aldosteronism or other conditions or treatment (e.g. corticoids/steroids) associated with sodium retention (see section 4.5).

Since this solution contains potassium, combination with potassium-sparing diuretics is not recommended. Plasma potassium must be particularly closely monitored in patients at risk of hyperkalaemia, e.g. in the presence of severe chronic renal failure (see section 4.5).
Precaution must be taken to use this medicine in combination with angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, suxamethonium, tacrolimus, cyclosporine or in case of severe digitalis intoxication (risk of cardiac symptoms).

Although Ionolyte has a potassium concentration similar to the concentration in plasma, it is insufficient to produce a useful effect in case of severe potassium deficiency and therefore it should not be used for this purpose.

Solutions containing magnesium salts should be used with caution to patients with renal impairment, severe heart rate disorders and in patients with myasthenia gravis. Patients should be monitored for clinical signs of excess magnesium, particularly when being treated for eclampsia. Administration in the postoperative period after neuromuscular block should be used with caution since magnesium salts can lead to a recurarisation effect (see section 4.5).

Infusion of Ionolyte may cause metabolic alkalosis because of the presence of acetate ions. However, it is not suitable to treat severe metabolic or respiratory acidosis.

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

4.5 Interaction with other medicinal products and other forms of interactions

Interactions related to the presence of sodium
Not recommended combinations: (see section 4.4)
Corticoids/steroids and carbenoxolone are associated with retention of sodium and water (with oedema and hypertension).

Interactions related to the presence of potassium
The following combinations increase the concentration of potassium in the plasma and may lead to potentially fatal hyperkalaemia notably in case of renal failure increasing the hyperkalaemic effects:
Not recommended combinations: (see section 4.4)
- Potassium-sparing diuretics: amiloride, spironolactone, triamterene, alone or in combination
- Angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin II receptor antagonists
- Tacrolimus, cyclosporine
- Suxamethonium

Interactions related to the presence of magnesium
Not recommended combinations: (see section 4.4)
Competitive and depolarising neuromuscular blockers

Alkalisation of urine
Precaution is to be taken, as alkalisation of the urine by bicarbonate resulting from acetate metabolism will increase the elimination of certain drugs (such as salicylates, lithium) and will decrease elimination of alkaline drugs like sympathomimetics (such as amphetamine).

4.6 Fertility, pregnancy and lactation

There are no adequate data from the use of Ionolyte in pregnant or lactating women.
At physiological doses, there are no concerns of effects on animal reproduction with either of the active substances of Ionolyte.

Ionolyte can be used safely during pregnancy and lactation as long as the electrolyte and fluid balance is controlled.

When another medicinal product is added to Ionolyte, the nature of the drug and its use during pregnancy and lactation have to be considered separately.

4.7 Effects on ability to drive and use machines

Ionolyte has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The undesirable effects are divided into: 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), not known (cannot be estimated from the available data)

For similar products, the following adverse reactions have been described:

Metabolism and nutrition disorders
During administration of electrolyte solutions, the following undesirable effects have been reported:
- Hyperhydration and heart failure in patients with cardiac disorder or pulmonary oedema (very common)
- Oedema due to water/sodium overload (unknown frequency)

General disorders and administration site conditions
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 and extravasation.

Investigations
In high doses the effects of dilution can commonly lead to a similar dilution of components of the blood, e.g. coagulation factors and other plasma proteins, and a decrease of the hematocrit.

Adverse reactions may be associated to the medicinal product added to the solution; the nature of the additive will determine the likelihood of any other undesirable effects.

In case of undesirable effect(s), the infusion must be discontinued.

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

In the event of accidental overdose, 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, e.g. administration of a diuretic. In oliguric or anuric patients hemofiltration or dialysis may be necessary in order to remove excessive fluid.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Electrolytes, ATC-Code: B05BB01

Ionolyte is an isotonic solution of electrolytes. The constituents of Ionolyte and their concentrations are designed to match those of plasma. The product is used for correction of disturbances in the serum electrolyte balance and in the acid-base balance. Electrolytes are given to achieve or to maintain normal osmotic conditions in the extracellular as well as the intracellular compartment. Acetate is metabolised into bicarbonate in hepatic and extrahepatic tissues (e.g. muscles and peripheral tissues) and produces a mild alkalising effect. Due to the amount of metabolisable anions, Ionolyte is suitable for patients with a tendency to acidosis.

The pharmacology of intravenously infused solutions with similar composition is known from long-standing use in clinical and emergency medicine.

The pharmacodynamic properties of this solution are those of its components (water, sodium, potassium, magnesium, acetate, and chloride). The main effect of Ionolyte is the expansion of the extracellular compartment including both the interstitial and intravascular fluids.
Ions, such as sodium, circulate through the cell membrane using various mechanisms of transport among which is the sodium pump (Na+/K+-ATPase). Sodium plays an important role in neurotransmission and cardiac electrophysiology.

Potassium is essential for numerous metabolic and physiological processes including nerve conduction, muscle contraction, and acid-base regulation. A normal concentration of potassium in plasma is about 3.5 to 5.0 mmoles per liter. Potassium is predominantly an intracellular cation, primarily found in muscle; only about 2% are present in the extracellular fluid. The passage of potassium into the cells and retention against the concentration gradient requires active transport via the Na+/K+-ATPase.

Chloride is mainly an extracellular anion found in low concentration in bone and in high concentration in some components of connective tissue such as collagen. Intracellular chloride concentration is high in red blood cells and gastric mucosa. The balance of anions and cations are regulated by the kidneys. Reabsorption of chloride generally follows reabsorption of sodium.

Magnesium is an activator of numerous enzyme systems and as such of general importance for metabolic functions. It is involved in the carbohydrate and fat metabolism, protein synthesis, and membrane transport and integrity. Nerve conduction and muscular contractility depend on magnesium.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of this solution are those of its components (water, sodium, potassium, magnesium, acetate and chloride).

The pharmacology of intravenously infused solutions with similar composition is known from the long-standing use in clinical and emergency medicine and from the fundamental understanding of the water and electrolyte balance regulation and metabolic processes in the body.

The cation Na+ and the anion Cl- are the predominant electrolytes in extracellular fluid. Maintenance of normal sodium balance is essential for proper blood volume and water distribution in the body. Fluid homeostasis is regulated by various related systems. The healthy body can compensate for widely divergent water and sodium chloride intakes by adaptation of the elimination. The kidneys, adrenals, pituitary gland, lungs and the sympathetic nervous system are mainly involved. Regulatory mechanisms for the body's water balance are associated with the cation Na+. Consequently, disturbances of water homeostasis cause sodium changes and vice versa. Furthermore, sodium is involved in all bio-electrical processes and in the function of numerous enzyme systems.

Chloride is essential for the maintenance of appropriate acid-base balance and plays an important role in the control of fluid homeostasis. High chloride concentrations exist in gastric fluids. Loss through diarrhoea, vomiting or other disturbances may result in hypochloraemia and metabolic alkalosis. Reduced chloride content compared to sodium chloride 0.9% solution helps to prevent the development of hyperchloremic metabolic acidosis.

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 of 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 feces and small amounts may also be excreted in sweat.
Acetate serves as a metabolic precursor of bicarbonate. It is rapidly activated to Acetyl-CoA and enters the corresponding biochemical pathways to be degraded to carbon dioxide. Bicarbonate is the principal extracellular buffer in the body, which is in a dynamic equilibrium with carbon dioxide and undissociated carbonic acid. Mainly the buffer capacity of this equilibrium adjusts the blood pH to its normal slightly basic value. Acetate has, after conversion to bicarbonate in a molar ratio, the corresponding anti-acidotic effect.

5.3 Preclinical safety data

Preclinical safety data of Ionolyte in animal are not relevant since the constituents are physiological components in animal and human plasma.

Toxic effects are not to be expected under the conditions of clinical application when used according to the treatment recommendations.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

6.2 Incompatibilities

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

6.3 Shelf life

a) Shelf life of the product as packaged for sale:
free*flex*bag: 3 years
KabiPac: 3 years

b) Shelf life after first opening of the container:
The product should be used immediately after opening.

6.4 Special precautions for storage

Do not refrigerate or freeze.

6.5 Nature and contents of container

Polyolefine bag (**free***flex*) with overwrap: 20 x 500 ml, 10 x 1000 ml
LDPE bottle (KabiPac): 10 x 500 ml, 20 x 500 ml, 10 x 1000 ml
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

For single use only.

To be used immediately after the bottle or bag is opened.
Any unused solution should be discarded.

Use only clear, particle-free solutions and undamaged containers.

Remove the overwrap from the Polyolefine (**free***flex*) bag prior to use.

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

PA2059/042/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of Last Renewal: 27th August 2020

10 DATE OF REVISION OF THE TEXT

November 2020