AUSTRALIAN PRODUCT INFORMATION IONOLYTE (SODIUM CHLORIDE, SODIUM ACETATE TRIHYDRATE, POTASSIUM CHLORIDE AND MAGNESIUM CHLORIDE HEXAHYDRATE)

1. NAME OF MEDICINE
Sodium chloride, sodium acetate trihydrate, potassium chloride and magnesium chloride hexahydrate.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Ionolyte solution for infusion is a clear and colourless solution.

1000 mL of Ionolyte solution for infusion contains:

Sodium chloride	6.02 g
Sodium acetate trihydrate	4.63 g
Potassium chloride	0.30 g
Magnesium chloride hexahydrate	0.30 g

Electrolytes per 1000 mL:

Sodium (Na^+)	137 mmol
Potassium (K^+)	4 mmol
Magnesium (Mg^{2+})	1.5 mmol
Chloride (Cl^-)	110 mmol
Acetate (CH_3COO^-)	34 mmol

List of excipients:

Sodium hydroxide	pH adjustment
Hydrochloric acid	pH adjustment
Water for Injections	q.s. to 1000 mL

Osmolality:	approx. 265 mOsm/kg water
Titratable acidity:	< 2.5 mmol NaOH/L
pH:	6.9 to 7.9

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM
Solution for infusion.

4. CLINICAL PARTICULARS
4.1 Therapeutic Indications
Ionolyte is indicated for:
- mild metabolic acidosis
- as a source of water and electrolytes

4.2 Dose and Method of Administration
As directed by the physician. Dosage and rate of administration is dependent on age, weight and clinical condition of the patient as well as laboratory determinations (including acid-base balance) and the concomitant therapy.

Product is for single use in one patient only. Discard any residue. Contains no antimicrobial preservatives. To be used immediately after the bag is opened.

Parenteral medicine products should be inspected visually for particulate matter and discolouration prior to the administration whenever solution and container permit.

All injections in **free***flex*® bags are intended for intravenous administration using sterile equipment.

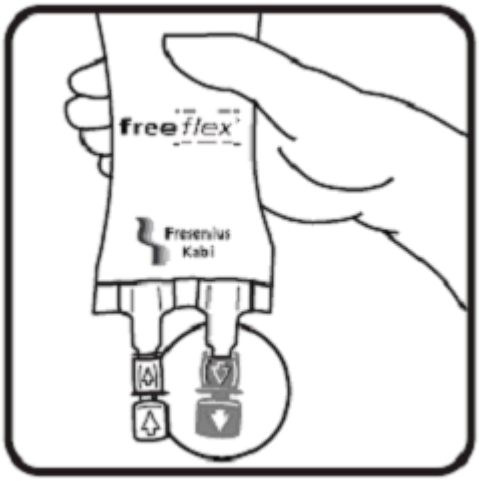
SPECIAL HANDLING INSTRUCTIONS

Before administering the product in plastic bags to patient, review these directions:

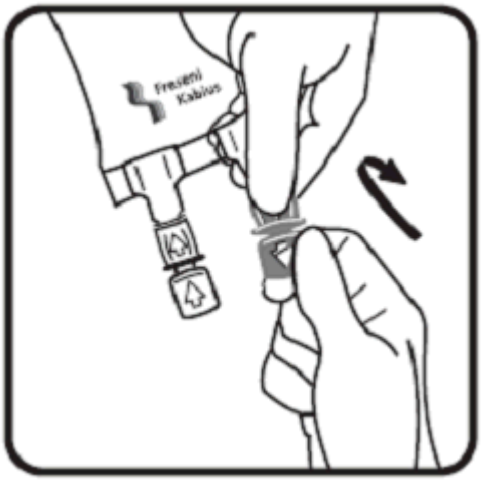
free*flex*® IV Solution Container

(1) Check the expiry date and the solution for visible particles or cloudiness, do not use unless the solution is clear. Inspect the container for damage or leakage, if damaged do not use.

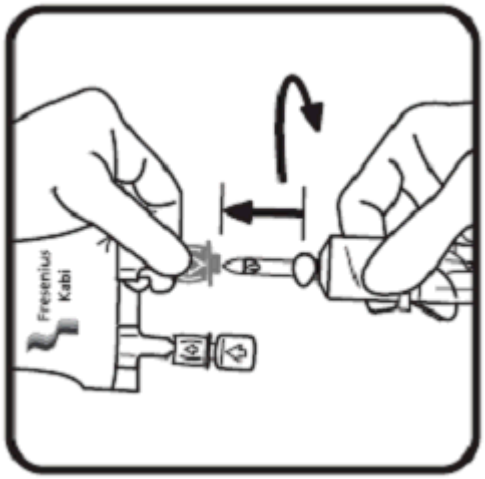
(2) Using the pre-cut corner tabs, peel open and remove the over-wrap.



(3) Identify the blue infusion (administration) port. **Use the BLUE port only to administer solution**.



(4) Break off the blue tamper-evident cover from the **free***flex*® blue infusion port.



(5) Close roller clamp. Insert the spike until the clear plastic collar of the port meets the shoulder of the spike. Use a non-vented standard infusion set and close air inlet. Hang the bag on the

infusion stand. Press drip chamber to get fluid level. Prime infusion set. Connect and adjust the flow rate.

Warnings

1. Do not remove the **free***flex*® IV container from its overwrap until immediately before use.
2. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
3. Do not administer unless the solution is clear, free from particles and the **free***flex*® IV container is undamaged.
4. Ionolyte should be used immediately after insertion of the administration set.
5. Use the BLUE port only to administer solution.
6. Do not vent.
7. If administered by pressure infusion, air should be withdrawn or expelled from the bag through the medication/administration port prior to infusion.
8. Discontinue the infusion if an adverse reaction occurs.
9. It is recommended that administration sets are changed at least once every 24 hours.
10. For single use only. Discard unused portion.

4.3 Contraindications

- 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 sodium chloride 0.9% 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 in patients with hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function, pre-eclampsia, aldosteronism or other conditions or treatment (e.g. corticoids/steroids) associated with sodium retention (please also refer to section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

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 (please also

refer to section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

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 in 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 (please also refer to section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

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.

Paediatric use
Safety and efficacy of Ionolyte in paediatric patients have not been established by adequate or well controlled trials, however, the use of electrolyte solutions in the paediatric population is referenced in the medical literature. The precautions and adverse reactions identified in this document should be observed in the paediatric population.

Use in the elderly
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or medicine therapy.

Effects on laboratory tests
No data available.

4.5 Interactions with Other Medicines and Other Forms of Interactions
Interactions related to the presence of sodium
Combinations not recommended: (please also refer to section 4.1 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)
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:
Combinations not recommended: (please also refer to section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

- 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
Combinations not recommended: (please also refer to section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)
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

Effects on fertility
Studies with Ionolyte have not been performed to evaluate the effect on fertility.

Use in pregnancy (No Category)
Animal reproduction studies have not been conducted with Ionolyte. It is also not known whether Ionolyte can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. Ionolyte should be given to a pregnant woman only if clearly needed.

Use in lactation
It is not known whether Ionolyte is excreted in human milk. Because many medicines are excreted in human milk, caution should be exercised when Ionolyte is administered to a nursing mother.

4.7 Effects on Ability to Drive and Use Machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse Effects (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 with 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 haematocrit.

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 Suspected Adverse Effects
Reporting suspected adverse reactions after registration 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 at https://www.tga.gov.au/reporting-problems.

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 haemofiltration or dialysis may be necessary in order to remove excessive fluid.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic Properties
Mechanism of Action
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, 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 approx. 3.5 to 5.0 mmoles per litre. 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 pump.

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.

Clinical Trials
Data not available.

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 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.

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

Carcinogenicity

Studies with Ionolyte have not been performed to evaluate carcinogenic.

Genotoxicity

Studies with Ionolyte have not been performed to evaluate mutagenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sodium hydroxide	pH adjustment
Hydrochloric acid	pH adjustment
Water for Injections	q.s. to 1000 mL

6.1 Incompatibilities

Additives may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with a pharmacist, if available. If, in the informed judgement of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

6.3 Shelf Life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special Precautions for Storage

Store below 30°C. Do not freeze.

6.5 Nature and Contents of Container

Ionolyte solution for intravenous infusion is a clear and colourless solution in **free***flex*® bags with overwrap available in the following pack sizes:

free*flex*® bags with overwrap	500 mL (Cartons of 20 bags)
free*flex*® bags with overwrap	1000 mL (Cartons of 10 bags)
free*flex*®+ (needle-free) bags with overwrap	500 mL (Cartons of 20 bags)
free*flex*®+ (needle-free) bags with overwrap	1000 mL (Cartons of 10 bags)

6.6 Special Precautions for Disposal

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physiochemical Properties

Chemical structure

Ionolyte solution for infusion is an isotonic solution of electrolytes

CAS Number

Sodium chloride (CAS No.: 7647-14-5), sodium acetate trihydrate (CAS No.: 6131-90-4), potassium chloride (CAS No.: 7447-40-7) and magnesium chloride hexahydrate (CAS No.: 7791-18-6).

7. MEDICINE SCHEDULE (POISONS STANDARD)

Australia: Not Scheduled

8.SPONSOR

Fresenius Kabi Australia Pty Limited
Level 2, 2 Woodland Way
Mount Kuring-gai NSW 2080
Australia
Tel: (02) 9391 5555

9. DATE OF FIRST APPROVAL

9 May 2014

10. DATE OF REVISION

21 July 2023

Summary table of Changes

Section Changed	Summary of New Information
all	New format
4.9	Remove “or 0800764766 (New Zealand)”
7	Remove reference to “New Zealand:General Sale Medicine”
8	Remove New Zealand address