

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Maintelyte solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of Maintelyte solution for infusion contains:

Glucose (as monohydrate) 50.00 g

Sodium Chloride 1.00 g

Sodium Acetate trihydrate 3.13 g

Potassium Chloride 1.50 g

Magnesium Chloride hexahydrate 0.30 g

Content of electrolytes per 1000 ml:

Na⁺ 40 mmol

K⁺ 20 mmol

Mg²⁺ 1.5 mmol

CH₃COO⁻ 23 mmol

Cl⁻ 40 mmol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

Clear solution, free from visible particles

pH: 4.5-6.5

Osmolarity: 402 mOsm/l (approx)

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Supplement of water, carbohydrates and electrolytes to patients where normal intake is insufficient or when there is a deficiency.

4.2 Posology and method of administration

Posology

Dosage, rate, and duration of administration are to be individualised and depend upon the indication for use, the patient's age, weight, clinical condition, and concomitant treatment, and on the patient's clinical and laboratory response to treatment.

Fluid balance, blood glucose, and serum electrolytes should be monitored before and during administration (see sections 4.4, 4.5, 4.6 and 4.8).

Recommended dose for adults is 2-3 litres infusion fluid per day.

Maintelyte solution for infusion: 1000 ml administered intravenously during 4 -12 hours (based on a patient weighing 70 kg).

Infusion rate: 1.2 – 3.5 ml/kg/hour.

Buffering capacity: In order to increase pH of Maintelyte solution from 5 to 7, approximately 7 mmol NaOH will be needed. In order to decrease the pH of Maintelyte solution from 5 to 4, approximately 13 mmol HCl will be needed.

Infusion rate should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycaemia. For information, the maximum glucose oxidation capacities is 5mg/kg/min for adults.

Paediatric population:

Currently, there are no dosing recommendations for use in children (Please see section 4.4: Use in pediatric patients).

Method of administration:

The solution should be administered by intravenous infusion (peripheral or central vein). Maintelyte solution for infusion **must not be administered subcutaneously**.

Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

Because of the presence of glucose, this solution should NOT be administered through the same infusion equipment as whole blood, as haemolysis and clumping of the blood cells can occur.

4.3 Contraindications

The solution is contra-indicated in patients presenting:

- Hyperkalaemia
- Severe renal insufficiency (with oliguria/anuria)
- Uncompensated cardiac or pulmonary failure
- The solution is also contraindicated in case of uncontrolled diabetes, other known glucose intolerances, hyperosmolar coma, hyperglycaemia, hyperlactataemia.
- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Fluid balance/renal function

Hyponatraemia

Treatment with intravenous fluids having a lower sodium concentration than the patient's serum sodium may cause hyponatraemia (see section 4.2). Children, patients with reduced cerebral compliance, patients with non-osmotic vasopressin release (e.g. in acute illness, trauma, post-operative stress, central nervous system diseases), and patients exposed to vasopressin agonists and other drugs that can lower serum sodium (see section 4.5) are at particular risk of acute hyponatraemia. Acute hyponatraemia can lead to acute brain oedema and life-threatening brain injury.

Risk of fluid and/or solute overload and electrolyte disturbances

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

Depending on the volume and rate of infusion, intravenous administration of Maintelyte solution can cause fluid and/or solute overload resulting in overhydration/hypervolaemia therefore high volume infusion must be used under specific monitoring in patients with cardiac, pulmonary or renal failure.

Use in patients with hypervolaemia or overhydration, or conditions that cause sodium retention and oedema

Maintelyte solution should be administered with particular caution to hypervolaemic or overhydrated patients. Solutions containing sodium chloride should be carefully administered to patients with hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function, pre-eclampsia, aldosteronism, or other conditions associated with sodium retention (see also 4.5).

Use in patients with severe renal impairment

Maintelyte solution should be administered with particular caution to patients with severe renal impairment. In such patients administration of Maintelyte solution may result in sodium and/or potassium or magnesium retention.

Electrolyte balance

Maintelyte solution's magnesium concentration is inadequate for the treatment of symptomatic hypomagnesemia.

Use in patients with or at risk for hyperkalaemia

The plasma potassium level of the patient should be particularly closely monitored in patients at risk of hyperkalaemia. Solutions containing potassium salts should be administered with caution to patients with cardiac disease or conditions predisposing to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration, or extensive tissue destruction as occurs with severe burns.

The following combinations are not recommended; they 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 (see section 4.5).

- Angiotensin converting enzyme inhibitors (ACEi) and, by extrapolation, angiotensin II receptor antagonists : hyperkalaemia, potentially lethal
- Tacrolimus, cyclosporine.

Use in patients with hypocalcaemia

Maintelyte solution contains no calcium, and an increase in plasma pH due to its alkalinizing effect may lower the concentration of ionized (not protein-bound) calcium. Maintelyte solution should be administered with particular caution to patients with hypocalcaemia.

Use in patients with or at risk for and from hypermagnesaemia

Solutions containing magnesium salts should be used with caution to patient 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 (see also in 4.5 "Interactions with other medicinal products and other forms of interaction").

Acid base balance

Use in patients with or at risk for alkalosis

Maintelyte solution should be administered with particular caution to patients with alkalosis or at risk for alkalosis. Excess administration of Maintelyte solution can result in metabolic alkalosis because of the presence of acetate ions. However, this solution is not suitable to treat severe metabolic or respiratory acidosis.

Other warnings

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including anaphylactoid reactions, have been reported with Maintelyte solution. The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic counter measures must be instituted as clinically indicated. Solutions containing glucose should be used with caution in patients with known allergy to corn or corn products (see section 4.8). Administration in the postoperative period after neuromuscular block should be used with caution since magnesium salts can lead to a recurring effect.

Refeeding syndrome

For patients who are severely malnourished or have undergone a long period of starvation, caution should be exercised initially when administering glucose. The dose may be gradually increased as glucose metabolism improves. During long-term parenteral treatment, other convenient nutritive supply must be given to the patient.

Use in patients with or at risk for hyperglycaemia

Solutions containing glucose should be used with caution in patients with impaired glucose tolerance or diabetes mellitus. In diabetic patients, the amount of infused glucose has to be taken into account and insulin requirements may be modified. If hyperglycaemia occurs, rate of infusion should be adjusted or insulin administered. Due to glucose presence, this solution is contra-indicated in the first 24 hours following head trauma and blood glucose concentration should be closely monitored during intracranial hypertension episodes. Hyperglycaemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after acute ischemic strokes. Caution is recommended in using dextrose-containing solutions in such patients.

Osmolarity

Maintelyte solution for infusion is an hypertonic solution of electrolytes and glucose (osmolarity: 402 mOsm/l (approx)). Administration of hypertonic solutions may cause venous irritation, including phlebitis. Hyperosmolar solutions should be administered with caution to patients with hyperosmolar states.

Use in pediatric patients

Safety and effectiveness of Maintelyte solution in children have not been established by adequate and well-controlled trials. The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy and should be determined by the consulting physician experienced in pediatric intravenous fluid therapy. Newborns – especially those born premature and with low birth weight - are at increased risk of developing hypo- or hyperglycaemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycaemic control in order to avoid potential long term adverse effects. Hypoglycaemia in the newborn can cause prolonged seizures, coma and brain damage. Hyperglycaemia has been associated with intraventricular hemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stay, and death. Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes.

The infusion of low sodium containing fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema and death. Therefore, acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

Use in elderly

When selecting the type of infusion solution and the volume/rate of infusion for a older people, consider that older people are generally more likely to have cardiac, renal, hepatic, and other diseases or concomitant drug therapy.

4.5 Interaction with other medicinal products and other forms of interactions

Interaction with sodium:

- Corticoids/Steroids and carbenoxolone may cause retention of sodium and water (with oedema and hypertension).

Interaction with potassium:

- Potassium-sparing diuretics (amiloride, spironolactone, triamterene, alone or in association).
- Angiotensin converting enzyme inhibitors (ACEi) and angiotensin II receptor antagonists.
- Tacrolimus and cyclosporine increase concentration of potassium in the plasma and the combination may lead to potentially fatal hyperkalaemia notably in case of a renal failure contributing to the hyperkalaemia.

Interaction with acetate:

Caution is advised when administering Maintelyte solution to patients treated with drugs for which renal elimination is pH dependent. Due to its alkalinizing effect (formation of bicarbonate), Maintelyte solution may interfere with the elimination of such drugs.

- Renal clearance of acidic drugs such as salicylates, barbiturates and lithium may be increase because of the alkalinisation of urine by the bicarbonate resulting from acetate and gluconate metabolism.
- Renal clearance of alkaline drugs, notably such as sympathomimetics (e.g. ephedrine, pseudoephedrine) and stimulants (e.g. quinidine, dexamphetamine sulphate, phenfluramine hydrochloride) may be decreased.

Interactions with magnesium

- Magnesium salts may potentiate the effect of depolarising neuromuscular blocker such as suxamethonium, vecuronium or tubocurarine. Therefore, the combination with these substances is not recommended.

Interaction with drugs that can increase the risk for hyponatraemia

Drugs that can lower serum sodium may increase the risk of acquired hyponatraemia following treatment with intravenous fluids inappropriately balanced to the need of the patient in terms of fluid volume and sodium content (see sections 4.2, 4.4, 4.6 and 4.8). Examples are diuretics, non-steroid anti-inflammatory drugs (NSAIDs), antipsychotics, selective serotonin reuptake inhibitors, opioids, antiepileptics, oxytocin, and chemotherapy

4.6 Fertility, pregnancy and lactation

When Maintelyte solution for infusion is administrated to pregnant women during labour, particularly if administered in combination with oxytocin, there may be an increased risk for hyponatraemia (see section 4.4, 4.5 and 4.8).

Intrapartum maternal intravenous infusion of glucose containing solutions may result in fetal insulin production, with an associated risk of fetal hyperglycaemia and metabolic acidosis as well as rebound hypoglycaemia in the neonate. Physicians should carefully consider the potential risks and benefits for each specific patient before administering Maintelyte solution.

4.7 Effects on ability to drive and use machines

Maintelyte solution has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

The following adverse reactions have been reported in the postmarketing experience, with unspecified Maintelyte solution, listed by MedDRA System Organ Class (SOC), then in order of severity, where feasible. The frequency of the adverse drug reactions listed in this section is not known (cannot be estimated from the available data).

<i>System Organ Class (SOC)</i>	<i>Not known (cannot be estimated from the available data)</i>
Immune system disorders	*Hypersensitivity /infusion reaction, including Anaphylactoid reaction
Metabolism and nutrition disorders	Hyperkalaemia, Hyperglycemia Hypervolaemia, Hyponatraemia
Nervous system disorders	Seizures, Hyponatraemic encephalopathy
Vascular disorders	Thrombophlebitis Venous thrombosis
General disorders and administration site conditions	Infusion site reactions (e.g., Burning sensation Pyrexia Injection site pain Injection site reaction Injection site phlebitis Injection site irritation Injection site infection Extravasation)
Metabolism and nutrition disorders	Electrolyte disturbance

* Potential manifestation in patients with allergy to corn, see section 4.4.

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 HPRC 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

Too fast infusion may lead to water and sodium overload with a risk of oedema, particularly when there is a defective renal sodium excretion. In this case renal dialysis may be necessary.

Excessive administration or rapid infusion or prolonged administration of glucose may lead to hyperglycaemia.

Excessive administration of potassium may lead to the development of hyperkalaemia, especially in patients with renal impairment. Symptoms include paresthesia of the extremities, muscle weakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest, and mental confusion. Treatment of hyperkalaemia involves the administration of calcium, insulin (with glucose) sodium bicarbonate, exchange resins or dialysis.

Excessive administration of magnesium may lead to hypermagnesaemia, important signs of which are loss of deep tendon reflexes and respiratory depression, both due to neuromuscular blockade. Other symptoms of hypermagnesaemia may include nausea, vomiting, flushing of the skin, thirst, hypotension due to peripheral vasodilatation, drowsiness, confusion, muscle weakness, bradycardia, coma, and cardiac arrest.

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

Excessive administration of compounds, such as sodium acetate, which are metabolized to form the bicarbonate anion may lead to hypokalaemia and metabolic alkalosis, especially in patients with impaired renal function. Symptoms may include mood changes, tiredness, shortness of breath, muscle weakness, and irregular heartbeat. Muscle hypertonicity, twitching, and tetany may develop especially in hypocalcaemic patients. Treatment of metabolic alkalosis associated with bicarbonate overdose consists mainly of appropriate correction of fluid and electrolyte balance.

Acute treatment:

The infusion should be interrupted immediately. Administration of diuretics and continuous monitoring of serum electrolytes, correction of electrolyte balance and acid-base balance.

When assessing an overdose, any additives in the solution must also be considered.

The effects of an overdose may require immediate medical attention and treatment.

A patient with supralethal hypermagnesaemia was successfully treated using assisted ventilation, calcium chloride, administered intravenously, and forced diuresis with mannitol infusions

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Maintenance solution, ATC code: B05BB02

The physiological balanced maintenance solutions cover the basal needs of fluid and electrolytes with a daily dose of 2000-3000 ml. The amount of glucose 50g/1000 ml is chosen with respect to the administered glucose (approx. 150g/day) which is needed to prevent a marked degradation of amino acids and production of ketone bodies.

Maintelyte solution for infusion is an hypertonic solution of electrolytes and glucose (osmolarity: 402 mOsm/l (approx)).

The pharmacological properties of Maintelyte solution for infusion are those of its components (glucose, sodium, potassium, magnesium, chloride and acetate).

Acetates are mainly metabolized by muscle and peripheral tissues to bicarbonate, without affecting the liver.

For this solution, glucose is the main source of energy, and this solution provides 200 kcal/L.

5.2 Pharmacokinetic properties

After intravenous administration glucose exhibits fast (approximately 20 minutes) and slow phases of equilibrium. Distribution is largely through extracellular water, and intracellular water of the liver.

In the postoperative state endogenous glucose production equals the amount of glucose taken up and metabolized by all the tissues and is about $2.3 \pm 0.1 \text{ mg/kg}^{-1} \cdot \text{min}^{-1}$.

Sodium homeostasis is complex and closely associated with fluid balance. Osmolality and volume of extracellular fluid are tightly regulated. Small changes in osmolality (plasma-sodium concentrations) are corrected by alterations of extracellular volume. The balance of plasma osmolality is achieved by the secretion or suppression of antidiuretic hormone (ADH; vasopressin), which primarily controls water excretion by the kidney.

A normal concentration of potassium in plasma is about 3.5 to 5.0 mmol per litre, but factors influencing between intracellular and extracellular shifts such as acid-base disturbances can distort the relationship between plasma concentrations and total body stores.

Parenterally administered magnesium is excreted mainly in the urine. Small amounts of magnesium are distributed into breast milk and it crosses into the placenta. The normal circulating level of total magnesium is 1.6 to 2.4 mg/dl (0.8 to 1.2 mmol/l).

Acetates, such as sodium acetate trihydrate, are metabolised to bicarbonate. Acetate can be metabolised by muscle and peripheral tissues into bicarbonate, thus avoiding the liver.

5.3 Preclinical safety data

There is no preclinical data relevant to the prescribing doctor besides the one already described in the other sections of this Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid, concentrated (for pH adjustment).

Water for injections

6.2 Incompatibilities

Incompatibility of the medicinal product to be added with the solution in Viaflo container must be assessed before addition.

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

The instruction for use of the medicinal product to be added must be consulted.

Before adding a drug, verify it is soluble and stable in water at the pH of Maintelyte solution for infusion (pH 4.5 to 6.5).

Glucose should not be administered concomitantly with blood in the same infusion set due to the risk of clotting of red blood cells.

6.3 Shelf life

05 May 2020

CRN009R7G

Page 6 of 8

Unopened: 3 years

In-use shelf-life:

Chemical and Physical stability of any additive at the pH of Maintelyte solution in the Viaflo container should be established prior to use.

From a microbiological point of view, the diluted product must 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 reconstitution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and contents of container

The bags known as Viaflo are composed of polyolefin/polyamide co-extruded plastic (PL 2442).

The bags are overwrapped with a protective plastic pouch composed of polyamide/polypropylene.

Bag size: 1000 ml.

Outer carton content: 10 bags of 1000 ml

6.6 Special precautions for disposal and other handling

After opening the container, the contents should be used immediately and should not be stored for a subsequent infusion.

The solution should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Do not administer unless the solution is clear and the seal is intact.

Administer immediately following the insertion of infusion set.

Do not remove unit from overwrap until ready for use.

The inner bag maintains the sterility of the product.

Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed.

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.

Additives may be introduced before infusion or during infusion through the medication port.

Adding other medication or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In case of adverse reaction, infusion must be stopped immediately.

Discard after single use.

Discard any unused solution.

Do not reconnect partially used bags.

1. Opening

- a. Remove the Viaflo container from the overpouch just before use.
- b. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution, as sterility may be broken.
- c. Check that the solution is clear and does not contain foreign matters. If so, discard the solution.

2. Preparation for administration

Use sterile material for preparation and administration.

- a. Suspend container from eyelet support.

- b. Remove plastic protector from outlet port at bottom of container:
 - Grip the small wing on the neck of the port with one hand.
 - Grip the large wing on the cap with the other hand and twist.
 - The cap will pop off.
- c. Use an aseptic method to set up the infusion.
- d. Attach administration set. Refer to complete directions accompanying set for connection, priming of the set and administration of the solution.

3. Techniques for injection of additive medications

Note that some additives may be incompatible.

When additive is used, verify isotonicity prior to parenteral administration. Thorough and careful aseptic mixing of any additive is mandatory. Solutions containing additives should be used immediately and not stored.

To add medication before administration

- a. Disinfect medication site.
- b. Use a syringe with 19 gauge (1,10 mm) to 22 gauge (0,70 mm) needle. Puncture resealable medication port and inject.
- c. Mix solution and medication thoroughly. For high-density medication such as potassium chloride, tap the ports gently while ports are upright and mix.

Caution: Do not store bags containing added medications.

To add medication during administration

- a. Close clamp on the set.
- b. Disinfect medication site.
- c. Use a syringe with 19 gauge (1,10 mm) to 22 gauge (0,70 mm) needle. Puncture resealable medication port and inject.
- d. Remove container from IV pole and/or turn to an upright position.
- e. Evacuate both ports by tapping gently while the container is in an upright position.
- f. Mix solution and medication thoroughly.
- g. Return container to in use position, re-open the clamp and continue administration.

7 MARKETING AUTHORISATION HOLDER

Baxter Holding B.V.
Kobaltweg 49
3542CE Utrecht
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA2299/045/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th October 2019

10 DATE OF REVISION OF THE TEXT

April 2020