Approved professional information for Neolyte® infusion

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

NEOLYTE® solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 200 ml contains:

Potassium chloride	224 mg
Calcium chloride dihydrate	73,4 mg or
Calcium chloride hexahydrate	109,4 mg
Magnesium chloride hexahydrate	20,4 mg
Sodium lactate	448 mg
as sodium lactate solution 60 %	
Phosphoric acid 85 %	86,36 mg
Dextrose anhydrous	20,0 g or
Dextrose monohydrate	22,0 g.

Content of electrolytes per 1 000 ml:

sodium ion (Na^+)	20 mmol/l
potassium ion (K^+)	15 mmol/l
chloride ion (Cl^-)	21 mmol/l
lactate	20 mmol/l
calcium ion (Ca^{2+})	2,5 mmol/l
magnesium ion (Mg^{2+})	0,5 mmol/l
phosphate	3,75 mmol/l.

Excipient with known effect:

Contains sugar (dextrose).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

A clear, colourless to light straw-coloured solution.

Osmolarity:	638 mOsm/l
pH (approximately):	4,0
Energy:	1 672 kilojoules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NEOLYTE is intended for neonates as maintenance therapy.

Correction of moderate or severe deficit due to malnutrition with inadequate potassium intake.

Marked loss of gastrointestinal secretions. Prolonged diuresis, metabolic acidosis, etc.

4.2 Posology and method of administration

NEOLYTE can be given on the basis of water requirements. Approximately 1 300 ml per square metre body surface per 24 hours. The dose can be increased to 3 000 ml per square metre per 24 hours.

Routine maintenance:

Calculate routine maintenance IV fluid rates for children and young people using the Holliday–Segar formula (100 ml/kg/day for the first 10 kg of weight, 50 ml/kg/day for the next 10 kg and 20

ml/kg/day for the weight over 20 kg). Be aware that over a 24-hour period, males rarely need more than 2 500 ml and females rarely need more than 2 000 ml of fluids.

Calculate routine maintenance IV fluid rates for term neonates according to their age, using the following as a guide:

Age:	**Requirement:**
Birth to day 1	50 – 60 ml/kg/day
Day 2	70 – 80 ml/kg/day
Day 3	80 –100 ml/kg/day
Day 4	100 – 120 ml/kg/day
Days 5 – 28	120 – 150 ml/kg/day

4.3 Contraindications

- Hypersensitivity to any of the active ingredients or excipients of NEOLYTE (see sections 2 and 6.1).
- Hypersensitivity to maize (corn) products (as corn starch may be used as raw material for dextrose production).
- Anuria or oliguria due to renal insufficiency.
- Patients with congestive heart failure.
- Severe impairment of renal function.
- Clinical states in which the administration of sodium and chloride is detrimental.
- Concomitant administration of ceftriaxone and NEOLYTE is contraindicated in newborns (≤ 28 days of age) due to risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream.

4.4 Special warnings and precautions for use

NEOLYTE is not for use in the treatment of lactic acidosis, severe metabolic acidosis or treatment of severe potassium deficiency. Although the solutions have potassium concentrations similar to that of plasma, it is insufficient to produce a useful effect in severe potassium deficiency.

Avoid administering NEOLYTE through the same infusion equipment as whole blood, as dextrose (as contained in NEOLYTE) may cause haemolysis and clumping (see section 4.5).

Ceftriaxone

Concomitant administration of NEOLYTE with ceftriaxone in newborns (≤ 28 days of age) is contraindicated due to the risk of fatal ceftriaxone-calcium salt precipitation (see section 4.3).
In patients older than 28 days, ceftriaxone must not be administered simultaneously with NEOLYTE (contains calcium), through the same infusion line (see sections 4.3 and 4.5).
If the same infusion line is used for sequential administration, the line must be thoroughly flushed between infusions with a compatible fluid.

Hypersensitivity reactions

The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted.

Osmolality

NEOLYTE is a hypertonic solution (638 mOsm/l). It is important to bear in mind that an administration of substantially hypertonic solution may cause venous irritation, including phlebitis, and may lead to a wide variety of complications, such as crenation (shrinkage) of red blood cells and general cellular dehydration. Hyperosmolar solutions should be administered with caution, if at all, to patients with hyperosmolar states.

Renal impairment

Normal kidney function must be ascertained. Administration should be discontinued if signs of renal insufficiency develop during infusion of NEOLYTE.

Close medical supervision should guide parenteral therapy.

In patients with diminished renal function, administration of NEOLYTE may result in sodium, calcium and/or potassium retention. If a patient receives prolonged therapy, or the rate of administration warrants review, clinical evaluation and laboratory monitoring for changes in fluid balance, electrolyte concentration and acid-base balance should be conducted.

Hyperkalaemia

NEOLYTE should be administered with particular caution to patients with hyperkalaemia or conditions predisposing to hyperkalaemia (e.g. potassium excretion impairment, adrenocortical insufficiency, acute dehydration, severe renal impairment or extensive tissue injury or burns) and patients with cardiac disease, as administration of IV potassium can rapidly result in severe hyperkalaemia without symptoms, which may lead to fatal adverse reactions.

Hypervolaemia, overhydration, sodium retention and oedema:

NEOLYTE should be administered with particular caution to patients

with conditions that may cause sodium retention, fluid overload and oedema.

It should be considered to withhold NEOLYTE altogether in hypervolaemic or overhydrated patients, including those with severe renal impairment, primary or secondary hyperaldosteronism or pre-eclampsia, due to the risk of potassium and/or sodium retention, fluid overload and oedema.

NEOLYTE should be used with caution in patients receiving corticosteroids or corticotropin due to potential sodium retention.

Fluid/solute overload and electrolyte disturbances

Depending on the volume and rate of infusion, intravenous administration of NEOLYTE can cause:

- Fluid and/or solute overloading resulting in dilution of the serum electrolyte concentrations, overhydration, congested states, including pulmonary congestion and oedema.
- Clinically relevant electrolyte disturbance and acid-base imbalance.

The risk of dilution states is inversely proportional to the electrolyte concentrations of the injections. The risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations of the injections.

Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

Alkalosis

NEOLYTE should be administered with particular caution to patients with alkalosis or at risk of alkalosis, because lactate is metabolised to bicarbonate and administration may result in, or worsen, metabolic alkalosis. The effect of the sodium lactate component in NEOLYTE on patients with metabolic or respiratory alkalosis should be monitored closely.

Increased lactate levels or impaired lactate utilisation

NEOLYTE should be administered with extreme caution in patients with conditions associated with increased lactate levels, impaired lactate utilisation such as cardiac disease, shock and severe hepatic insufficiency or otherwise at risk of alkalosis. Hyperlactataemia (i.e. high lactate levels) can develop in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. In addition, NEOLYTE may not produce its alkalinising action in patients with severe hepatic insufficiency since lactate metabolism may be impaired. Seizure may be precipitated by the alkalosis induced by lactate, but this is uncommon.

Lactate-containing solutions, such a NEOLYTE, should be administered with particular caution to neonates and infants less than 6 months of age.

Hyponatraemia

Dextrose (glucose) intravenous infusions, such as NEOLYTE, are usually isotonic solutions. In the body, however, glucose-containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolism. Monitoring of serum sodium is particularly important for hypotonic fluids. NEOLYTE is hypertonic with an osmolality of 638 mOsm/l.

Depending on the tonicity of the solution, the volume and rate of infusion, and depending on a patient's underlying clinical condition and capability to metabolise glucose, intravenous administration of glucose can cause electrolyte disturbances, most importantly hypo- or hyperosmotic hyponatraemia.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia. Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (brain oedema) characterised by headache, nausea, seizures, lethargy and vomiting. Patients with brain oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Hyperglycaemia

NEOLYTE should be used with caution in patients with impaired glucose tolerance or diabetes mellitus, as rapid infusion can lead to hyperglycaemia.

Hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and impairing recovery after acute ischaemic strokes. Caution is recommended in using NEOLYTE in such patients. Early hyperglycaemia has also been associated with poor outcomes in patients with severe traumatic brain injury. NEOLYTE should therefore be used with caution in patients with head injury, in particular during the first 24 hours following the trauma.

If hyperglycaemia occurs, the rate of NEOLYTE administration should be reduced and/or insulin administered, or the insulin dose adjusted.

Newborns, especially those born prematurely and with low birth mass, are at increased risk of developing hypo- or hyperglycaemia and therefore need close monitoring during treatment with intravenous dextrose solutions (such as NEOLYTE) 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 haemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotising enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stay and death.

Hypercalcaemia

NEOLYTE (intravenous solutions containing calcium salts) should be used with caution in patients with:

- hypercalcaemia or conditions predisposing to hypercalcaemia, such as patients with severe renal impairment and granulomatous diseases associated with increased calcitriol synthesis, such as sarcoidosis
- calcium renal calculi or a history of renal calculi.

4.5 Interaction with other medicines and other forms of interaction

NEOLYTE should not be administered simultaneously with:

- Ceftriaxone, as precipitation of calcium salts can occur (see sections 4.3 and 4.4).
- Blood preparations through the same administration set, because of a possibility of coagulation (see section 4.4).
- Medicines that can cause hyperkalaemia or increased risk of hyperkalaemia, such as potassium-sparing diuretics (amiloride, spironolactone, triamterene), angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARAs), immunosuppressants (tacrolimus or ciclosporin) or potassium supplements. Simultaneous administration of these

medicines can result in severe and potentially fatal hyperkalaemia, particularly in patients with severe renal insufficiency.

- Digoxin, as calcium may increase the effects of digoxin and lead to serious or fatal cardiac dysrhythmias. Therefore, larger volumes or faster infusion rates should be used with caution in patients treated with digitalis glycosides.

Caution is advised when administering NEOLYTE to patients treated with:

- Thiazide diuretics or vitamin D as concomitant use of these can increase the risk of hypercalcaemia.
- Medicines that may increase the risk of sodium and fluid retention such as carbenoxolone and corticosteroids.
- Medicines with pH-dependent renal elimination. Due to the alkalinising action of lactate (formation of bicarbonate), NEOLYTE may interfere with the elimination of medicines that are pH dependent for renal elimination:
    - Renal clearance of acidic medicines, such as salicylates, barbiturates and lithium, may be increased.
    - Renal clearance of alkaline medicines, such as sympathomimetics such as pseudoephedrine, dexamphetamine sulphate and fenfluramine may be decreased.
- Medicines leading to an increased vasopressin effect. The medicines listed below increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hyponatraemia following treatment with intravenous fluids (see sections 4.4 and 4.8).
    - Medicines stimulating vasopressin release such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3,4-methylenedioxy-*N*-metamphetamine, ifosfamide, antipsychotics and opioids.

- Medicines potentiating vasopressin action such as chlorpropamide, non-steroidal anti-inflammatory medicines (NSAIDs) and cyclophosphamide.
- Vasopressin analogues such as desmopressin, oxytocin, vasopressin and terlipressin.

- Medicines that may increase the risk of hyponatraemia, such as diuretics and antiepileptics (e.g. oxcarbazepine).

Use of intravenous infusions containing glucose may necessitate review of a patient's oral hypoglycaemic or insulin requirements. Close monitoring of serum glucose may be required.

4.6 Fertility, pregnancy and lactation

Not applicable, as NEOLYTE is intended for neonates.

4.7 Effects on ability to drive and use machines

Not applicable as NEOLYTE is only intended for neonates.

4.8 Undesirable effects

Immune system disorders:

Frequency not known:

Hypersensitivity/infusion reactions, including anaphylactic/anaphylactoid reactions with the following manifestations: angioedema, chest pain, chest discomfort, bronchospasm, dyspnoea, cough, urticaria, rash, pruritus, erythema, nausea, pyrexia.

Metabolism and nutrition disorders

Frequency not known:

Hyperkalaemia, hyponatraemia, hypervolaemia, oedema (see section 4.4).

Psychiatric disorders:

Frequency not known:

Anxiety.

Nervous system disorders:

Frequency not known:

Headache, hyponatraemic encephalopathy, dysgeusia, oral hypaesthesia, paraesthesia.

Cardiac disorders:

Frequency not known:

Hypotension, decreased heart rate, tachycardia, chest pain, chest discomfort.

Respiratory, thoracic and mediastinal disorders:

Frequency not known:

Respiratory distress, dyspnoea, cough.

Gastrointestinal disorders:

Frequency not known:

Nausea, throat irritation.

Skin and subcutaneous tissue disorders:

Frequency not known:

Rash, pruritis, erythema.

General disorders and administration site conditions

Frequency not known:

Infusion site reactions, including infusion site pruritus, infusion site erythema and infusion site anaesthesia (numbness), phlebitis, infusion site inflammation, infusion site swelling, infusion site rash, infusion site pain, infusion site burning and pyrexia, flushing.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of NEOLYTE is important. It allows continued monitoring of the benefit/risk balance of NEOLYTE. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Dangerous cardiotoxicity as a result of hyperkalaemia. Toxic effects on heart and skeletal muscle as a result of reduction in serum sodium concentration. Intravenous injection of 10 % calcium gluconate solution counteracts the toxic effect on the heart.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 24 Mineral substitutes, electrolytes.

Pharmacotherapeutic group: Electrolytes with carbohydrates.

ATC code: B05BB02.

Mechanism of Action

Plasma phosphate concentrations are higher in children than in adults. Phosphorus is present in plasma and extracellular fluid, in cell membranes and intracellular fluid. In the extracellular fluid, phosphate is primarily in inorganic form and only a small component of esterified phosphate is present. Plasma phosphate concentration is inversely related to the action of vitamin D and thus to the rate of renal hydroxylation. A reduction of the plasma phosphate concentration permits the presence of more calcium in the blood and inhibits deposit of new bone salt. An increased plasma concentration of the phosphate anion facilitates the effect of calcitonin on calcium deposition in

bone. The ratio of sodium phosphate and monosodium phosphate in extracellular fluid is 4:1 at a pH of 7,4. Familial hypophosphataemia causes a decrease in erythrocyte concentrations.
Potassium, magnesium, calcium, sodium and chlorides restore the electrolyte balance in the body in intracellular deficits, anion losses, losses of intestinal fluids and general loss of fluids and electrolytes.
Dextrose is given intravenously to increase the volume of the circulating blood and to prevent shock and haemorrhage and counteract dehydration.
Sodium lactate is also administered intravenously for dehydrated infants and children.

Clinical efficacy and safety

No data from clinical trials.

5.2 Pharmacokinetic properties

As NEOLYTE is directly administered to the systemic circulation, the bioavailability (absorption) of the active components is complete (100 %). Excess calcium is predominantly excreted via the renal system, as in the case of potassium and sodium excretion.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection.

6.2 Incompatibilities

Ceftriaxone must not be mixed with NEOLYTE (see sections 4.3 and 4.4).

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

200 ml flexible PVC or **free***flex* bags.

6.6 Special precautions for disposal and other handling

Additives may be incompatible. Do not use unless the solution is clear. Check for minute leaks by squeezing the bag. Destroy any unused portion.

Health professionals should ensure that all the air has been removed from the tubing and administration set prior to placement in the patient. Health professionals should ensure that NEOLYTE is administered at the correct temperature, rate and volume of infusion appropriate to the size and condition of the infant. Discontinue infusion if any adverse reaction occurs.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten

Port Elizabeth 6020

South Africa

8. REGISTRATION NUMBER

R/24/243

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26 May 1986

10. DATE OF REVISION OF THE TEXT

24 June 2021