1.3.1.1 PROFESSIONAL INFORMATION

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE

PHYSIONEAL 40 GLUCOSE 1,36 % w/v / 13,6 mg/ml

PHYSIONEAL 40 GLUCOSE 2,27 % w/v / 22,7 mg/ml

PHYSIONEAL 40 GLUCOSE 3,86 % w/v / 38,6 mg/ml

(SOLUTION FOR PERITONEAL DIALYSIS)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PHYSIONEAL 40 GLUCOSE 1,36 % w/v / 13,6 mg/ml

Small bag "A"	
Glucose monohydrate	41,25 g/l
equivalent to anhydrous glucose	37,5 g/l
Calcium chloride dihydrate	0,507 g/l
Magnesium chloride hexahydrate	0,140 g/l
Large bag "B"	
Sodium chloride	8,43 g/l
Sodium bicarbonate	3,29 g/l
Sodium lactate	2,63 g/l
Final solution after mixing	
Glucose monohydrate	15,0 g/l
equivalent to anhydrous glucose	13,6 g/l
Sodium chloride	5,38 g/l
Calcium chloride dihydrate	0,184 g/l
Magnesium chloride hexahydrate	0,051 g/l

Sodium bicarbonate	2,10 g/l
Sodium lactate	1,68 g/l

1 000 ml of final solution after mixing corresponds to 362,5 ml of solution A and 637,5 ml of solution B. The pH of the final solution is 7,4.

Composition of the final solution after mixing in mmol/l	
Anhydrous glucose ($C_6H_{12}O_6$)	75,5 mmol/l
Sodium (Na^+)	132 mmol/l
Calcium (Ca^{++})	1,25 mmol/l
Magnesium (Mg^{++})	0,25 mmol/l
Chloride (Cl^-)	95 mmol/l
Bicarbonate (CHO_3^-)	25 mmol/l
Lactate ($C_3H_5O_3^-$)	15 mmol/l
Osmolarity	**344 mosmol/l**

PHYSIONEAL 40 GLUCOSE 2,27 % w/v / 22,7 mg/ml

Small bag "A"	
Glucose monohydrate	68,85 g/l
equivalent to anhydrous glucose	62,6 g/l
Calcium chloride dihydrate	0,507 g/l
Magnesium chloride hexahydrate	0,140 g/l
Large bag "B"	
Sodium chloride	8,43 g/l
Sodium bicarbonate	3,29 g/l
Sodium lactate	2,63 g/l

Final solution after mixing	
Glucose monohydrate	25,0 g/l
equivalent to anhydrous glucose	22,7 g/l
Sodium chloride	5,38 g/l
Calcium chloride dihydrate	0,184 g/l
Magnesium chloride hexahydrate	0,051 g/l
Sodium bicarbonate	2,10 g/l
Sodium lactate	1,68 g/l

1 litre of final solution after mixing corresponds to 362,5 ml of solution A and 637,5 ml of solution B. The pH of the final solution is 7,4.

Composition of the final solution after mixing in mmol/l	
Anhydrous glucose	126 mmol/l
Sodium	132 mmol/l
Calcium	1,25 mmol/l
Magnesium	0,25 mmol/l
Chloride	95 mmol/l
Bicarbonate	25 mmol/l
Lactate	15 mmol/l
Osmolarity	**395 mosmol/l**

PHYSIONEAL 40 GLUCOSE 3,86 % w/v / 38,6 mg/ml

Small bag "A"	
Glucose monohydrate	117,14 g/l
equivalent to anhydrous glucose	106,5 g/l
Calcium chloride dihydrate	0,507 g/l
Magnesium chloride hexahydrate	0,140 g/l

Large bag “B”	
Sodium chloride	8,43 g/l
Sodium bicarbonate	3,29 g/l
Sodium lactate	2,63 g/l
Final solution after mixing	
Glucose monohydrate	42,5 g/l
equivalent to anhydrous glucose	38,6 g/l
Sodium chloride	5,38 g/l
Calcium chloride dihydrate	0,184 g/l
Magnesium chloride hexahydrate	0,051 g/l
Sodium bicarbonate	2,10 g/l
Sodium lactate	1,68 g/l

1 litre of final solution after mixing corresponds to 362,5 ml of solution A and 637,5 ml of solution B. The pH of the final solution is 7,4.

Composition of the final solution after mixing in mmol/l	
Anhydrous glucose	214 mmol/l
Sodium	132 mmol/l
Calcium	1,25 mmol/l
Magnesium	0,25 mmol/l
Chloride	95 mmol/l
Bicarbonate	25 mmol/l
Lactate	15 mmol/l
Osmolarity	**483 mosmol/l**

Excipient(s) with known effect:

Sugar content: contains sugar:

PHYSIONEAL 40 GLUCOSE 1,36 % w/v / 13,6 mg/ml: Anhydrous glucose: 13,6 g/l

PHYSIONEAL 40 GLUCOSE 2,27 % w/v / 22,7 mg/ml: Anhydrous glucose: 22,7 g/l

PHYSIONEAL 40 GLUCOSE 3,86 % w/v / 38,6 mg/ml: Anhydrous glucose: 38,6 g/l

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for peritoneal dialysis.

Chamber “A” – A clear, colourless to yellow solution practically free of visible particles.

Chamber “B” – A clear, colourless to yellow solution practically free of visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PHYSIONEAL 40 GLUCOSE is indicated whenever peritoneal dialysis is employed.

PHYSIONEAL 40 GLUCOSE is indicated in patients in whom solutions based on lactate buffer only, with a low pH, cause abdominal inflow pain or discomfort.

4.2 Posology and method of administration

Posology

The mode of therapy, frequency of treatment, exchange volume, duration of dwell and length of dialysis should be selected by the physician. To avoid the risk of severe dehydration, hypovolaemia and to minimise the loss of proteins, it is advisable to select the PHYSIONEAL 40 GLUCOSE peritoneal dialysis solution with the lowest level of osmolarity consistent with fluid removal requirements for each exchange.

Adults

Patients on continuous ambulatory peritoneal dialysis (CAPD) typically perform 4 cycles per day (24 hours). Patients on automated peritoneal dialysis (APD) typically perform 4-5 cycles

at night and up to 2 cycles during the day. The fill volume depends on body size, usually from 2.0 to 2.5 litres.

Elderly

As for Adults

Paediatric population

The safety and efficacy of PHYSIONEAL 40 GLUCOSE in paediatric patients have not been established. Therefore, the clinical benefits of PHYSIONEAL 40 GLUCOSE have to be balanced versus the risks of side effects in this patient category.

For paediatric patients > 2 years old, 800 to 1 400 ml/m^2 per cycle up to a maximum amount of 2 000 ml, as tolerated, has been recommended. Fill volumes of 200 to 1 000 ml/m^2 are recommended in children less than 2 years of age.

Method of administration

Precautions to be taken before handling or administering the medicinal product

PHYSIONEAL 40 GLUCOSE is for intraperitoneal administration only and single use only. Not for intravenous administration. A strict aseptic technique must be used during administration and with the bag change procedure. In case of damage the container should be discarded.

The solution should be warmed in the overpouch to body temperature (37 °C) before use. However only dry heat (for example, heating pad, warming plate) should be used. Solutions should not be heated in water or in a microwave oven due to the potential for patient injury or discomfort.

After removal of the overpouch, immediately break the interchamber frangible pin to mix the two solutions.

Wait until the upper chamber has completely drained into the lower chamber. Mix gently by pushing with both hands on the lower chamber walls. The intraperitoneal solution must be infused within 24 hours after mixing. Discard any unused remaining solution after 24 hours.

Do not administer if the solution is discoloured, cloudy, contains particulate matter, shows evidence of leakage between chambers or to the exterior, or if seals are not intact

The drained fluid should be inspected for the presence of fibrin or cloudiness, which may indicate the presence of peritonitis.

Precaution to be taken before manipulating or administering the product, see section 6.6.
For instructions on dilution of the medicine before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
PHYSIONEAL 40 GLUCOSE should not be used in patients with:

- uncorrectable mechanical defects that prevent effective peritoneal dialysis or increase the risk of infection.
- documented loss of peritoneal function or extensive adhesions that compromise peritoneal function.

4.4 Special warnings and precautions for use

Patient conditions requiring caution of use

Peritoneal dialysis should be done with caution in patients with:

- abdominal conditions, including disruption of the peritoneal membrane and diaphragm by surgery, from congenital anomalies or trauma until healing is complete, abdominal tumours, abdominal wall infection, hernias, faecal fistula, colostomy or ileostomy,

frequent episodes of diverticulitis, inflammatory or ischemic bowel disease, large polycystic kidneys, or other conditions that compromise the integrity of the abdominal wall, abdominal surface, or intra-abdominal cavity

- other conditions including recent aortic graft replacement and severe pulmonary disease.

General Monitoring

- When prescribing the solution to be used for an individual patient, consideration should be given to the potential interaction between the dialysis treatment and therapy directed at other existing illnesses. Serum potassium levels should be monitored carefully in patients treated with cardiac glycosides
- An accurate fluid balance record must be kept and the body weight of the patient should carefully be monitored to avoid over- or underhydration with severe consequences including congestive heart failure, volume depletion and shock.
- Protein, amino acids, water soluble vitamins and other medicines may be lost during peritoneal dialysis with PHYSIONEAL 40 GLUCOSE and may require replacement.
- Serum electrolyte concentrations (particularly bicarbonate, potassium, calcium and phosphate), blood chemistry (including parathyroid hormone) and haematological parameters should be evaluated periodically.

Use in diabetic patients

In patients with diabetes, blood glucose levels should be monitored and the dosage of insulin or other treatment for hyperglycaemia should be adjusted.

Secondary hyperparathyroidism

In patients with secondary hyperparathyroidism, the benefits and risks of the use of dialysis solution with 1,25 mmol/l calcium content such as PHYSIONEAL 40 GLUCOSE should be carefully considered as it might worsen hyperparathyroidism.

Metabolic alkalosis

Patients taking antacids and calcium carbonate should have their bicarbonate levels monitored.

Metabolic alkalosis may occur in patients with a plasma bicarbonate level above 30 mmol/l, especially if higher dialysis volumes are used. Plasma bicarbonate should be monitored regularly.

Encapsulating Peritoneal Sclerosis (EPS)

Encapsulating Peritoneal Sclerosis (EPS) has been reported in patients using PHYSIONEAL 40 GLUCOSE as part of their peritoneal dialysis therapy.

Peritonitis

If peritonitis occurs, the choice and dosage of antibiotics should be based upon the results of identification and sensitivity studies of the isolated organism(s) when possible. Prior to identification of the involved organism(s), broad-spectrum antibiotics may be indicated.

Hypersensitivity

PHYSIONEAL 40 GLUCOSE solution should be used with caution in patients with a known allergy to maize or maize products. Hypersensitivity reactions such as those due to a maize starch allergy, including anaphylactic/anaphylactoid reactions, may occur. Stop the infusion immediately and drain the solution from the peritoneal cavity if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Use in patients with elevated lactate levels

Patients with elevated lactate levels should use PHYSIONEAL 40 GLUCOSE with caution. It is recommended that patients with conditions known to increase the risk of lactic acidosis [e.g., severe hypotension, sepsis, acute renal failure, inborn errors of metabolism, treatment with medicines such as metformin and nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)] must be monitored for occurrence of lactic acidosis before the start of treatment and during treatment with PHYSIONEAL 40 GLUCOSE solution.

Overinfusion

- Overinfusion of PHYSIONEAL 40 GLUCOSE solutions into the peritoneal cavity may be characterised by abdominal distension/abdominal pain and/or shortness of breath.
- Treatment of PHYSIONEAL 40 GLUCOSE overinfusion is to drain the solution from the peritoneal cavity.

Use of higher glucose concentrations

Excessive use of PHYSIONEAL 40 GLUCOSE peritoneal dialysis solution with a higher dextrose (glucose) during a peritoneal dialysis treatment may result in excessive removal of water from the patient.

Addition of potassium

- Potassium is omitted from PHYSIONEAL 40 GLUCOSE solutions due to the risk of hyperkalaemia.
- In situations in which there is a normal serum potassium level or hypokalaemia, the addition of potassium chloride (up to a concentration of 4 mEq/l) may be indicated to prevent severe hypokalaemia and should be made after careful evaluation of serum and total body potassium, only under the direction of a physician

Improper administration

- Improper clamping or priming sequence may result in infusion of air into the peritoneal cavity, which may result in abdominal pain and/or peritonitis.
- In case of infusion of unmixed solution, the patient should immediately drain the solution and use a newly mixed bag.

Paediatric population

Safety and efficacy in paediatric patients have not been established.

4.5 Interactions with other medicines and other forms of interaction

- No interaction studies have been performed.
- Incompatibilities must be checked before admixture. PHYSIONEAL 40 GLUCOSE should be used immediately after adding any medicine
- Blood concentration of dialysable medicine may be reduced during dialysis. A possible compensation for losses must be taken into consideration.
- Plasma levels of potassium in patients using cardiac glycosides must be carefully monitored as there is a risk of digitalis intoxication. Potassium supplements may be necessary.

4.6 Fertility, pregnancy and lactation

- Safety in pregnancy and lactation has not been established.
- PHYSIONEAL 40 GLUCOSE is not recommended during pregnancy and in women of childbearing potential not using contraception**.**
- It is unknown whether PHYSIONEAL 40 metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded.

4.7 Effects on ability to drive and use machines

PHYSIONEAL 40 GLUCOSE may cause dizziness. Patients experiencing dizziness should avoid driving and use of machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most commonly reported adverse reactions during treatment are alkalosis occurring in approximately 10 % of patients. In most cases, it was based on serum bicarbonate values only and was usually not associated with clinical symptoms.

b. Tabulated summary of adverse reactions

Undesirable effects of peritoneal dialysis include procedure and solution related problems.

Those which are related to the procedure include:

Gastrointestinal disorders:

Frequent: abdominal pain, bleeding, peritonitis (which is followed by abdominal pain, cloudy effluent and sometimes fever), infection around the catheter (signs of inflammation: redness and secretion), catheter blockage, ileus shoulder pain, hernia of the abdominal cavity.

Those which are generally related to peritoneal dialysis solutions such as PHYSIONEAL 40 GLUCOSE are seen less frequently than those related to the procedure and include:

Gastrointestinal disorders:

Frequent: peritonitis

Less frequent: peritoneal membrane failure, abdominal pain, dyspepsia, flatulence and nausea.

Frequency not known: encapsulating peritoneal sclerosis and cloudy peritoneal effluent

General disorders and administration site conditions:

Frequent: oedema and asthenia

Less frequent: weakness, tiredness, chills, facial oedema, hernia, malaise and thirst.

Frequency not known: pyrexia

Musculoskeletal and connective tissue disorders:

Less frequent: musculoskeletal pain.

Nervous system disorders:

Less frequent: headache, fainting and dizziness.

Respiratory, thoracic and mediastinal disorders:

Less frequent: respiratory symptoms associated with pulmonary oedema, dyspnoea and cough.

Metabolism and nutrition disorders:

Frequent: fluid retention

Less frequent: electrolyte disturbances (e.g. hypokalaemia, hypocalcaemia), metabolic alkalosis, hypervolaemia, anorexia, dehydration, hyperglycaemia and lactic acidosis.

Blood and lymphatic system disorders:

Frequency not known: eosinophilia

Psychiatric disorders:

Less frequent: insomnia

Vascular disorders:

Frequent: hypertension

Less frequent: hypotension

Skin and subcutaneous tissue disorders:

Frequency not known: angioedema and rash

Investigations:

Frequent: weight increased

Less frequent: PCO2 increased, Blood lactate dehydrogenase increased, Laboratory test abnormal PCO2 increased, Alanine aminotransferase increased, C reactive protein increased, Creatinine renal clearance decreased, Gammaglutamyltransferase increased

c. Description of selected adverse reactions

Not applicable

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

For reporting of side effects directly to the HCR, contact +27 11 635 0134 or email Adcock.aereports@adcock.com

4.9 Overdose

Possible consequences of overdose include hypervolaemia, hypovolaemia, electrolyte disturbances or (in diabetic patients) hyperglycaemia.

Management of overdose:

Hypervolaemia may be managed by using hypertonic peritoneal dialysis solutions and fluid restriction.

Hypovolaemia may be managed by fluid replacement either orally or intravenously, depending on the degree of dehydration.

Electrolyte disturbances shall be managed according to the specific electrolyte disturbance verified by blood test. The most probable disturbance, hypokalaemia, may be managed by the oral ingestion of potassium or by the addition of potassium chloride in the peritoneal dialysis solution prescribed by the treating physician.

Hyperglycaemia (in diabetic patients) shall be managed by adjusting the insulin dose according to the insulin scheme prescribed by the treating physician.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group and ATC code: Peritoneal Dialytics, Hypertonic solutions: ATC code: B05DB

Mechanism of action

For patients with renal failure peritoneal dialysis is used to remove toxic substances produced by nitrogen metabolism and which are normally excreted by the kidneys, and for aiding the regulation of fluid and electrolyte as well as acid base balances. Peritoneal dialysis fluid is administered through a catheter into the peritoneal cavity.

Pharmacodynamic effects

Glucose produces a solution hyperosmolar to the plasma, creating an osmotic gradient which facilitates fluid removal from the plasma to the solution. Transfer of substances

between the patient's peritoneal capillaries and the dialysis fluid is made across the peritoneal membrane according to the principles of osmosis and diffusion. After dwell time, the solution is saturated with toxic substances and must be changed. With the exception of lactate, present as a bicarbonate precursor, electrolyte concentrations in the fluid have been formulated in an attempt to normalise plasma electrolyte concentrations. Nitrogenous waste products, present in high concentration in the blood, cross the peritoneal membrane into the dialysis fluid.

5.2 Pharmacokinetic properties

Intraperitoneally administered glucose, buffer, electrolytes, are absorbed into the blood and metabolised by the usual pathways. Glucose is metabolised (1 g of glucose = 4 kilocalories or 17 kilojoules) into CO_2 and H_2O).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Medicines compatibility must be checked before admixture and the pH and the salts of the solution must be taken into account.

6.3 Shelf life

Before mixing: 2 years

After mixing: After reconstitution, use within 24 hours.

6.4 Special precautions for storage

Store at or below 25 °C. Do not freeze.

Store in the original package

6.5 Nature and contents of container

- The PHYSIONEAL 40 GLUCOSE solution is hermetically sealed inside a flexible 5 litre two-chambered Viaflex poly (vinyl chloride) container, with the following fill volumes: 1,5 litre, 2 litre and 2,5 litre.
- The upper chamber is fitted with an injection port for medicine admixture to the glucose with electrolytes solution. The lower chamber is fitted with a port for connection to a suitable administration set allowing dialysis operations. The lineo connector that may equip the Y transfer line of the twin bag, contains 10,5 % of Povidone iodine ointment
- The bag is sealed inside a transparent overpouch obtained by thermic fusion and made of multilayer copolymers.
- Container volumes after reconstitution: 1 500 ml (544 ml of solution A and 956 ml of solution B), 2 000 ml (725 ml of solution A and 1 275 ml of solution B), 2 500 ml (906 ml of solution A and 1 594 ml of solution B).

Pack types:

The single bag is a two-chamber bag (small bag “A” and large bag “B”) to be used in Automated Peritoneal Dialysis.

The twin bag is a two-chamber bag (small bag “A” and large bag “B”) plus a drain bag with an integrated disconnect system plus an empty drain bag to be used in Continuous Ambulatory Peritoneal Dialysis.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

- Aminoglycosides should not be administered with penicillins in the same bag due to chemical incompatibility

* In case of damage the container should be discarded. After removal of the overpouch, immediately break the interchamber frangible pin to mix the two solutions.
* **PLEASE NOTE:** If medicines are added, they should be added through the medication port in the top chamber before breaking the interchamber frangible pin. The product should be used immediately after adding any medicines.
* Do not administer unless solution is clear. Discard any unused remaining solution.
* Wait until the upper chamber has completely drained into the lower chamber. Mix gently by pushing with both hands on the lower chamber walls. The intraperitoneal solution must be infused within 24 hours after mixing.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Critical Care (Pty) Ltd.

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Aeroton,

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2013

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8. REGISTRATION NUMBER(S)

PHYSIONEAL 40 GLUCOSE 1,36% w/v / 13,6 mg/ml: 37/34/0584

PHYSIONEAL 40 GLUCOSE 2,27% w/v / 22,7 mg/ml: 37/34/0585

PHYSIONEAL 40 GLUCOSE 3,86% w/v / 38,6 mg/ml: 37/34/0586

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Approved: 25 November 2005

10. DATE OF REVISION OF THE TEXT

Date of current amendment: 17 November 2021

Meera Patel

Digitally signed by Meera Patel
Date: 2022.03.02 11:08:31 +02'00'