PRESCRIBING INFORMATION

PHYSIONEAL 40 Glucose 1.36%
PHYSIONEAL 40 Glucose 2.27%
PHYSIONEAL 40 Glucose 3.86%

Glucose, Calcium Chloride, Magnesium Chloride, Sodium Chloride, Sodium Bicarbonate, Sodium Lactate

Solution for Peritoneal Dialysis

In VIAFLEX Plastic Container

Manufacturer's Standard

Vantive ULC
6675 Millcreek Drive, Unit 2
Mississauga Ontario L5N 5M4
Canada

Date of Preparation:
May 23, 2024

Submission Control No: 284256

Prescribing Information

Directions for Use for Health Professionals

NAME OF THE MEDICINAL PRODUCT

PHYSIONEAL 40 Glucose 1.36%
1.36% w/v (13.6 mg/mL)
Solution for Peritoneal Dialysis, Mfr. Std.

PHYSIONEAL 40 Glucose 2.27%
2.27% w/v (22.7 mg/mL)
Solution for Peritoneal Dialysis, Mfr. Std.

PHYSIONEAL 40 Glucose 3.86%
3.86% w/v (38.6 mg/mL)
Solution for Peritoneal Dialysis, Mfr. Std.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Formula Before mixing:	**PHYSIONEAL 40 Glucose**		
Chamber "A" (glucose bag) contains:			
	1.36%	**2.27%**	**3.86%**
Glucose Monohydrate	41.25 g/L	68.85 g/L	117.4 g/L
Equivalent to Anhydrous Glucose	37.5 g/L	62.6 g/L	106.5 g/L
Calcium Chloride Dihydrate	0.507 g/L	0.507 g/L	0.507 g/L
Magnesium Chloride Hexahydrate	0.140 g/L	0.140 g/L	0.140 g/L
Chamber "B" (buffer bag) contains:			
	1.36%	**2.27%**	**3.86%**
Sodium Chloride	8.43 g/L	8.43 g/L	8.43 g/L
Sodium Bicarbonate	3.29 g/L	3.29 g/L	3.29 g/L
Sodium (S)-Lactate	2.63 g/L	2.63 g/L	2.63 g/L
Formula After mixing: **The mixed solution contains:**			
	1.36%	**2.27%**	**3.86%**
Glucose monohydrate	15.0 g/L	25.0 g/L	42.5 g/L
Equivalent to Anhydrous Glucose	13.6 g/L	22.7 g/L	38.6 g/L
Sodium Chloride	5.38 g/L	5.38 g/L	5.38 g/L
Calcium Chloride Dihydrate	0.184 g/L	0.184 g/L	0.184 g/L
Magnesium Chloride Hexahydrate	0.051 g/L	0.051 g/L	0.051 g/L
Sodium Bicarbonate	2.10 g/L	2.10 g/L	2.10 g/L
Sodium (S)-Lactate	1.68 g/L	1.68 g/L	1.68 g/L

1000 mL of final solution after mixing corresponds to 362.5 mL of chamber A and 637.5 mL of chamber B.

Composition of the final solution (mmol/L) after mixing:			
	1.36%	**2.27%**	**3.86%**
Anhydrous Glucose ($C_6H_{12}O_6$)	75.5	126	214
Sodium (Na^+)	132	132	132
Calcium (Ca^{++})	1.25	1.25	1.25
Magnesium (Mg^{++})	0.25	0.25	0.25
Chloride (Cl^-)	95	95	95
Bicarbonate (HCO_3^-)	25	25	25
Lactate ($C_3H_5O_3^-$)	15	15	15

PHARMACEUTICAL FORM

Solution for peritoneal dialysis.
Sterile, clear, colourless solution.
The pH of the final solution is approximately 7.4.

	Osmolarity (mOsmol/L) (mixed solution)		
Glucose Concentration of Solution	**1.36%**	**2.27%**	**3.86%**
PHYSIONEAL 40	344	395	483

The number '40' in the name specifies the buffer concentration of the solution (15 mmol/l of lactate + 25 mmol/l of bicarbonate = 40 mmol/l).

INDICATIONS AND CLINICAL USE

PHYSIONEAL 40 is indicated for:

- Peritoneal dialysis for the treatment of acute and chronic renal failure with manifestations of severe water retention and severe electrolyte imbalance.
- Intoxication with dialyzable substances where adequate alternate treatments are not available.

Bicarbonate/lactate based PHYSIONEAL 40 peritoneal dialysis solutions with a physiological pH are particularly indicated in patients in whom solutions based on lactate buffer only, with a low pH, cause abdominal inflow pain or discomfort.

DOSAGE AND ADMINISTRATION

- PHYSIONEAL 40 is intended for intraperitoneal administration only. Not for intravenous administration.
- Peritoneal dialysis solutions may be warmed to 37°C (98.6°F) to enhance patient comfort. 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 glucose chamber A has completely drained into the buffer chamber B. Mix gently by pushing with both hands on the lower chamber walls. The intraperitoneal solution must be infused within 24 hours after mixing.
- PHYSIONEAL 40 should be administered at a rate that is comfortable for the patient. The volume administered is determined by the prescribing physician.
- The mode of therapy, frequency of treatment, exchange volume, duration of dwell and length of dialysis should be initiated and supervised by the prescribing physician.
- To avoid the risk of severe dehydration, hypovolemia and to minimise the loss of proteins, it is advisable to select the peritoneal dialysis solution with the lowest level of osmolarity consistent with fluid removal requirements for each exchange. PHYSIONEAL 3.86% glucose-containing solution is a high osmotic pressure fluid and using it for all exchanges may cause dehydration. (See section **WARNINGS AND PRECAUTIONS)**
- Patients on continuous ambulatory peritoneal dialysis (CAPD) typically perform 4 cycles per day (24 hours) (Ronco et al. 2000; Keshaviah et al. 1994). Patients on automated peritoneal dialysis (APD) typically perform 3-5 cycles at night and up to 2 cycles during the day (Blake et al. 1996; Blake et al. 2011). It has been reported in literature that, the fill volume per exchange depends on body size, usually from 2.0 to 2.5 liters per 1.73 m^2 (Ronco et al. 2000; Keshaviah et al. 1994).
- Aseptic technique should be employed throughout the peritoneal dialysis procedure.
- 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.
- Discard any unused remaining solution.
- For single use only

Special Populations:

Pediatrics
- Safety and effectiveness in pediatric patients has not been established.
- Therefore the clinical benefits of PHYSIONEAL 40 have to be balanced versus the risk of side effects in this patient category. For pediatric patients >2 years old, 800 to 1400 mL/m2 per cycle up to a maximum amount of 2000 mL, as tolerated is recommended.

Geriatrics
- More than 30% of the patients in the clinical trials were older than 65. The evaluation of the results obtained for this group does not show any difference to the rest of the patients.

CONTRAINDICATIONS

PHYSIONEAL 40 is contraindicated for use in patients with:
- Uncorrectable mechanical defects that prevent effective PD or increase the risk of infection
- Documented loss of peritoneal function or extensive adhesions that compromise peritoneal function
- Severe respiratory insufficiency
- Malnutrition
- Severe disorders of lipid metabolism
- Pregnancy, unless under the close supervision of a doctor

WARNINGS AND PRECAUTIONS

Warnings
- Encapsulating Peritoneal Sclerosis (EPS) is considered to be a known, rare complication of peritoneal dialysis therapy. EPS has been reported in patients using peritoneal dialysis solutions including PHYSIONEAL 40.
- 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.
- Solutions containing dextrose should be used with caution in patients with a known allergy to corn or corn products. Hypersensitivity reactions such as those due to a corn 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.
- Patients with elevated lactate levels should use lactate-containing peritoneal dialysis solutions with caution. It is recommended that patients with conditions known to increase the risk of lactic acidosis [e.g., severe hypotension or sepsis, hepatic failure and/or renal failure, inborn errors of metabolism, treatment with drugs 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 lactate-based peritoneal dialysis solutions.
- 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.

- Diabetics require careful monitoring of blood-glucose levels during and following dialysis with glucose-containing solutions. Dosage of insulin or other treatments for hyperglycemia should be adjusted.
- This product may contain fructose as an impurity in the dextrose material. Exercise caution when this product is used in patients with hereditary fructose intolerance. In these patients, fructose may result in hypoglycemia, metabolic acidosis, liver toxicity which manifests as vomiting, nausea, sweating, jaundice, hemorrhage, seizures or coma or even death. The severity of the reactions is dependent on the amount and duration of fructose intake.

Precautions

- PHYSIONEAL 40 is intended for intraperitoneal administration only. Not for intravenous administration.
- 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.
- Safety and effectiveness in pediatric patients has not been established.
- In patients with plasma bicarbonate level above 30 mmol/L, the risk of possible metabolic alkalosis should be weighed against the benefits of treatment with this product.
- Protein, amino acids, water soluble vitamins and other medicines may be lost during peritoneal dialysis and may require replacement.
- 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.
- Peritoneal dialysis should be done with caution in patients with: 1) abdominal conditions, including disruption of the peritoneal membrane and diaphragm by surgery, from congenital anomalies or trauma until healing is complete, abdominal tumors, abdominal wall infection, hernias, fecal fistula, colostomy, large polycystic kidneys, or other conditions that compromise the integrity of the abdominal wall, abdominal surface, or intra-abdominal cavity; and 2) other conditions including aortic graft placement (Misra et al. 1998) and severe pulmonary disease. When assessing peritoneal dialysis as the mode of therapy in these situations, the benefits to the patient must be weighed against the possible complications.
- Overinfusion of PHYSIONEAL 40 solutions into the peritoneal cavity may be characterized by abdominal distension/abdominal pain and/or shortness of breath.
- Treatment of PHYSIONEAL 40 overinfusion is to drain the solution from the peritoneal cavity.
- Excessive use of PHYSIONEAL 40 peritoneal dialysis solution with a higher dextrose (glucose) during a peritoneal dialysis treatment may result in excessive removal of water from the patient.
- Potassium is omitted from PHYSIONEAL 40 solutions due to the risk of hyperkalemia.
    - In situations in which there is a normal serum potassium level or hypokalemia, the addition of potassium chloride (up to a concentration of 4 mEq/L) may be indicated to prevent severe hypokalemia and should be made after careful evaluation of serum and total body potassium, only under the direction of a physician.
- Serum electrolyte concentrations (particularly bicarbonate, potassium, magnesium, calcium and phosphate), blood chemistry (including parathyroid hormone and lipid parameters) and haematological parameters should be evaluated periodically.
- In patients with secondary hyperparathyroidism, the benefits and risks of the use of dialysis solution with a low calcium content such as PHYSIONEAL 40 should be carefully considered as it might worsen hyperparathyroidism.
- 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.

DRUG INTERACTIONS

No interaction studies have been conducted with PHYSIONEAL 40. Blood concentration of other dialysable drugs 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.

PREGNANCY AND LACTATION

There is no clinical experience with Physioneal 40 during pregnancy and lactation. No data are available from animal studies. Use of peritoneal dialysis in pregnancy is contraindicated unless under the close supervision of a doctor. The risk-benefit must be assessed.

ADVERSE REACTIONS

The adverse reactions within this section represent those adverse reactions that may be associated with the use of PHYSIONEAL 40 or in conjunction with performing the peritoneal dialysis procedure.

Adverse Reactions from Clinical Trials

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The adverse reactions within this section represent those reported in clinical trials involving PHYSIONEAL 35 and PHYSIONEAL 40. In clinical trials with PHYSIONEAL 40 alkalosis occurred in approximately 10% of patients. Alkalosis was not observed in clinical trials with PHYSIONEAL 35.

PHYSIONEAL 35 and PHYSIONEAL 40 Clinical Trial Adverse Reactions			
System Organ Class	**Preferred Term**	**Frequency[a]**	**Percentage of patients**
NEOPLASMS, BENIGN AND MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	Benign neoplasm of skin	Uncommon	0.3

METABOLISM AND NUTRITIONAL DISORDERS	Alkalosis[b]	Common	3.7
	Hypokalemia	Common	1.3
	Fluid retention	Common	1.0
	Hypercalcemia	Common	1.0
	Hypervolemia	Uncommon	0.7
	Anorexia	Uncommon	0.3
	Dehydration	Uncommon	0.3
	Hyperglycemia	Uncommon	0.3
	Hyperphosphatemia	Uncommon	0.3
	Lactic acidosis	Uncommon	0.3
PSYCHIATRIC DISORDERS	Insomnia	Uncommon	0.3
NERVOUS SYSTEM DISORDERS	Dizziness	Uncommon	0.7
	Headache	Uncommon	0.3
	Hypertonia	Uncommon	0.3
CARDIAC DISORDERS	Arrhythmia	Uncommon	0.3
	Cardiomegaly	Uncommon	0.3
VASCULAR DISORDERS	Hypertension	Common	2.3
	Hypotension	Uncommon	0.3
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Dyspnea	Uncommon	0.7
	Cough	Uncommon	0.3
	Respiratory acidosis	Uncommon	0.3
GASTROINTESTINAL DISORDERS	Peritonitis	Common	1.3
	Peritoneal membrane failure[c]	Uncommon	0.7
	Abdominal pain	Uncommon	0.7
	Dyspepsia	Uncommon	0.7
	Flatulence	Uncommon	0.7
	Nausea	Uncommon	0.7
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	Pruritus	Common	1.0
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Edema	Common	2.3
	Asthenia	Common	1.0
	Chills	Uncommon	0.7
	Facial edema	Uncommon	0.7
	Hernia	Uncommon	0.3
	Malaise	Uncommon	0.3
	Thirst	Uncommon	0.3
INJURY POISONING AND PROCEDURAL COMPLICATIONS	Procedural complication	Uncommon	0.3

INVESTIGATIONS	Weight increased	Common	1.3
	Blood lactate dehydrogenase increased	Uncommon	0.7
	Laboratory test abnormal	Uncommon	0.7
	PCO_2 increased	Uncommon	0.7
	Alanine aminotransferase increased	Uncommon	0.3
	C reactive protein increased	Uncommon	0.3
	Creatinine renal clearance decreased	Uncommon	0.3
	Gamma-glutamyltransferase increased	Uncommon	0.3

a) Frequency has been evaluated using the following criteria: 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), very rare (<1/10,000).

b) Reported in PHYSIONEAL 40 only (N=4/46)

c) MedDRA LLT (lower level term) = lack of ultrafiltration; PT (preferred term) = peritoneal membrane failure; HLT (high level term) = peritoneal and retroperitoneal disorders; HLGT (high level group term) = peritoneal and retroperitoneal conditions; SOC = gastrointestinal disorders.

Adverse Reactions: General

Adverse reactions to peritoneal dialysis include mechanical and solution related problems as well as the results of contamination of equipment or improper technique in catheter placement.

Post-Marketing Adverse Reactions

In addition to the adverse reactions noted in clinical trials, the following adverse reactions have been reported in the post-marketing experience. These reactions are listed by MedDRA System Organ Class (SOC), then by Preferred Term in order of severity.

INFECTIONS AND INFESTATIONS: Peritonitis bacterial, Catheter site infection

BLOOD AND LYMPHATIC SYSTEM DISORDERS: Eosinophilia

GASTROINTESTINAL DISORDERS: Encapsulating peritoneal sclerosis, Peritoneal cloudy effluent, Abdominal discomfort

SKIN AND SUBCUTANEOUS TISSUE DISORDERS: Angioedema, Rash

MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS: Musculoskeletal pain

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Catheter related complication, Pyrexia

Examples of peritoneal dialysis therapy related class effects include: bleeding, ileus, tiredness, muscle cramping

OVERDOSE

There is potential for overdose resulting in hypervolemia, hypovolemia, electrolyte disturbances or hyperglycemia. Excessive use of PHYSIONEAL 40 peritoneal dialysis solution with 3.86% glucose during a peritoneal dialysis treatment can result in significant removal of water from the patient.

Management of overdose:

- Hypervolemia may be managed by using hypertonic peritoneal dialysis solutions and fluid restriction. Hypovolemia may be managed by fluid replacement either orally or intravenously, depending on the degree of dehydration.
- Electrolyte disturbances may be managed according to the specific electrolyte disturbance verified by blood test. The most probable disturbance, hypokalemia, 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.
- Hyperglycemia in diabetic patients may be managed by adjusting the insulin dose.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Pharmacodynamics properties

Solutions for Peritoneal Dialysis (code ATC: B 05DB00).

For patients with renal failure, peritoneal dialysis is a procedure for removing toxic substances produced by nitrogen metabolism and normally excreted by the kidneys, and for aiding the regulation of fluid and electrolyte as well as acid base balances.

This procedure is accomplished by administering peritoneal dialysis fluid through a catheter into the peritoneal cavity. 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. Glucose produces a solution hyperosmolar to the plasma, creating an osmotic gradient which facilitates fluid removal from the plasma to the solution.

In-vitro and *ex-vivo* studies have shown evidence of improved biocompatibility indicators of PHYSIONEAL 40 in comparison with standard lactate buffered solution. In addition, clinical studies in limited numbers of patients with abdominal inflow pain have confirmed some symptomatic benefit. To date, however, there are no data available which indicate that clinical complications overall are reduced or that regular use of such solutions might translate into meaningful benefits over the longer-term.

Pharmacokinetic Properties

Intraperitoneally administered glucose, buffer, electrolytes and water 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, provided all calories are spent as energy. Excess calories will be stored as fat.

Preclinical safety data

Complete preclinical evaluation of safety pharmacology, repeated dose toxicity, toxicity to reproduction, genotoxicity and carcinogenicity of PHYSIONEAL 40 has not been performed and is partly not applicable.

PHARMACEUTICAL PARTICULARS

List of excipients

Carbon Dioxide
Water for Injection

Incompatibilities

Consult with pharmacist familiar with peritoneal dialysis, if available. If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Incompatibilities have to be checked before admixture. The product should be used immediately after any drug addition.

Aminoglycosides should not be mixed with penicillins due to chemical incompatibility.

Compatibility has been demonstrated with insulin in PHYSIONEAL 40 in the VIAFLEX container.

Shelf life after mixing

The product, once removed from its overpouch and mixed, should be used within 24 hours.

Special precautions for storage

Store at 15ºC to 25ºC.

Nature and contents of container

The PHYSIONEAL 40 solution is hermetically sealed inside a two-chambered bag manufactured from medical grade plasticised PVC.

The glucose chamber “A” is fitted with an injection port for drug admixture to the glucose with electrolytes solution. The buffer chamber “B” is fitted with a port for connection to a suitable administration set allowing dialysis operations.

The bag is sealed inside a transparent overpouch obtained by thermic fusion and made of multilayer copolymers.

Container volumes after reconstitution: 1500 mL (544 mL of glucose chamber A and 956 mL of buffer chamber B), 2000 mL (725 mL of glucose chamber A and 1275 mL of buffer chamber B), 2500 mL (906 mL of solution A and 1594 mL of solution B).

Pack sizes:
The single bag is a two-chamber bag (small bag/glucose chamber "A" and large bag/buffer chamber "B") to be used in Automated Peritoneal Dialysis (APD). The twin bag is a two-chamber bag (small bag/glucose chamber "A" and large bag/buffer chamber "B") plus an empty drain bag to be used in CAPD.

PHYSIONEAL 40 is available in the following pack sizes:

1.5 l	5 units per box	single two-chamber bag	Luer connector
1.5 l	5 units per box	twin two-chamber bag	Luer connector
2.0 l	4 units per box	single two-chamber bag	Luer connector
2.0 l	4 units per box	twin two-chamber bag	Luer connector
2.5 l	4 units per box	single two-chamber bag	Luer connector
2.5 l	4 units per box	twin two-chamber bag	Luer connector

The pH of chamber A is approximately 4.5. The pH of chamber B is approximately 7.5.

Instructions for use and handling

- In the case of damage, the container should be discarded.
- Aseptic technique should be employed throughout the peritoneal dialysis procedure.
- Peritoneal dialysis solutions may be warmed to 37˚C (98.6˚F) to enhance patient comfort. 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.
- Drugs should be added through the medication port in the glucose chamber before breaking the interchamber frangible pin. Drug compatibility must be checked before admixture and the pH and salts of the solution must be taken into account. The product should be used immediately after any drug addition.
- The pH and salts of the solution must be taken into account for compatibility before adding to the solution.
- After removal of the overpouch, immediately break the interchamber frangible pin to mix the two solutions. Wait until the glucose chamber has completely drained into the buffer chamber. Mix gently by pushing with both hands on the buffer chamber walls. The intraperitoneal solution must be infused within 24 hours after mixing.
- Discard any unused remaining solution.
- For single use only.

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READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICATION

PART III: PATIENT MEDICATION INFORMATION

PHYSIONEAL 40 Glucose 1.36%
PHYSIONEAL 40 Glucose 2.27%
PHYSIONEAL 40 Glucose 3.86%

Glucose, Calcium Chloride, Magnesium Chloride, Sodium Chloride, Sodium Bicarbonate, Sodium Lactate

Solution for Peritoneal Dialysis

In VIAFLEX Plastic Container

Read this carefully before you start using PHYSIONEAL 40 solution and each time you get a refill. This leaflet is a summary and will not tell you everything about PHYSIONEAL 40 solution. Talk to your doctor, nurse, or pharmacist about your medical condition and treatment and ask if there is any new information about PHYSIONEAL 40 solution.

ABOUT THIS MEDICATION

What the medication is used for:
PHYSIONEAL 40 solution is a sterile peritoneal dialysis solution used in patients whose kidneys are not working properly. It removes waste products and water from the blood.

PHYSIONEAL 40 solution can also be used in some cases of drug intoxication.

PHYSIONEAL 40 solution has not been studied for use in children (younger than 18 years old). If PHYSIONEAL 40 solution is considered for use in these patients, the doctor will weigh the risks of side effects against the benefits for the patient.

What it does:
PHYSIONEAL 40 solution contains glucose which draws fluid and wastes from your blood stream into your peritoneal cavity (the space inside your abdomen). The fluids and wastes are removed from your body when the PHYSIONEAL 40 solution is drained.

When it should not be used:
Do not use PHYSIONEAL 40 solution if you:

- have a problem involving your abdominal wall or cavity that cannot be corrected by surgery (e.g. hernia, ileus, adhesions, imperfections in the muscle that separate the abdomen from the chest, or tumours)
- have a problem that increases your risk of an abdominal infection (e.g., skin infections, burns, bowel perforations or recent abdominal surgery)
- have severe peritoneal scarring
- have severe shortness of breath
- are malnourished
- cannot break down fats
- are pregnant, unless under the close supervision of a doctor

What the medicinal ingredients are:
Glucose
Calcium Chloride
Magnesium Chloride
Sodium Chloride
Sodium Bicarbonate
Sodium Lactate

What the nonmedicinal ingredients are:
Hydrochloric acid concentrated (for pH adjustment),
Sodium hydroxide (for pH adjustment)
Carbon Dioxide
Water for injection

What dosage forms it comes in:
PHYSIONEAL 40 solution is available in a Viaflex bag with 2 chambers holding 5000 mL of final solution after mixing. The number 40 in the name specifies the buffer concentration of the solution (15 mmol/L of lactate + 25 mmol/L of bicarbonate = 40 mmol/L)

WARNINGS AND PRECAUTIONS

BEFORE you use PHYSIONEAL 40 solution talk to your doctor, nurse or pharmacist if you:

- have diabetes. Blood glucose levels should be monitored and your dosage of insulin or other treatment for hyperglycemia should be adjusted by your doctor.
- have secondary hyperparathyroidism, the benefits and risks of the use of dialysis solution with 1.25mmol/L calcium content should be carefully considered with your doctor as it might worsen hyperparathyroidism.
- have elevated lactate levels or have a condition known to increase the risk of lactic acidosis (severe low blood pressure, sepsis, liver or kidney failure, inborn errors of metabolism, taking drugs such as metformin and nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs))
- take cardiac glycosides, such as digoxin.
- are breastfeeding.

If you are allergic to corn or corn products, undesirable allergic reactions, including development of rash, hives, throat and/or facial swelling, wheezing, shortness of breath, low blood pressure, and other 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 allergic reaction develop and seek immediate medical help.

Tell your doctor, nurse or pharmacist about any other conditions you have that may affect the inside, outside or the wall of your abdomen.

Patients on PHYSIONEAL 40 solution may experience high or low levels of potassium, calcium, or magnesium in their blood. Your doctor will monitor your blood test results.

Keep a written note of your weight, a record of the volume liquids added to your body including peritoneal dialysis solutions infused and liquids drunk and the volume of liquids removed from your body including the volume of the peritoneal dialysis solution drained and urine volume, together with any other measurements which your doctor has asked you to record. Contact your doctor, nurse or pharmacist if your drained volume is more than expected.

Protein, amino acids, water soluble vitamins and other medicines may be removed during peritoneal dialysis. **Your doctor may recommend supplementation to your diet and other changes.**

Improper clamping or priming sequence may result in infusion of air into the peritoneal cavity, which may result in abdominal pain and/or peritonitis (inflamed peritoneum) or infection.

INTERACTIONS WITH THIS MEDICATION

As with most medicines, interactions with other drugs are possible. Tell your doctor, nurse, or pharmacist about all the medicines you take, including drugs prescribed by other doctors, vitamins, minerals, natural supplements, or alternative medicines.

The blood concentration of drugs that can be removed from the body using dialysis may be reduced by peritoneal dialysis.

Tell your doctor, nurse of pharmacist about all the medicines you take, including insulin, blood pressure medicines and heart medicines called cardiac glycosides (such as digoxin). Your dose of these medicines may need to be changed when you use PHYSIONEAL 40 solution.

PROPER USE OF THIS MEDICATION

PHYSIONEAL 40 solution is to be administered into your peritoneal cavity. This is the cavity in your abdomen (belly) between your skin and the peritoneum. The peritoneum is the membrane surrounding your internal organs such as your intestines and liver. This solution is only for intrapertioneal usage, and will be adminisered via a catheter directly to the peritoneal cavity. It is not for intravenous use.

Always use this medicine exactly as instructed by the medical team specialised in peritoneal dialysis. Check with them if you are not sure.

Usual adult dose:

- The kind of treatment, frequency of treatment, exchange volume, the time that the dialysis solution remains in the abdominal cavity and length of dialysis will be selected by your doctor. Infuse PHYSIONEAL 40 solution at a rate that is comfortable for you.
- Patients on continuous ambulatory peritoneal dialysis (CAPD) typically perform 4 cycles per day (24 hours).
- Patients on automated peritoneal dialysis (APD) typically perform 3-5 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 liters per 1.73 m^2.To reduce the risk of dehydration, it is important to use the solution(s) your doctor has chosen for you.

Directions for use:

- Detailed instructions and training on the peritoneal dialysis exchange procedure will be given to you, in a specialized training centre, before you use PHYSIONEAL 40 solution at home.
- You should practice infection free technique throughout the bag change procedure.
- Examine the bag before use and discard the package if it is broken, damaged, or the solution is discoloured, cloudy or any solids are floating in the solution.
- To make using PHYSIONEAL 40 solution more comfortable, you can warm it to 37˚C (98.6˚F) before use. This should only be done using dry heat, such as a heating pad or cycler warming plate. To avoid increased risk of infection, do not place PHYSIONEAL 40 solution in water to heat the bags. Do not microwave.

- After the removal of the overpouch, check that the interchamber frangible pin is not broken. **If the seal is already broken, even partially, discard the bag.**
- Just before infusion prepare the solution by breaking the interchamber fragile pin. Wait until the glucose chamber A has completely drained into the buffer chamber B before you start the infusion. Mix gently by pushing with both hands on the lower chamber walls. **Do not infuse without breaking the interchamber fragile pin. If the solution is accidently infused without breaking the interchamber fragile pin immediately drain the solution and use a newly mixed bag. Inform your doctor.**
- The solution should be infused within 24 hours after mixing.
- When draining the fluid after the dwell, always check your drained fluid for cloudiness or fibrin. Fibrin looks like clumps or stringy material in the drained solution. Cloudy drained fluid or fibrin may mean you have an infection. Call your doctor if your drained fluid is cloudy or contains fibrin.
- Your doctor may prescribe other injectable drugs to be added directly into the PHYSIONEAL 40 bag. In that situation, add the drug through the medication port in the SMALL chamber before breaking the interchamber pin. Use the product immediately after addition of the drug. You should use infection free technique when adding any medications to PHYSIONEAL 40 solution.
- PHYSIONEAL 40 solution is for single use only. **Discard any unused remaining solution.**

Overdose:

If you think you have taken too much PHYSIONEAL 40 solution, contact your doctor, nurse, pharmacist, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
If you have missed an exchange, continue with the next scheduled treatment.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:

- Rash, itching
- Weakness, fatigue, tiredness
- Headache

If any of these affects you severely, tell your doctor, nurse or pharmacist.

Sometimes, too much PHYSIONEAL 40 solution can get into your peritoneal cavity. If you experience abdominal distention, feeling of fullness and, or shortness of breath, contact your doctor, nurse, pharmacist or peritoneal dialysis unit.

Encapsulating Peritonitis Sclerosis (EPS) is a rare but serious side effect that happens to patients taking PHYSIONEAL 40 solution. In EPS the bowels become blocked due to the growth of a thick layer of fibrin within the peritoneum. Symptoms include fever, abdominal discomfort, constipation, nausea, vomiting or lack of appetite, lack or decreased bowel movements or of passing gas. If this happens to you seek immediate medical help.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor, nurse or pharmacist		Seek immediate medical help
	Only if severe	In all cases	
Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			√
Dehydration: dizziness, weakness, fainting, thirst, dry mouth, constipation, muscle cramps	√		
Catheter Blockage/Infection: Redness, pus, swelling or pain around exit site of your catheter			√
Peritonitis (infection in the peritoneal cavity): cloudy or bloody drained fluid, abdominal pain, fever, redness, nausea, upset stomach, vomiting, lack of appetite, weight loss, constipation		√	
Edema: Swollen ankles or legs, swelling of the eyes or face	√		
Irregular heartbeat	√		
High Blood Pressure: headaches, vision problems, dizziness, shortness of breath	√		
Shortness of breath or chest pain		√	
Abnormal Bleeding		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor, nurse or pharmacist		Seek immediate medical help
	Only if severe	In all cases	
Increased Blood Sugar: frequent urination, thirst, and hunger	√		
Electrolyte Imbalance: weakness, drowsiness, muscle pain or cramps, irregular heartbeat		√	

This is not a complete list of side effects. For any unexpected effects while taking PHYSIONEAL 40 solution, contact your doctor, nurse or pharmacist.

HOW TO STORE IT

Store in the original package. Store at 15°C to 25°C. **Do not freeze.** Do not use PHYSIONEAL 40 solution after the expiry date on the label.

Keep PHYSIONEAL 40 solution out of reach and sight of children.

Do not use PHYSIONEAL 40 solution unless the solution is clear and the container undamaged. Once PHYSIONEAL 40 is removed from its overpouch and mixed it should be used within 24 hours. Any unused portion should be discarded.

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.
3 ways to report:

- **Online at MedEffect (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php);**
- **By calling 1-866-234-2345 (toll-free)**
- **By completing a Consumer Side Effect Reporting Form and sending it by:**
  - **Fax to 1-866-678-6789 (toll-free), or**
  - **Mail to: Canada Vigilance Program**
    Health Canada, Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php)

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

If you want more information about PHYSIONEAL 40 solution:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); or by contacting the sponsor, Vantive ULC, at 1-800-387-8399

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