

NEW ZEALAND DATA SHEET

1 PHYSIONEAL 40

Physioneal 40, 1.36%w/v solution dialysis

Physioneal 40, 2.27%w/v solution dialysis

Physioneal 40, 3.86%w/v solution dialysis

PHYSIONEAL 40 GLUCOSE CLEAR FLEX

Physioneal 40 Glucose 1.36%w/v / 13.6mg/mL CLEAR-FLEX solution dialysis

Physioneal 40 Glucose 2.27%w/v / 22.7mg/mL CLEAR-FLEX solution dialysis

Physioneal 40, Glucose 3.86%w/v / 38.6mg/mL CLEAR-FLEX solution dialysis.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition of the solution in each compartment before mixing in g/L						
	Viaflex Bag			CLEAR FLEX Bag		
Active Ingredients	Glucose 1.36%	Glucose 2.27%	Glucose 3.86%	Glucose 1.36%	Glucose 2.27%	Glucose 3.86%
Glucose Bag "A"						
Anhydrous Glucose	37.50	62.60	106.50	18.2	30.3	51.5
Calcium Chloride (Dihydrate)	0.507	0.507	0.507	0.245	0.245	0.245
Magnesium Chloride (Hexahydrate)	0.140	0.140	0.140	0.068	0.068	0.068
Buffer Bag "B"						
Sodium Chloride	8.43	8.43	8.43	19.95	19.95	19.95
Sodium Bicarbonate	3.29	3.29	3.29	9.29	9.29	9.29
Sodium Lactate	2.63	2.63	2.63	6.73	6.73	6.73

Final Solution After Mixing			
Anhydrous Glucose	13.6	22.7	38.6
Sodium Chloride	5.38	5.38	5.38
Calcium Chloride (Dihydrate)	0.184	0.184	0.184
Magnesium Chloride (Hexahydrate)	0.051	0.051	0.051
Sodium Bicarbonate	2.10	2.10	2.10
Sodium Lactate	1.68	1.68	1.68

NEW ZEALAND DATA SHEET

1000mL of final solution after mixing corresponds to:

- Viaflex Bag: 362.5mL of solution A (Glucose) and 637.5mL of solution B (Buffer).
- CLEAR FLEX Bag: 750mL of solution A (Glucose) and 250mL of solution B (Buffer).
- The pH of the final solution is 7.4.
- Hydrochloric acid (Solution A) and Sodium hydroxide (Solution B) are used for pH adjustment in the CLEAR FLEX presentation.

Composition of the final solution after mixing in mmol/L			
	Glucose 1.36%	Glucose 2.27%	Glucose 3.86%
Anhydrous glucose (C ₆ H 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 ₃ H ₅ O ₃ ⁻)	15	15	15
Osmolarity*	344mOsmol/L	395mOsmol/L	483mOsmol/L

*Osmolarity is equivalent to osmolality in infinitely diluted conditions, including total dissociation of ingredients.

3 PHARMACEUTICAL FORM

Dialysis Solutions.

PHYSIONEAL 40 and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** are sterile, clear, colourless glucose solutions for peritoneal dialysis.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

PHYSIONEAL 40 and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX**, are indicated for use in peritoneal dialysis in patients with acute or chronic renal failure.

4.2 Dose and method of administration

Dosage

Intraperitoneal administration only. Not for intravenous administration.

Product is for single use in one patient only.

Adult

- 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 peritoneal dialysis solution with the lowest level of osmolality consistent with fluid removal requirements for each exchange.
- 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.

NEW ZEALAND DATA SHEET

Children

To date, there are no data from clinical studies in paediatric patients. Safety and effectiveness in paediatric patients has not been established.

Elderly

The evaluation of the results obtained for this group does not show any difference to the rest of the patients.

Instructions for Use and Handling - General

Preparation for Administration

- Prior to exchange assemble supplies on exchange area, wash hands and wipe surface. Prior to opening overpouch, check for the correct solution type, expiration date, and amount (volume).
- The solution should be warmed to 37°C in the overpouch to enhance patient comfort. However, only dry heat (e.g. heating pad, warming plate) should be used. Solutions should not be heated in water or in a microwave oven.
- Aseptic technique should be employed throughout the peritoneal dialysis procedure. Lift the dialysate bag to check for any leaks are contained within the overpouch. If leaks are discovered do not use as sterility may be impaired. In case of damage the container should be discarded.
- Open overpouch and remove contents. Ensure the pull ring is attached to the solution administration port. Do not use if pull ring is not attached as sterility may be impaired.
- Do not administer if the solution is discoloured, cloudy, contains particulate matter or shows evidence of leakage 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.
- The pH and salts of the solution must be taken into account for compatibility before adding to the solution.
- Contains no antimicrobial preservative.
- The mode of therapy, frequency of treatment, exchange volume, duration of dwell and length of dialysis should be selected by a physician.

Viaflex Bag – Instruction for use and handling

- Detailed instruction on the CAPD exchange procedure is given to patients by means of training in a specialised training centre, prior to home use.
- After the removal of the overpouch, inspect the container for signs of leakage. Leaks may occur between the chambers or to the exterior. Check that the interchamber frangible pin is not broken by pressing firmly on the large and small chambers. If the frangible pin is already broken, or if any leak is detected, do not use bag.
- 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 of mixing.
- After the frangible pin has been broken, check the integrity of the bag for any signs of leakage. If leaks are detected, do not use bag.
- Medicines should be added through the medication port in the glucose chamber before breaking the interchamber frangible pin. The product should be used immediately after any medicine addition. **DO NOT STORE.**
- There is no incompatibility with insulin in **PHYSIONEAL 40** in the Viaflex container. Consult with pharmacist familiar with peritoneal dialysis, if available. If, in the informed judgement of the physician, it is deemed advisable to introduce additives, use aseptic technique.

NEW ZEALAND DATA SHEET

CLEAR FLEX bag – Instruction for use and handling

- Detailed instructions on the Peritoneal Dialysis exchange procedure is given to patients by means of training in a specialised training centre, prior to home use.
- After the removal of the overpouch, inspect the container for signs of leakage. Leaks may occur between the chambers or to the external environment. Check that the long and short seals are not opened at any point by pressing firmly on the large and small chambers. If one of the seals is opened, even partially, or if any leak is detected, do not use bag.
- After removal of the overpouch, immediately open the long-seal (interchamber seal) to mix the two solutions and then open the short Safety Moon seal (access seal) to allow administration of the mixed solution. The intraperitoneal solution must be infused within 24 hours of mixing.
- Patients must be instructed to open both the long and the short seals prior to infusion. If only the short-seal opens, infusion of the unmixed solution can cause abdominal pain, hypernatremia and severe metabolic alkalosis. In case of infusion of unmixed solution, the patient should immediately drain the solution and use a newly mixed bag.
- After short and long seals have been opened, check the integrity of the bag for any signs of leakage. If leaks are detected, do not use bag. Report and return faulty bags.
- Medicines should be added through the medication site in the larger 'glucose' chamber before opening the interchamber peel seal. The product should be used immediately after any medicine addition. DO NOT STORE.
- There is no incompatibility with cefazolin, heparin, low molecular weight heparin, insulin, vancomycin and **PHYSIONEAL 40** in the CLEARFLEX container. Gentamicin and tobramycin can be added only if the solution is used immediately after medicine addition. 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.

4.3 Contraindications

PHYSIONEAL 40 and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX**, are contraindicated for use 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

- For single use in one patient only.
- 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) where possible. Prior to identification of the involved organism(s), broad-spectrum antibiotics may be indicated.
- Solutions containing glucose 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 that can be associated with acute renal failure, inborn errors of metabolism, treatment with drugs such as metformin and nucleoside/

NEW ZEALAND DATA SHEET

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 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 hyperglycaemia should be adjusted.
- The use of **PHYSIONEAL** in CLEAR FLEX container is not recommended in patients requiring a fill volume < 1600mL due to the risk of undetected mis-infusion (administration of the buffer chamber only)
- Patients must be instructed to open both the long and the short seals prior to infusion. If only the short-seal opens, infusion of the unmixed solutions can cause abdominal pain, hypernatremia and severe metabolic alkalosis. In case of infusion of unmixed solution, the patient should immediately drain the solution and use a newly mixed bag.
- 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, faecal fistula or 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, and advanced pregnancy; and
 - 2) other conditions including aortic graft placement and severe pulmonary disease, malnutrition or severe disorders of lipid metabolism. In the individual case, the benefits for the patient must be weighed against the possible complications.
- **PHYSIONEAL 40** and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** are intended for intraperitoneal administration only. Not for intravenous administration.
- Do not administer if the solution is discoloured, cloudy, contains particulate matter or 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 paediatric patients have not been established.
- An accurate fluid balance record must be kept and the body weight of the patient should carefully be monitored to avoid over- or under-hydration 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 and may require replacement.
- In renal failure patients, serum electrolyte concentrations (particularly bicarbonate, potassium, magnesium, calcium and phosphate), blood chemistry (including parathyroid hormone) and haematological parameters should be evaluated periodically.
- In patients with secondary hyperparathyroidism, the benefits and risks of the use of dialysis solution with low calcium content such as **PHYSIONEAL 40** and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** should be carefully considered as it might worsen hyperparathyroidism.
- In patients with plasma bicarbonate level above 30mmol/L, the risk of possible metabolic alkalosis should be weighed against the benefits of treatment with this product. Serum bicarbonate levels should be monitored regularly.
- Over infusion of **PHYSIONEAL 40** or **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** solutions into the peritoneal cavity may be characterised by abdominal distension/abdominal pain and/or shortness of breath.

NEW ZEALAND DATA SHEET

- Treatment of **PHYSIONEAL 40** or **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** over infusion is to drain the solution from the peritoneal cavity.
- Excessive use of **PHYSIONEAL 40** or **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** peritoneal dialysis solution with a higher glucose during peritoneal dialysis treatment may result in excessive removal of water from the patient.
- Potassium is omitted from **PHYSIONEAL 40** and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** solutions due to the risk of hyperkalaemia.
- In situations in which there is normal serum potassium level or hypokalaemia, the addition of potassium chloride (up to a concentration of 4mEq/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.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been conducted with **PHYSIONEAL 40** or **PHYSIONEAL 40 GLUCOSE CLEAR FLEX**.

Blood concentration of dialyzable 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.

4.6 Fertility, pregnancy and lactation

Fertility

Potential effects on male and female fertility are unknown.

Pregnancy (Category B2)

The potential effects of **PHYSIONEAL 40** and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** on reproduction have not been adequately studied in animals. There is insufficient experience with the use of dialysis fluids in pregnant women.

Women of childbearing potential should be treated with **PHYSIONEAL 40** or **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** only when adequate contraceptive precautions have been taken.

Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing **PHYSIONEAL 40** or **PHYSIONEAL 40 GLUCOSE CLEAR FLEX**.

Lactation

There are no available data from animal studies on the effects of **PHYSIONEAL 40** administered during lactation. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing **PHYSIONEAL 40** or **PHYSIONEAL 40 GLUCOSE CLEAR FLEX**.

4.7 Effects on ability to drive and use machines

End stage renal disease (ESRD) patients undergoing peritoneal dialysis may experience undesirable effects, which could affect the ability to drive or use machines.

4.8 Undesirable effects

The main adverse events reported for pivotal study REP-RENAL-REG-029 were alkalosis, acidosis and peritonitis. These adverse events were reported by 97.2% and 95.7% of subjects in the control and physiological treatment groups respectively. Subjects treated with **PHYSIONEAL 40** recorded significantly more alkalosis events than those treated with **Dianeal**. For pivotal study REP-RENAL-REG-30A, the main adverse events reported were pruritus and sweating.

NEW ZEALAND DATA SHEET

In clinical trials with **PHYSIONEAL 40** the following adverse reactions have been noted: benign neoplasm of the skin, alkalosis, fluid retention, hypercalcaemia, hypervolaemia, anorexia, dehydration, hyperglycaemia, hyperphosphataemia, lactic acidosis, insomnia, dizziness, hypertonia, arrhythmia, cardiomegaly, hypertension, hypotension, dyspnoea, cough, respiratory acidosis, peritoneal membrane failure, dyspepsia, flatulence, nausea, pruritis, oedema, asthenia, chills, facial oedema, malaise, thirst, procedural complication, weight increase, blood lactate dehydrogenase increased, laboratory test abnormal PCO₂ increased, alanine aminotransferase increased, C reactive protein increased, creatinine renal clearance decreased, and gamma glutamyltransferase increased.

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

Those which are related to the procedure, include 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, and hernia of the abdominal cavity. Those which are generally related to peritoneal dialysis solutions, are seen less frequently than those related to the procedure and include weakness, fainting, tiredness, muscle cramping, headache, respiratory symptoms associated with pulmonary oedema and electrolyte disturbances (e.g. hypokalaemia, hypocalcaemia).

Post marketing experience from August 1998 until September 2001 indicate that, with the exception of data from 1999, adjusted peritonitis incidence rates submitted to the European Dialysis Solutions Registry were similar for both **PHYSIONEAL 40** and **Dianeal** solutions.

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 DISORDER:

Eosinophilia.

GASTROINTESTINAL DISORDERS:

Sclerosing encapsulating peritonitis, Peritoneal cloudy effluent, Abdominal discomfort.

SKIN AND SUBCUTANEOUS TISSUE DISORDER:

Angiodema, Rash.

MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS:

Musculoskeletal pain.

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:

Catheter related complications, Pyrexia.

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. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

NEW ZEALAND DATA SHEET

4.9 Overdose

Possible consequences of overdose include hypervolaemia, hypovolaemia, electrolyte disturbances or (in diabetic patients) hyperglycaemia. Excessive use of **PHYSIONEAL 40**, or **PHYSIONEAL 40 GLUCOSE 3.86%w/v / 38.6mg/mL CLEAR FLEX** peritoneal dialysis solution with 3.68% glucose during a peritoneal dialysis treatment can result in significant removal of water from the patient.

For advice on the management of overdose please contact the National Poisons Centre on phone number: 0800 764 766 [0800 POISON] in New Zealand (or 131126 in Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

Peritoneal Dialytics, Hypertonic solutions.

ATC code

B05DB.

For use in patients with renal failure to aid the regulation of fluid and electrolytes 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 metabolic 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

Clinical Trials

To date a total of 226 patients have been exposed to **PHYSIONEAL 40** in a total of 6 controlled clinical trials. The exposure time ranged from single dwells (18 patients) to up to one year's exposure (70 patients in 6-month study, 43 continued for full year). No pregnant or lactating women or children were studied and there is no long-term survival data.

Most of the trials were designed to demonstrate equivalence with the control product. In all studies there were no significant changes in the residual renal function (RRF), weekly Kt/V and normalised creatinine clearances when patients switched from **Dianeal PD4** to **PHYSIONEAL 40**, and no statistically significant differences between the control (**Dianeal PD4**) arms of these studies and the **PHYSIONEAL 40** arms. Ultrafiltration is maintained when the buffer is changed from pure lactate to a bicarbonate/lactate combination. There was no difference between **PHYSIONEAL 40** and **Dianeal PD4** with regard to maintenance of calcium and magnesium homeostasis. Acid-base homeostasis was assessed from measurement of the plasma bicarbonate. In all studies the change from baseline (or between group differences) was always within the pre-defined equivalence targets. **PHYSIONEAL 40** thus corrects acidosis as well as **Dianeal**.

There did not seem to be any obvious trends across the various **PHYSIONEAL 40** trials regarding deaths or withdrawals due to adverse events.

NEW ZEALAND DATA SHEET

Pivotal Study: REP-RENAL-REG-029

Study design

Randomised, open-label, comparative study to assess the bioequivalence of a bicarbonate based peritoneal dialysis [bicarb/lactate 25/15mmol/L] solution compared to lactate (40mmol/L) buffer solution.

Primary Variable

Plasma bicarbonate levels.

The two preparations were considered equivalent if the 90% confidence intervals for the treatment difference fell entirely within ± 3.0 mmol/L

Results

Base line demographics and plasma bicarbonate levels for subjects in study REP-RENAL-REG-029:

REP-RENAL-REG-029	ITT population	
	Control	PHYSIONEAL 40
Total No. Randomised	36	70
Mean Age (yrs)	56.6	55.1
Range	23 - 76	26 - 77
Gender % Males	50	60
Previous peritonitis (% subjects)	14.3	18.9
Duration of dialysis at baseline (yrs)	1.6	1.8
Duration of CAPD at baseline (yrs)	1.3	1.5
Bicarbonate at baseline mmol/L (SD)	26.3 (3.4)	26.4 (3.0)
Bicarbonate at 3 months (SD)	27.3 (3.0)	28.0 (2.9)
Treatment difference	0.79 (90% CI 0.26, 1.31)	
Bicarbonate at 6 months (SD)	27.2 (3.1)	27.9(2.9)
Treatment difference	0.78 (90% CI 0.31, 1.26)	

After three to six months there were small statistically significant treatment differences in plasma bicarbonate levels. 90% of confidence intervals for the treatment differences were within ± 3 mmol/L of bicarbonate and the treatments are considered to be equivalent. There were no statistically significant correlations between bicarbonate levels and age or normalised Residual Renal Function at 6 months for either treatment, but there was a significant negative correlation between calcium carbonate dose and bicarbonate levels in the **PHYSIONEAL 40** group.

Subjects treated with **PHYSIONEAL 40** recorded significantly more alkalosis events than those treated with the lactate (40mmol/L) buffer solution.

Pivotal Study: REP-RENAL-REG-030-A

Study design

Study designed to subjectively evaluate inflow pain during CAPD with a 28mM bicarbonate solution, **PHYSIONEAL 40** and **Dianeal** in 18 subjects who had previously experienced pain during dialysis treatment. This was a single-blind, randomised crossover study where pain was assessed during two single infusions of each solution over a one to three-week period, with each participant receiving six

NEW ZEALAND DATA SHEET

single infusions in random order. Test solutions were: bicarbonate 38mM (pH 7.0 - 7.4); Bicarbonate lactate 25/15mM (pH 7.0 - 7.4) and **Dianeal PD4** (40mM lactate) (pH 5.0 - 5.2). All three solutions contained 3.86% glucose in a two-litre bag.

Primary Variable

The primary endpoint variable was pain during the infusion and subjects were evaluated over a three-hour period that included the dwell and drain times of the solution. Pain severity was measured on a five-point visual analogue scale (none, mild, moderate, severe and very severe). The McGill Pain Questionnaire (MPQ) was used to assess the pain severity/intensity and provide verbal descriptors of pain.

Results

Baseline demographics and subjective pain scores (range 0 - 5) for subjects in study REP-RENAL-REG-030A:

REP-RENAL-REG-030 A	ITT population
Total No. Randomised	18
Mean Age (yrs)	53.5
Range	27 - 75
Gender % Males	56
Previous peritonitis in last 6 months (% subjects)	50
Duration of dialysis at baseline (mean yrs)	2.0

Evaluable population				
	Dianeal	Bicarb.	PHYSIONEAL 40	P value
Total No. of infusions	34	34	34	
Peak pain score during infusion (Range)	1.50 (0 - 3)	0.59 (0 - 3)	0.44 (0 - 2)	0.0001
Treatment difference	PHYSIONEAL 40 vs Dianeal PD4			0.001
Peak pain score during dwell (Range)	0.44 (0 - 3)	0.47 (0 - 3)	0.21 (0 - 2)	0.083
Treatment difference	PHYSIONEAL 40 vs Dianeal PD4			0.001
Peak pain score during drain (Range)	0.15 (0 - 1)	0.32 (0 - 3)	0.06 (0 - 2)	0.035
Treatment difference	PHYSIONEAL 40 vs Dianeal PD4			0.325

There was a statistically significant treatment difference in peak pain scores during the infusions (P = 0.0001). **PHYSIONEAL 40** solution produced lower pain scores than **Dianeal**. However, this difference has not been confirmed from larger studies. Numerous variables could affect pain related to the dialysis procedure (including ones related to the dialysis solution, such as catheter placement, that can affect the validity of clinical trials).

NEW ZEALAND DATA SHEET

5.2 Pharmacokinetic properties

Intraperitoneally administered glucose, buffer, electrolytes and water are absorbed into the blood and metabolised by the usual pathways. Glucose is metabolised (1g of glucose = 4 kilocalories or 17 kilojoules) into CO₂ and H₂O.

5.3 Preclinical safety data

Carcinogenicity and genotoxicity

Long-term carcinogenicity studies of **PHYSIONEAL 40** and **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** have not been done. **PHYSIONEAL 40** was not mutagenic in bacterial gene mutation assays.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PHYSIONEAL 40

Carbon dioxide
Water for injection.

PHYSIONEAL 40 GLUCOSE CLEAR FLEX

Hydrochloric acid
Sodium hydroxide
Water for injection.

6.2 Incompatibilities

This medicine must not be mixed with other medicines except those mentioned in section 4.2.

6.3 Shelf life

The shelf life of the product in the overpouch is 2 years.

Shelf life after reconstitution

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

6.4 Special precautions for storage

PHYSIONEAL 40 in Viaflex bags: store below 30°C. Do not freeze.

PHYSIONEAL 40 in CLEAR FLEX bags: store below 25°C. Do not freeze.

6.5 Nature and contents of container

Viaflex Container

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

The upper chamber is fitted with an injection port for drug 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 bag is sealed inside a transparent overpouch obtained by thermic fusion and made of multilayer copolymers.

Container volumes after reconstitution:

1500mL (544mL of solution A and 956mL of solution B),
2000mL (725mL of solution A and 1275mL of solution B) and
2500mL (906mL of solution A and 1594mL of solution B).

NEW ZEALAND DATA SHEET

PHYSIONEAL 40 Glucose Viaflex is available in the presentations in the following table:

TT50- (ARTG)	Product Name	Container Size
TT50-7047/1 (119077)	PHYSIONEAL 40 Glucose 1.36% w/v Peritoneal Dialysis Solution Twin Bag	1.5L, 2L, 2.5L
TT50-7047/1 (97418)	PHYSIONEAL 40 Glucose 1.36% w/v Peritoneal Dialysis Solution Bag	1.5L, 2L, 2.5L
TT50-7047/1a (119078)	PHYSIONEAL 40 Glucose 2.25% w/v Peritoneal Dialysis Solution Twin Bag	1.5L, 2L, 2.5L
TT50-7047/1a (97426)	PHYSIONEAL 40 Glucose 2.25% w/v Peritoneal Dialysis Solution Bag	1.5L, 2L, 2.5L
TT50-7047/1b (119079)	PHYSIONEAL 40 Glucose 3.86% w/v Peritoneal Dialysis Solution Twin Bag	1.5L, 2L, 2.5L
TT50-7047/1b (97431)	PHYSIONEAL 40 Glucose 3.86% w/v Peritoneal Dialysis Solution Bag	1.5L, 2L, 2.5L
Not all presentations may be available.		

CLEAR FLEX Container:

The **PHYSIONEAL 40 GLUCOSE CLEAR FLEX** solution is stored inside a two-chamber bag made of a coextruded film (CLEAR FLEX film) of polypropylene, polyamide and a blend of polypropylene, styrene-ethylene/butylene-styrene and polyethylene.

The bag is sealed inside a transparent overpouch made of multilayer copolymers.

On the glucose chamber an injection site is welded for medicine admixture to the glucose with electrolytes solution. On the buffer chamber a valve system is welded for connection to a suitable administration set allowing dialysis operations. The bag is wrapped inside a transparent overpouch made of multilayer copolymers.

Container volume after reconstitution is 5000mL (3750mL of solution A and 1250mL of solution B). The pH of chamber A is approximately 2.1. The pH of chamber B is approximately 9.0.

PHYSIONEAL 40 GLUCOSE CLEAR FLEX are available in the following container sizes:

TT50- (ARTG)	Product Name	Container Size
TTT50-7047/3 (97418)	PHYSIONEAL 40 Glucose 1.36% w/v CLEAR FLEX Peritoneal Dialysis Solution Bag	5L
TTT50-7047/3a (97426)	PHYSIONEAL 40 Glucose 2.25% w/v CLEAR FLEX Peritoneal Dialysis Solution Bag	5L
TTT50-7047/3b (97431)	PHYSIONEAL 40 Glucose 3.86% w/v CLEAR FLEX Peritoneal Dialysis Solution Bag	5L
Not all presentations may be available.		

NEW ZEALAND DATA SHEET

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

PHYSIONEAL 40 and PHYSIONEAL 40 GLUCOSE CLEAR FLEX are distributed in New Zealand by:

Baxter Healthcare Ltd
33 Vestey Drive
Mt Wellington
Auckland 1060.

Baxter Healthcare Ltd
PO Box 14 062
Panmure
Auckland 1741

Phone (09) 574 2400.

PHYSIONEAL 40 and PHYSIONEAL 40 GLUCOSE CLEAR FLEX are supplied in Australia by:

Baxter Healthcare Pty Ltd
1 Baxter Drive
Old Toongabbie
NSW 2146.

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:

PHYSIONEAL 40

1 March 2007

PHYSIONEAL 40 GLUCOSE CLEAR FLEX

7 November 2013.

10 DATE OF REVISION OF THE TEXT

7 May 2018.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Reformatted to SPC style.

Based on Australian PI approved 21 June 2013, most recent amendment 16 October 2014; and CCDS10220140731.

Please refer to the Medsafe website (www.medsafe.govt.nz) for most recent data sheet.

Baxter, Dianeal, PHYSIONEAL 40 and PHYSIONEAL 40 GLUCOSE CLEAR FLEX are trademarks of Baxter International Inc.