1 DIANEAL(solution, dialysis)

Dianeal 1mmol/L Calcium with 1.5%w/v Glucose Monohydrate

Dianeal 1mmol/L Calcium with 2.5%w/v Glucose Monohydrate

Dianeal 1mmol/L Calcium with 4.25%w/v Glucose Monohydrate

Dianeal PD-4 with 0.55%w/v Glucose Monohydrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dianeal PD-4 and 1mmol/L Calcium dialysis solutions are sterile, nonpyrogenic and contain no bacteriostatic or antimicrobial agents or added buffers.

Each 1000mL of Dianeal dialysis solution contains:

Component	Content
Glucose, BP	0.55% -- 5.5g 1.5 % -- 15.0g 2.5 % -- 25.0g or 4.25% -- 42.5g
Sodium Chloride, BP	- - 5.38g
Sodium Lactate	- - 4.48g
Magnesium Chloride Hexahydrate, BP	- - 50.8g
Calcium Chloride Dihydrate, BP	PD-2 - 257mg, PD-4 - 183mg, or 1mmol/L Calcium 147mg
Water For Injections, BP	QS

Dianeal *1mmol/L Calcium dialysis solution*

		with 1.5% Glucose	with 2.5% Glucose	with 4.25% Glucose
Glucose .H2O		76mmol/L	126mmol/L	214mmol/L
Sodium		132mmol/L	132mmol/L	132mmol/L
Calcium		1.00mmol/L	1.00mmol/L	1.00mmol/L
Magnesium		0.25mmol/L	0.25mmol/L	0.25mmol/L
Chloride		96mmol/L	96mmol/L	96mmol/L
Lactate		40mmol/L	40mmol/L	40mmol/L
Approximate Osmolality		344mOs	394mOs	482mOs

	with 0.55% Glucose			
Glucose .H2O	28mmol/L			
Sodium	132mmol/L			
Calcium	1.25mmol/L			
Magnesium	0.25mmol/L			
Chloride	96mmol/L			
Lactate	40mmol/L			
Approximate Osmolality	297mOs			

Potassium is omitted from Dianeal solutions because dialysis may be performed to correct hyperkalaemia.

Because average plasma magnesium levels in chronic Continuous Ambulatory Peritoneal Dialysis (CAPD) patients have been observed to be elevated (Nolph *et al.* 1981), the magnesium concentration of this formulation has been reduced to 0.25mmol/L.

Because average serum bicarbonate levels in chronic CAPD patients have been observed to be somewhat lower than normal values (Nolph *et al*. 1981), the bicarbonate precursor (lactate) concentration of this formulation has been raised to 40mmol/L.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution, dialysis.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Dianeal PD-4 and 1mmol/L Calcium dialysis solution is indicated for use in chronic renal failure patients being maintained on Continuous Ambulatory Peritoneal Dialysis (CAPD).

4.2 Dose and method of administration

Dianeal PD-4 and 1mmol/L Calcium dialysis solutions are intended for intraperitoneal administration only. The mode of therapy (Continuous Ambulatory Peritoneal Dialysis), frequency of treatment, formulation, exchange volume, duration of dwell and length of dialysis should be selected by the physician responsible for and supervising the treatment of the individual patient.

To avoid the risk of severe dehydration and hypovolaemia and to minimise the loss of protein, it is advisable to select the peritoneal dialysis solution with the lowest level of osmolality consistent with the fluid removal requirements for that exchange.

As the patient's body weight becomes closer to the ideal dry weight, lowering the glucose concentration of Dianeal is recommended. Dianeal 4.25% glucose containing solution is a high osmotic pressure fluid and using it alone may cause dehydration (see section 4.4).

Heating the dialysis solution to 37°C (while in the overpouch) may decrease discomfort and heat loss and result in increased clearances of urea when compared to solution at room temperature (Gross and McDonald 1967). Only dry heat (eg. 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.

The addition of heparin to the dialysis solution may be indicated to aid in prevention of catheter blockage in patients with peritonitis, or when the solution drainage contains fibrinous or proteinaceous material (Ribot *et al.* 1966). 1000 to 2000 International Units of heparin per litre of solution has been recommended (Furman *et al.* 1978).

Continuous Ambulatory Peritoneal Dialysis (CAPD)
For maintenance dialysis of chronic renal failure patients.

In this technique, typically 1.5 to 2.0 litres of dialysis solution (depending upon patient size) are instilled into the peritoneal cavity and the peritoneal access device is then clamped. The solution remains in the cavity for dwell times of 4 - 6 hours during the day and approximately eight hours overnight. At the conclusion of each dwell period, the access device is opened, the solution drained and fresh solution instilled. The procedure is repeated 3 - 5 times per day, 6 -7 days per week. Typically the majority of exchanges will utilise 1.5% and 2.5% Glucose containing peritoneal dialysis solutions, with 4.25% Glucose containing solutions being used when extra fluid removal is required. Patient weight is used as the indicator of the need for fluid removal (Popovich *et al.* 1978).

Directions for Use
Dianeal dialysis solutions are intended for intraperitoneal administration only. Do not use for intravenous administration. Do not administer if the solution is discoloured, cloudy, contains particulate matter or shows evidence of leakage or if seals are not intact.

Use aseptic technique throughout the peritoneal dialysis procedure. To add medication:

1. Prepare medication site. If the resealable rubber plug on the medication port is missing or partially removed, do not use product if medication is to be added.
2. Using syringe with 19-22 gauge needle, puncture resealable rubber plug at target area and inject.
3. Mix solution and medication thoroughly. For high density medication such as potassium chloride, squeeze medication port while port is upright and mix thoroughly.

Preparation for Administration

1. Place container on table or suspend from support.
2. Remove protector from outlet port of container.
3. Attach solution transfer set; refer to complete directions accompanying set.

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.

4.3 Contraindications

Dianeal is contraindicated in patients with:

- hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- pre-existing severe lactic acidosis
- 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.

Do not administer unless the solution is clear and the seal is intact.

4.4 Special warnings and precautions for use

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 Dianeal. Infrequently, fatal outcomes of EPS have been reported with Dianeal.

Improper clamping or priming sequence may result in infusion of air into the peritoneal cavity, which may result in abdominal pain and/or 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.

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 severe lactic acidosis should not be treated with lactate-based peritoneal dialysis solutions (see section 4.3). It is recommended that patients with conditions known to increase the risk of lactic acidosis [eg. Severe hypotension or sepsis that can be associated with acute 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, calcium and magnesium levels should be monitored carefully in patients treated with cardiac glycosides.

Azotaemic diabetics require careful monitoring of insulin requirements during and following dialysis with glucose-containing solutions. Dianeal products contain varying concentrations of glucose, ranging between 0.55 to 4.25%. In diabetic patients, blood glucose levels should be regularly monitored, and the dosage of insulin or other treatments for hyperglycaemia should be adjusted.

Aseptic technique must be used throughout the procedure and at its termination in order to reduce the possibility of infection. 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.

Peritoneal dialysis should be done with great care, if at all, in patients with a number of abdominal conditions including disruption of the peritoneal membrane and diaphragm by surgery or from congenital anomalies or trauma until healing is complete, abdominal tumours, extensive adhesions, bowel distension, undiagnosed abdominal disease, abdominal wall infection, hernias or burns, faecal fistula, colostomy or ileostomy, frequent episodes of diverticulitis, inflammatory or ischaemic bowel disease, tense ascites, obesity, and large polycystic kidneys, or other conditions that compromise the integrity of the abdominal wall, abdominal surface, or intra-abdominal cavity. Peritoneal dialysis should also be done with caution in patients with other conditions including aortic graft replacement and severe pulmonary disease. When assessing peritoneal dialysis as the mode of therapy in such extreme situations, the benefits to the patient must be weighed against the possible complications.

Protein, amino acids, water-soluble vitamins, and other medicines may be lost during peritoneal dialysis and may require replacement.

Patients should be carefully monitored to avoid over- and under-hydration. An accurate fluid balance record must be kept and the weight of the patient carefully monitored to avoid over- or under-hydration and severe consequences including congestive heart failure, volume depletion, and shock. Excessive use of Dianeal PD-4 and 1mmol/L Calcium dialysis solutions with 4.25% Glucose during peritoneal dialysis treatment can result in significant removal of water from the patient. Over-infusion of a Dianeal volume into the peritoneal cavity may be characterised by abdominal distension, abdominal pain and/or shortness of breath (see section 4.9).

Routine periodic evaluation of blood chemistries (including parathyroid hormone and lipid parameters), serum electrolyte concentrations (particularly bicarbonate, potassium, magnesium, calcium and phosphate) and haematologic factors, as well as other indicators of patient status, should be performed for stable patients undergoing maintenance peritoneal dialysis.

Potassium is omitted from Dianeal PD-4 and 1mmol/L Calcium dialysis solutions because dialysis may be performed to correct hyperkalaemia. IN SITUATIONS WHERE THERE IS NORMAL SERUM POTASSIUM OR HYPOKALAEMIA, ADDITION OF POTASSIUM CHLORIDE (up to 4mEq/L) TO PREVENT SEVERE HYPOKALAEMIA SHOULD BE MADE AFTER CAREFUL EVALUATION OF SERUM AND TOTAL BODY POTASSIUM AND ONLY UNDER THE DIRECTION OF A PHYSICIAN.

Not for use in the treatment of lactic acidosis.

Low Calcium Dianeal PD solution should be considered with patients with hypercalcaemia. Patients receiving this solution should have their calcium levels monitored for the development of hypocalcaemia or worsening of hypercalcaemia. In these circumstances, adjustments to the dosage of the phosphate binders and/or Vitamin D analogs should be considered by the physician.

Hyperphosphataemia may develop from use of 1mmol/L Calcium Solutions which may subsequently lead to secondary hyperparathyroidism. Dialysis using 1mmol/L Calcium Solution requires close and continuous monitoring of PTH and bone metabolism.

Because average plasma magnesium levels in chronic CAPD patients have been observed to be elevated (Nolph *et al.* 1981), the magnesium concentration of this formulation has been reduced to 0.25mmol/L. Serum magnesium levels should be monitored and if low, oral magnesium supplements, oral magnesium containing phosphate binders, or peritoneal dialysis solutions containing higher magnesium concentrations may be used.

4.5 Interaction with other medicines and other forms of interaction

No clinical drug interaction studies have been conducted with **Dianeal**.

Additives may be incompatible (see section 6.2). Consult with pharmacist familiar with peritoneal dialysis, if available. When introducing additives, refer to directions for use accompanying drugs to obtain full information on additives, and use aseptic techniques. Mix thoroughly. Do not store.

Refer to manufacturer's directions accompanying drugs to obtain full information on additives.

Significant losses of protein, amino acids and water soluble vitamins, as well as other dialysible medicines may occur during peritoneal dialysis. Replacement therapy should be provided as necessary.

4.6 Fertility, pregnancy and lactation

Effects on fertility

Studies to evaluate the carcinogenic or mutagenic potential of this product, or its potential to affect fertility adversely, have not been performed.

Pregnancy

There are no adequate data from the use of **Dianeal** in pregnant women. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing **Dianeal**.

Breast-feeding

There are no adequate data from the use of **Dianeal** in lactating women. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing **Dianeal**.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

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. Abdominal pain, bleeding, peritonitis, subcutaneous infection around a chronic peritoneal catheter, catheter blockage, difficulty in fluid removal, and ileus are among the complications of the procedure. Solution-related adverse reactions may include electrolyte and fluid imbalances, hypovolaemia, hypervolaemia, hypertension, hypotension, and muscle cramping and hyperphosphataemia (which may induce secondary hyperparathyroidism).

The following adverse reactions have been reported in post-marketing experience:

Infections and Infestations

Fungal peritonitis, bacterial peritonitis, catheter-related infection.

Metabolism and Nutrition Disorders

Hypovolaemia, hypervolaemia, fluid retention, hypokalaemia, hyponatraemia, dehydration and hypochloraemia.

Vascular Disorders

Hypotension and hypertension.

Respiratory, Thoracic and mediastinal Disorders

Dyspnoea.

Gastrointestinal Disorders
Sclerosing Encapsulating Peritonitis, peritonitis, peritoneal cloudy effluent, vomiting, diarrhoea, nausea, constipation, abdominal pain, abdominal distension, abdominal discomfort.

Skin and Subcutaneous Disorders
Stevens-Johnson syndrome, urticaria, rash (including pruritic, erythematous and generalised) and Pruritus.

Musculoskeletal and connective Tissue Disorders
Myalgia, muscle spasms and musculoskeletal pain.

General Disorders and Administration Site Conditions
generalised oedema, pyrexia, malaise, infusion site pain and catheter-related complication.

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/

4.9 Overdose
Overdose by over infusion of a **Dianeal** volume into the peritoneal cavity is characterised by abdominal pain and distension and shortness of breath.

There is a potential for overdose resulting in hypervolaemia, hypovolaemia, electrolyte disturbances or hyperglycaemia. Excessive use of **Dianeal** peritoneal dialysis solution with 4.25% glucose during a peritoneal dialysis treatment can result in significant removal of water from the patient.

Treatment of **Dianeal** overdose by over infusion is to release the **Dianeal** from the peritoneal cavity by drainage of the **Dianeal** volume contained within the peritoneal cavity. Hypovolaemia 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 testing. 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 may be managed by adjusting the insulin dose or oral medications.

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.
ATC code: B05D.

Dianeal is a peritoneal dialysis solution of electrolytes, lactate and dextrose and is pharmacologically inactive.

Mechanism of action
Peritoneal dialysis is a procedure for removing toxic substances and metabolites normally excreted by the kidneys, and for aiding in the regulation of fluid and electrolyte balance.

The procedure is accomplished by instilling peritoneal dialysis fluid through a conduit into the peritoneal cavity. 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 which are controlled by osmosis and diffusion across the peritoneal membrane (between the plasma of the patient and the dialysis fluid). Toxic substances and metabolites, present in high concentration in the blood, cross the peritoneal membrane into the dialysing fluid. Glucose in the dialysing fluid is used to produce a solution hyperosmolar to the plasma, creating an osmotic gradient which facilitates transfer of extracellular fluid into the peritoneal cavity. After a period of time (dwell time), the fluid is drained by gravity from the cavity.

These medicines have been given provisional consent under Section 23 of the Medicines Act. This means that further evidence is awaited.

5.2 Pharmacokinetic properties
Not applicable.

5.3 Preclinical safety data
Animal reproduction studies have not been conducted with **Dianeal** dialysis solution.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Hydrochloric acid for pH adjustment
Water for Injections q.s.

6.2 Incompatibilities
Additives may be incompatible (see section 4.5). Consult with pharmacist familiar with peritoneal dialysis, if available. When introducing additives, refer to directions for use accompanying drugs to obtain full information on additives, and use aseptic techniques. Mix thoroughly. Do not store.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store at or below 30°C.

6.5 Nature and contents of container
Not all pack sizes and presentations may be marketed.

Dianeal 1mmol/L Calcium dialysis solution is available with 1.5% (TT50-5546/4a) and 2.5% (TT50-5546/5) Glucose concentrations in selected fill volumes and configurations:

Single Bag	6000 mL in 5000 mL nominal size container (System III)
Twin Bag	2500 mL in 3000 mL nominal size container.

Dianeal 1mmol/L Calcium dialysis solution is available 4.25% (TT50-5546/5b) Glucose concentrations in selected fill volumes and configurations:

Single Bag	6000 mL in 5000 mL nominal size container (System III).

Dianeal PD-4 dialysis solution is available with 0.55% (TT50-5545/4)
Glucose concentrations in selected fill volumes and configurations.

Single Bag	5000 mL in 5000 mL nominal size container (System III)
Twin Bag	2500 mL in 3000 mL nominal size container

Dianeal Freeline Solo Twin Bag
The Solution contained in the Freeline Solo Products can be **Dianeal** PD-4 or 1mmol/L Calcium. The solution bag is attached to a Y set and an empty container. Freeline Solo is a completely disposable exchange package. A fresh sterile pack is used for each exchange and this system requires only one connection per exchange.

6.6 Special precautions for disposal

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

The product is for single use in one patient only. Discard any residue immediately after use. Do not use if container is damaged or if solution is not clear.

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

Dianeal dialysis solution is 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.

Dianeal dialysis solution is manufactured and distributed 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:

Dianeal 1mmol/L Calcium with 1.5%w/v Glucose Monohydrate	12 September 2013
Dianeal 1mmol/L Calcium with 2.5%w/v Glucose Monohydrate	12 September 2013
Dianeal 1mmol/L Calcium with 4.25%w/v Glucose Monohydrate	12 September 2013
Dianeal PD-4 with 0.55%w/v Glucose Monohydrate	12 September 2013

10 DATE OF REVISION OF THE TEXT

24 November 2020.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Trade name corrected throughout document.

REFERENECES

Chang, T.M.S. 1977. Criteria, evaluation, and perspective of various microencapsulated charcoal hemoperfusion systems. Dialysis and Transplantation: 50 - 53

Furman, K.I. *et al.* 1978. Activity of intraperitoneal heparin during peritonal dialysis. Clin Nephrol 9: 15 - 18

Gross, M. and McDonald, Jr., H.P. 1967. Effect of dialysate temperature and flow rate on peritoneal clearance. JAMA 202: 363 - 365

Mattocks, A.M. and El-Bassiouni, E.A. 1971. Peritoneal dialysis: a review. J. Pharm Sciences 60: 1767 - 1782

Nolph. K.D. *et al.* 1981. Considerations for dialysis solution modifications. In Peritoneal Dialysis, eds. Robert C. Atkins et al. Chapter 25. New York: Churchill Livingston.

Popovich, R.P. *et al.* 1978. Continuous ambulatory peritoneal dialysis. Annals Intern Med 8: 449 - 456

Ribot, S. *et al.* 1966. Complications of peritoneal dialysis. AM J. Med Sciences 252: 505 – 517.

Based on Australian PI latest amendment 2 October 2014.

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