

Dianeal[®] Peritoneal Dialysis Solutions

Name of the medicine

Dianeal PD-2, PD-4 and 1 mmol/L Calcium Peritoneal Dialysis Solutions.

Description

Dianeal PD-2, PD-4 and 1 mmol/L Calcium Peritoneal Dialysis Solutions are sterile, nonpyrogenic and contain no bacteriostatic or antimicrobial agents or added buffers.

Each 1000 mL of Dianeal Peritoneal Dialysis Solution contains:

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

Dianeal PD-2 Peritoneal Dialysis Solution:

	with 0.55% Glucose	with 1.5% Glucose	with 2.5% Glucose	with 4.25% Glucose
Glucose .H ₂ O	28 mmol/L	76 mmol/L	126 mmol/L	214 mmol/L
Sodium	132 mmol/L	132 mmol/L	132 mmol/L	132 mmol/L
Calcium	1.75 mmol/L	1.75 mmol/L	1.75 mmol/L	1.75 mmol/L
Magnesium	0.25 mmol/L	0.25 mmol/L	0.25 mmol/L	0.25 mmol/L
Chloride	96 mmol/L	96 mmol/L	96 mmol/L	96 mmol/L
Lactate	40 mmol/L	40 mmol/L	40 mmol/L	40 mmol/L
Approximate Osmolality	298 mOs	346 mOs	396 mOs	485 mOs

Dianeal PD-4 Peritoneal Dialysis Solution

	with 0.55% Glucose	with 1.5% Glucose	with 2.5% Glucose	with 4.25% Glucose
Glucose .H ₂ O	28 mmol/L	76 mmol/L	126 mmol/L	214 mmol/L
Sodium	132 mmol/L	132 mmol/L	132 mmol/L	132 mmol/L
Calcium	1.25 mmol/L	1.25 mmol/L	1.25 mmol/L	1.25 mmol/L
Magnesium	0.25 mmol/L	0.25 mmol/L	0.25 mmol/L	0.25 mmol/L
Chloride	96 mmol/L	96 mmol/L	96 mmol/L	96 mmol/L
Lactate	40 mmol/L	40 mmol/L	40 mmol/L	40 mmol/L
Approximate Osmolality	297 mOs	345 mOs	395 mOs	483 mOs

Dianeal 1 mmol/L Calcium Peritoneal Dialysis Solution

	with 0.55% Glucose	with 1.5% Glucose	with 2.5% Glucose	with 4.25% Glucose
Glucose .H ₂ O	28 mmol/L	76 mmol/L	126 mmol/L	214 mmol/L
Sodium	132 mmol/L	132 mmol/L	132 mmol/L	132 mmol/L
Calcium	1.00 mmol/L	1.00 mmol/L	1.00 mmol/L	1.00 mmol/L
Magnesium	0.25 mmol/L	0.25 mmol/L	0.25 mmol/L	0.25 mmol/L
Chloride	96 mmol/L	96 mmol/L	96 mmol/L	96 mmol/L
Lactate	40 mmol/L	40 mmol/L	40 mmol/L	40 mmol/L
Approximate Osmolality	296 mOs	344 mOs	394 mOs	482 mOs

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 0.25 mmol/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 40 mmol/L.

Dianeal Freeline Solo Twin Bag

The Solution contained in the Freeline Solo Products can be Dianeal PD-2, PD-4 or 1 mmol/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.

Pharmacology

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.

Indications

Dianeal PD-2, PD-4 and 1 mmol/L Calcium Peritoneal Dialysis Solution is indicated for use in chronic renal failure patients being maintained on Continuous Ambulatory Peritoneal Dialysis (CAPD).

Contraindications

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

Dianeal is contraindicated in patients with:

- 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.

Precautions

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.

Patients with severe lactic acidosis should not be treated with lactate-based peritoneal dialysis solutions (see **Contraindications**). It is recommended that patients with conditions known to increase the risk of lactic acidosis [eg. 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-2, PD-4 and 1 mmol/L Calcium 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 **Overdosage** for treatment of over-infusion).

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-2, PD-4 and 1 mmol/L Calcium 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 4 mEq/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 1 mmol/L Calcium Solutions which may subsequently lead to secondary hyperparathyroidism. Dialysis using 1 mmol/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 0.25 mmol/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.

Use in Pregnancy & Lactation

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

Interactions with Other Medicines

No clinical drug interaction studies have been conducted with Dianeal.

Additives may be incompatible. 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 dialysable medicines may occur during peritoneal dialysis. Replacement therapy should be provided as necessary.

Adverse 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.

Dosage and Administration

Dianeal PD-2, PD-4 and 1 mmol/L Calcium 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 **Precautions**).

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 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.

Overdosage

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.

Presentation

Dianeal PD-2 Peritoneal Dialysis Solution is available with 0.55%, 1.5%, 2.5% and 4.25% Glucose concentrations in selected fill volumes and configurations.

Single Bag - 500 mL in 1000 mL nominal size container (System III)
1000 mL in 1000 mL nominal size container (System III)
1500 mL in 2000 mL nominal size container (System III)
2000 mL in 2000 mL nominal size container (System II)
2000 mL in 2000 mL nominal size container (System III)
2500 mL in 3000 mL nominal size container (System III)
3000 mL in 3000 mL nominal size container (System III)
5000 mL in 5000 mL nominal size container (System III)
6000 mL in 5000 mL nominal size container (System III)

Twin Bag - 1500 mL in 2000 mL nominal size container
2000 mL in 2000 mL nominal size container
2500 mL in 3000 mL nominal size container
3000 mL in 3000 mL nominal size container

Dianeal PD-4 Peritoneal Dialysis Solution is available with 0.55%, 1.5%, 2.5% and 4.25% Glucose concentrations in selected fill volumes and configurations.

Single Bag - 1000 mL in 1000 mL nominal size container (System III)
1500 mL in 2000 mL nominal size container (System III)
2000 mL in 2000 mL nominal size container (System II)
2000 mL in 2000 mL nominal size container (System III)
2500 mL in 3000 mL nominal size container (System III)
3000 mL in 3000 mL nominal size container (System III)
5000 mL in 5000 mL nominal size container (System III)
6000 mL in 5000 mL nominal size container (System III)

Twin Bag - 1500 mL in 2000 mL nominal size container
2000 mL in 2000 mL nominal size container
2500 mL in 3000 mL nominal size container
3000 mL in 3000 mL nominal size container

Dianeal 1mmol/L Calcium Peritoneal Dialysis Solution is available with 0.55%, 1.5%, 2.5% and 4.25% Glucose concentrations in selected fill volumes and configurations.

Single Bag - 2000 mL in 2000 mL nominal size container (System III)
2500 mL in 3000 mL nominal size container (System III)
3000 mL in 3000 mL nominal size container (System III)
5000 mL in 5000 mL nominal size container (System III)
6000 mL in 5000 mL nominal size container (System III)

Twin Bag - 1500 mL in 2000 mL nominal size container
2000 mL in 2000 mL nominal size container
2500 mL in 3000 mL nominal size container
3000 mL in 3000 mL nominal size container

Poison Schedule of the Medicine: *Unscheduled*

Name and Address of the sponsor:

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