

Dianeal® Low Calcium (2.5 mEq/l) Peritoneal Dialysis Solution with 1.5% and 2.5% Dextrose

For Peritoneal Dialysis

For Intraperitoneal administration only

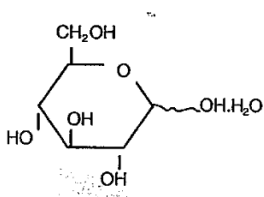
Description

Dianeal peritoneal dialysis solutions are sterile, nonpyrogenic solutions for intraperitoneal administration only. They contain no bacteriostatic or antimicrobial agents.

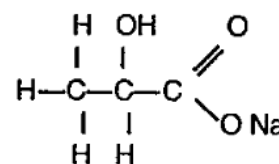
Composition, calculated osmolarity, pH, and ionic concentrations are shown in the following table.

	Composition/ 100 mL					Osmolarity (mOsmol/L)(calc)	pH	Ionic Concentration (mEq/L)					How Supplied		
	Dextrose Hydrated, USP	Sodium Chloride, USP (NaCl)	Sodium Lactate, (C ₃ H ₅ NaO ₃)	Calcium Chloride, USP (CaCl ₂ · 2H ₂ O)	Magnesium Chloride, USP (MgCl ₂ · 6H ₂ O)			Sodium	Calcium	Magnesium	Chloride	Lactate	Fill Volume (mL)	Container Size (mL)	Code
Dianeal PD4 Peritoneal Dialysis Solution with 1.5% Dextrose	1.5 g	538 mg	448 mg	18.3 mg	5.08 mg	344	5.2 (4.0 to 6.5)	132	2.5	0.5	96	40	2000	2000	THB9766
													5000	5000	THB4826
Dianeal PD4 Peritoneal Dialysis Solution with 2.5% Dextrose	2.5 g	538 mg	448 mg	18.3 mg	5.08 mg	395	5.2 (4.0 to 6.5)	132	2.5	0.5	96	40	2000	2000	THB9776
													5000	5000	THB5202
Dianeal PD4 Peritoneal Dialysis Solution with 4.25% Dextrose	4.25 g	538 mg	448 mg	18.3 mg	5.08 mg	483	5.2 (4.0 to 6.5)	132	2.5	0.5	96	40	2000	2000	THB9796
													5000	5000	THB5203

* Note: not all pack sizes are marketed.



(D-Glucopyranose monohydrate)
Dextrose Hydrated, USP



Sodium Lactate

The plastic container is fabricated from polyvinyl chloride (PL146 Plastic). Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period. The amount of water that can permeate from inside the solution container into the overpouch is insufficient to affect the solution significantly. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials.

Pharmacodynamics

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 dialysis fluid and the patient's peritoneal capillaries is made across the peritoneal membrane according to the principles of osmosis and diffusion. After a few hours of dwell time, the solution is saturated with toxic substances and must be changed. With 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 dialysing fluid. Glucose produces a solution hyperosmolar to the plasma, creating an osmotic gradient which facilitates fluid removal from the plasma to the solution, necessary to compensate for the overhydration observed in chronic renal failure patients.

Pharmacokinetics

Intraperitoneally administered glucose is absorbed into the blood and metabolised by the usual pathways.

Indication

Dianeal Low Calcium peritoneal dialysis solutions are indicated for use in chronic renal failure patients being maintained on continuous ambulatory peritoneal dialysis when nondialytic medical therapy is judged to be inadequate.

Contraindications

DIANEAL is contraindicated in patients with:

- pre-existing severe lactic acidosis.
- uncorrectable mechanical defects that prevent effective PD or increase the risk of infection
- documented loss of peritoneal function or extensive abdominal adhesions that compromise peritoneal function

Special Warnings and Precautions for Use

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 DIANEAL. Infrequently, fatal outcomes of EPS have been reported with DIANEAL.
- 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), broadspectrum antibiotics, with coverage for both gram positive and gram negative organisms, is recommended.
- 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 Contraindications) 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 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.
- Diabetics require careful monitoring of blood-glucose levels during and following dialysis with dextrose (glucose)-containing solutions. Dosage of insulin or other treatments for hyperglycemia should be adjusted.

PRECAUTIONS

- DIANEAL is intended for intraperitoneal administration only. Not for intravenous administration.
- Do not administer if the solution is discolored, 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.
- Protein, amino acids, water-soluble vitamins, and other medicines may be lost during peritoneal dialysis and may require replacement.
- 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 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 2) other conditions including aortic graft placement and severe pulmonary disease.

- Patients should be carefully monitored to avoid over- and underhydration. An accurate fluid balance record should be kept and the patient's body weight monitored.
- Excessive use of DIANEAL peritoneal dialysis solution with higher dextrose (glucose) during a peritoneal dialysis treatment may result in excessive removal of water from the patient.
- Potassium is omitted from DIANEAL 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 hematological parameters should be evaluated periodically.
- Low Calcium DIANEAL PD solution should be considered for use in patients with hypercalcemia. Patients receiving this solution should have their calcium levels monitored for the development of hypocalcemia or worsening of hypercalcemia. In these circumstances, adjustments to the dosage of the phosphate binders and/or vitamin D analogs, and/or calcimimetics should be considered by the physician.
- DIANEAL brands contain varying concentrations of dextrose (glucose), ranging between 1.5% and 4.25%. In diabetic patients blood glucose levels should be regularly monitored, and the dosage of insulin or other treatment for hyperglycemia should be adjusted.
- Overinfusion of a DIANEAL volume into the peritoneal cavity may be characterized by abdominal distension/abdominal pain and/or shortness of breath.
- Treatment of DIANEAL overinfusion is to drain DIANEAL from the peritoneal cavity.
- Improper clamping or priming sequence may result in infusion of air into the peritoneal cavity, which may result in abdominal pain and/or peritonitis.

Interactions with Other Medicinal Products and Other Forms of Interaction

No interaction studies have been conducted with DIANEAL. The blood concentration of dialyzable drugs may be reduced by peritoneal dialysis.

Pregnancy and Lactation: Category C

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.

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.

Adverse Reactions

The adverse reactions within this section represent those adverse reactions that are thought to have an association with the use of DIANEAL or in conjunction with performing the peritoneal dialysis procedure.

1. Adverse Reactions from Clinical Trials

There are no data available on adverse reactions from controlled clinical trials conducted to evaluate the safety of DIANEAL.

2. Post-Marketing Adverse Reactions

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

INFECTIONS AND INFESTATIONS: Fungal peritonitis, Peritonitis bacterial, Catheter related infection

METABOLISM AND NUTRITION DISORDERS: Hypovolemia, Hypervolemia, Fluid retention, Hypokalemia, Hyponatremia, Dehydration, Hypochloremia

VASCULAR DISORDERS: Hypotension, Hypertension

RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS: Dyspnea

GASTROINTESTINAL DISORDERS: Sclerosing encapsulating peritonitis, Peritonitis, Peritoneal cloudy effluent, Vomiting, Diarrhea, Nausea, Constipation, Abdominal pain, Abdominal distension, Abdominal discomfort

SKIN AND SUBCUTANEOUS DISORDERS: Stevens-Johnson syndrome, Urticaria, Rash, (including pruritic, erythematous and generalized), Pruritus

MUSCULOSKELETAL, CONNECTIVE TISSUE DISORDERS: Myalgia, Muscle spasms, Musculoskeletal pain

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Generalized edema, Pyrexia, Malaise, Infusion site pain, Catheter related complication

Overdose

There is a potential for overdose resulting in hypervolemia, hypovolemia, electrolyte disturbances or hyperglycemia. Excessive use of DIANEAL peritoneal dialysis solution with 4.25% dextrose (glucose) during a peritoneal dialysis treatment can result in significant removal of water from the patient.

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.
- Refer to directions for use accompanying drugs to obtain full information on additives. (Some drug additives may be incompatible with DIANEAL.)

- Addition of Potassium

Potassium is omitted from DIANEAL solutions because dialysis may be performed to correct hyperkalemia. In situations where 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. The decision to add potassium chloride should be made by the physician after careful evaluation of serum potassium.

- Addition of Insulin

Addition of insulin to DIANEAL was evaluated in 6 insulin-dependent diabetic patients undergoing CAPD for ESRD. No interference of DIANEAL with insulin absorption from the peritoneal cavity or with insulin's ability to control blood glucose was observed. Appropriate monitoring of blood glucose should be performed when initiating DIANEAL in diabetic patients and insulin dosage adjusted if needed.

- Addition of Heparin

No human drug interaction studies with heparin were conducted. In vitro studies demonstrated no evidence of incompatibility of heparin with DIANEAL.

- Addition of Antibiotics

No formal clinical drug interaction studies have been performed. In vitro studies of the following anti-infectives have demonstrated stability with the product: Amphotericin B, Ampicillin, Azlocillin, Cefapirin, Cefazolin, Cefepime, Cefotaxime, Ceftazidime, Ceftriaxone, Ciprofloxacin, Clindamycin, Cotrimoxazole, Ceferoxamine, Erythromycin, Gentamicin, Linezolid, Mezlocillin, Miconazole, Moxifloxacin, Nafcillin, Ofloxacin, Penicillin G, Piperacillin, Teicoplanin, Ticarcillin, Tobramycin, and Vancomycin. However, Aminoglycosides should not be mixed with Penicillins due to chemical incompatibility.

Dosage and Administration

Dianeal solutions are intended for intraperitoneal administration only. Not for intravenous administration.

Parental drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

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.

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 liters.

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

As the patient's body weight becomes closer to the ideal dry weight, lowering the dextrose (glucose) concentration of DIANEAL is recommended.

Peritoneal dialysis solutions may be warmed in the overpouch 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. Aseptic technique must be employed throughout the peritoneal dialysis procedure.

Do not administer if the solution is discolored, 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.

Pediatrics

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. Fill volumes of 200 to 1000 mL/m² are recommended in children less than 2 years of age.

Intermittent Peritoneal Dialysis (IPD)

For maintenance dialysis of chronic renal failure patients

The cycle of instillation, dwell and removal of dialysis fluid is repeated sequentially over a period of hours (8 to 36 hours) as many times per week as indicated by the condition of patient. For chronic renal failure patients, maintenance dialysis is often accomplished by periodic dialysis (3 to 5 times weekly) for shorter time periods (8 to 14 hours per session) (Mattocks and El-Bassiouni 1971).

Continuous Ambulatory Peritoneal Dialysis (CAPD) and Continuous Cyclic Peritoneal Dialysis (CCPD)

For maintenance dialysis of chronic renal failure patients

In CAPD, 1.5 to 3.0 liters of dialysis solution (depending upon patient size) are instilled into the peritoneal cavity of adults and the peritoneal access device is then clamped (Kim et al. 1984; Twardowski and Janicka 1981; Twardowski and Burrows 1984). For children, 30 to 50 mL/kg body weight with a maximum of 2 liters has been recommended (Potter et al. 1981; Irwin et al. 1981). The solution remains in the cavity for dwell times of 4 to 8 hours during the day and 8 to 12 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 to 5 times per day, 6 to 7 days per week. Solution exchange volumes and frequency of exchanges should be individualized for adequate biochemical and fluid volume control (Moncrief et al. 1982; Twardowski et al. 1983). The majority of exchanges will utilize 1.5% or 2.5% dextrose containing peritoneal dialysis solutions, with 3.5% or 4.25% dextrose 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).

In CCPD, the patient receives 3 or 4 dialysis exchanges during the night which range from 2½ to 3 hours dwell duration. Typically 1.5 to 2.0 liters of dialysis solution (depending upon patient size) are delivered each cycle by an automatic peritoneal dialysis cyclor machine. After the last outflow during the night, an additional exchange is infused by the cyclor machine into the peritoneum. The equipment is then disconnected from the patient, and the dialysate remains in the peritoneum for 14 to 15 hours during the day until the next nocturnal cycle (Diaz-Buxo et al. 1981). Combinations of 1.5% or 2.5% dextrose containing peritoneal dialysis solutions are usually used for the nighttime exchanges, while 3.5% or 4.25% dextrose is used when extra fluid removal is required such as during the daytime exchange. Patient weight is used as the indicator of the need for fluid removal (Popovich et al. 1978) so therapy should be individualized according to the patient's need for ultrafiltration.

It is recommended that adult patients being placed on chronic peritoneal dialysis or, in the case of pediatric patients, the selected caretaker, (as well as the patient, when suitable), should be appropriately trained in a program which is under the supervision of a physician. Training materials are available from Baxter Healthcare Corporation, Deerfield, IL 60015, USA to facilitate this training.

Directions for Use

AMBUFLEX

Use aseptic technique.

For complete system preparation, see directions accompanying ancillary equipment.

Warming the DIANEAL Low Calcium peritoneal dialysis solution, if desired, should be done in the overpouch using dry heat only. For patient comfort, the solution should be at body temperature (37T/98.6T). The solution container should be comfortably warm to the touch. Exceeding 45°C (113°F) solution temperature may be detrimental to the solution: do not overheat. If the warming method itself exceeds 45°C (113°F), frequently check the solution container and remove it from the heat source when the container becomes warm to the touch.

To Open

Tear overpouch down side at slit and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. If supplemental medication is desired, follow directions below before preparing for administration. Check for minute leaks by squeezing container firmly.

To Add Medication

Additives may be incompatible (See section Incompatibilities).

If the resealable rubber plug on the medication port is missing or partially removed. do not use product if medication is to be added.

1. Prepare medication site.
2. Using a syringe with a 1 inch long 19 to 25 gauge needle, puncture resealable medication port and inject.
3. Position container with ports up and evacuate the medication port by squeezing and tapping it.
4. Mix solution and medication thoroughly.

Preparation for Administration

1. Place container on table or suspend from support (depending on technique).
2. Remove protector from outlet port of container.
3. Attach appropriate solution set to container. Refer to complete directions in hardware manual and/or directions accompanying set.

Discard unused portion.

For single use only.

TWINBAG

Use aseptic technique.

Discard any unused remaining solution.

For single use only.

Preparation for Administration

1. Tear overpouch down side at a slit and remove the solution. Check for minute leaks by squeezing container firmly.
2. Remove pull ring from the outlet port.
3. Attach Twinbag to transfer set as directed by your healthcare professional.
4. Clamp the solution tubing and open the seal of the outlet port on the fluid bag by breaking the frangible.
5. Suspend the container from eyelet support in the upper part of the bag.
6. Instill / drain the dialysis fluid in the Twinbag in the procedure described below.

Administration:

1. Drain intraperitoneal waste fluid via the waste fluid bag by opening the twist clamp on the transfer set.
2. After draining, close transfer set and remove clamp from the solution line to wash the circuit with about 100 ml of fresh dialysis fluid (for 10 seconds). Watch the solution flow into the drain bag.
3. Clamp the drain line tubing and open the transfer set to instill the fresh dialysis fluid.
4. After infusion, close transfer set and disconnect Twinbag from the transfer set.
5. Attach a fresh minicap to the tip of the transfer set to complete the procedure.

Store below 30°C.

Manufactured by : Baxter Manufacturing (Thailand) Co., Ltd.

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References

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