Baxter

DIANEAL® Peritoneal Dialysis Solution
Twinbag System For Continuous Ambulatory Peritoneal Dialysis (CAPD)
For intraperitoneal administration only

Description

DIANEAL Low Calcium Peritoneal Dialysis Solutions are sterile, nonpyrogenic solutions in Twinbag containers for intraperitoneal administration only. They contain no bacteriostatic or antimicrobial agents. Clear, colorless to light yellow solution.

Twinbag containers are designed with an integrated "Y" set and drain container for infusion and drainage of Dianeal Low Calcium when disconnection of the "Y" set from the transfer set during dwell is desired.

Composition

DIANEAL Low Calcium Peritoneal Dialysis Solution with 1.5% Dextrose (in 100 mL)

Dextrose Anhydrous, USP	1.36 g
equivalent to Dextrose Hydrous, USP	1.5 g
Sodium Chloride, USP (NaCl)	538 mg
Sodium Lactate ($C_3H_5NaO_3$)	448 mg
Calcium Chloride, USP ($CaCl_2.2H_2O$)	18.3 mg
Magnesium Chloride, USP ($MgCl_2.6H_2O$)	5.08 mg

DIANEAL Low Calcium Peritoneal Dialysis Solution with 2.5% Dextrose (in 100 mL)

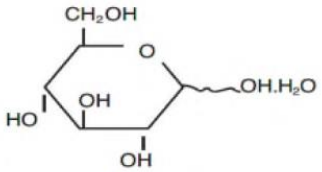
Dextrose Anhydrous, USP	2.27 g
equivalent to Dextrose Hydrous, USP	2.5 g
Sodium Chloride, USP (NaCl)	538 mg
Sodium Lactate ($C_3H_5NaO_3$)	448 mg
Calcium Chloride, USP ($CaCl_2.2H_2O$)	18.3 mg
Magnesium Chloride, USP ($MgCl_2.6H_2O$)	5.08 mg

Excipient used for DIANEAL Low Calcium Peritoneal Dialysis is Water For Injection.

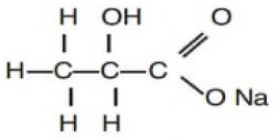
The calculated osmolarity, pH and ionic concentrations are shown in the following table.

	OSMOLARITY ((mOsmol/L) (calc))	pH	Ionic Concentration (mEq/L)					How Supplied		
			Sodium	Calcium	Magnesium	Chloride	Lactate	Fill Volume (mL)	Container Size (mL)	Code
DIANEAL Low Calcium Peritoneal Dialysis Solution with 1.5% Dextrose	344	5.2 (4.0 to 6.5	132	2.5	0.5	95	40	2000	2000	THB9766

DIANEAL Low Calcium Peritoneal Dialysis Solution with 2.5% Dextrose	395	5.2 (4.0 to 6.5	132	2.5	0.5	95	40	2000	2000	THB9776



Dextrose Hydrous, USP
(D-Glucopyranose monohydrate)



Sodium Lactate

The plastic container “Y” set is fabricated from polyvinyl chloride (PL-146® Plastic). Exposure to temperatures above 30°C/86°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.

Clinical 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 normalize plasma electrolyte concentrations resulting from osmosis and diffusion across the peritoneal membrane (between the patient's plasma and the dialysis fluid). Toxic substances and metabolites, present in high concentration in the blood, cross the peritoneal membrane into the dialyzing fluid. Dextrose in the dialyzing fluid is used to produce a solution hyperosmolar to the plasma, creating an osmotic gradient which facilitates fluid removal from the patient's plasma into the peritoneal cavity. After a period of time, (dwell time), the fluid is drained by gravity from the cavity.

The solution does not contain potassium. 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 beneficial to prevent severe hypokalemia. Addition of potassium chloride should be made after careful evaluation of serum and total body potassium and only under the direction of a physician. Clinical studies have demonstrated that the use of this solution resulted in significant increases in serum CO_2 and decreases in serum magnesium levels. The decrease in magnesium levels did not

cause clinically significant hypomagnesemia.

Indications and Usage

DIANEAL Low Calcium peritoneal dialysis solutions in Twinbag containers 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.

Precautions

DIANEAL Low Calcium is intended for intraperitoneal administration only. Not for Intravenous Injection.

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.

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.

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

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

Potassium is omitted from DIANEAL Low Calcium solutions due to the risk of hyperkalemia.

Low Calcium DIANEAL PD solution should be considered with 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 Low Calcium brands contain varying concentrations of dextrose (glucose), ranging between 1.5% and 4.25%. The level of glucose in the blood should be regularly monitored, particularly in diabetic patients. Appropriate countermeasures should be administered to patients with or at risk of hyperglycemia under the direction of a physician

Overinfusion of a DIANEAL Low Calcium volume into the peritoneal cavity may be characterized by abdominal distension/abdominal pain and/or shortness of breath.

Treatment of DIANEAL Low Calcium overinfusion is to drain DIANEAL Low Calcium from the peritoneal cavity.

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.

Laboratory tests:

Serum electrolytes, magnesium, bicarbonate levels and fluid balance should be periodically monitored.

Carcinogenesis, mutagenesis, impairment of fertility:

Long term animal studies with DIANEAL peritoneal dialysis solution have not been performed to evaluate the carcinogenic potential, mutagenic potential or effect on fertility.

Pregnancy and Lactation

Pregnancy 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.

Pediatric use:
Safety and effectiveness in children have not been established.

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.

Solution-related adverse reactions may include disequilibrium syndrome, allergic symptoms.

Post-Marketing Adverse Reactions

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: 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

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 adhesions that compromise peritoneal function.

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.

Use aseptic technique. Contamination of Luer lock connector may result in peritonitis.

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

Peritoneal dialysis should be done with caution in patients with abdominal conditions including disruption of the peritoneal membrane and diaphragm by surgery or from congenital anomalies or trauma, until healing is complete, abdominal tumors, bowel

distension, undiagnosed abdominal disease, abdominal wall infection, hernias, fecal fistula, colostomy or ileostomy, frequent episodes of diverticulitis, inflammatory or ischemic bowel disease, tense ascites, 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 placement 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.

An accurate fluid balance record must be kept and the weight of the patient carefully monitored to avoid over or under hydration with severe consequences, including congestive heart failure, volume depletion, and shock.

Excessive use of DIANEAL peritoneal dialysis solution with 4.25% dextrose (glucose) during a peritoneal dialysis treatment may result in excessive removal of water from the patient.

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. 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. For example, rapid potassium removal may create arrhythmias in cardiac patients using digitalis or similar drugs; digitalis toxicity may be masked by elevated potassium or magnesium, or by hypocalcemia. Correction of electrolytes by dialysis may precipitate signs and symptoms of digitalis excess. Conversely, toxicity may occur at suboptimal dosages of digitalis if potassium is low or calcium high. 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.

Stable patients undergoing maintenance peritoneal dialysis should have routine periodic evaluation of blood chemistries and hematologic factors, as well as other indicators of patient status.

During solution drainage, fibrin strands may be observed in the solution and may become attached to the connector frangible closure. In occasional instances, partial or complete obstruction of draining may occur. Manipulation of the connector frangible closure in the tubing may free the fibrin obstruction.

After removing overpouch, check for minute leaks by squeezing container firmly. If leaks are found, discard the solution because the sterility may be impaired.

After the pull ring has been removed from the outlet, check for broken connector frangible seal as evidenced by continuous fluid flow from port. A few drops of solution within the connector or protector cap may be present. If a continuous stream or droplets of fluid are noted, discard solution because sterility may be impaired.

Drug Interactions

Additives may be incompatible. Consult with a pharmacist if available. When introducing additives, use aseptic techniques. Mix thoroughly. Do not store. Refer to manufacturers directions accompanying drugs to obtain full information on additives.

Dosage and Administration

For maintenance dialysis of chronic renal failure patients.

DIANEAL Low Calcium solutions are intended for intraperitoneal administration only. Not for intravenous administration.

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.

In CAPD (Continuous Ambulatory Peritoneal Dialysis), 1.5 to 3.0 Liters of Dialysis Solution (depending upon patients size), are instilled into the peritoneal cavity of adults and peritoneal access device is then clamped. For children, 30 to 50 ml/kg body weight with a maximum of 2 Liters has been recommended. The solution remains in the cavity for dwell times of 4-8 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. The majority of exchange will utilize 1.5% or 2.5% dextrose containing peritoneal dialysis solutions, with 4.25% dextrose containing solutions being used when extra fluid removal is required. Patient weight is used as the indicator of the need for the fluid removal.

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 each exchange.

As the patient's body weight becomes closer to the ideal dry weight, lowering the dextrose (glucose) concentration of DIANEAL is recommended. DIANEAL 4.25% dextrose (glucose)-containing solution has the highest osmolarity of the Dianeal solutions and using it for all exchanges may cause dehydration.

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.

Discard any unused remaining solution.

For single use only.

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.

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. The decision to add potassium chloride should be made by the physician after careful evaluation of serum potassium.
    - 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, cefazolin, cefepime, cefotaxime, ceftazidime, ceftriaxone, ciprofloxacin, clindamycin, cotrimoxazole, deferoxamine, 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

Over dosage

Symptoms: Overdose by overinfusion of a DIANEAL volume into the peritoneal cavity is characterized by abdominal distension and shortness of breath. Other than that, 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.

Management of Overdose:

- The DIANEAL volume contained within the peritoneal cavity should be drained
- Hypervolemia may be managed by using hypertonic peritoneal dialysis solutions and fluid restriction. Hypovolemia may be managed by fluid replacement either orally or intravenously, depending on the degree of dehydration.
- Electrolyte disturbances may be managed according to the specific electrolyte disturbance verified by blood testing. The most probable disturbance, hypokalemia, may be managed by the oral ingestion of potassium or by the addition of potassium chloride in the peritoneal dialysis solution prescribed by the treating physician.

Directions for Use

Use aseptic technique

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 the protector 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 100ml 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 the 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.

Presentation

- Dianeal Low Calcium Peritoneal Dialysis Solution with 1.5% Dextrose (2L)
  Reg No DKI2366600142A1
- Dianeal Low Calcium Peritoneal Dialysis Solution with 2.5% Dextrose (2L)
  Reg No DKI2366600142B1

Store below 30°C.

Manufactured by:
Baxter Manufacturing (Thailand) Co., Ltd
7/398 Moo 6, Mab Yang Porn, Pluak Daeng, Rayong
Thailand 21140

Imported and Marketed by:
PT. Kalbe Farma Tbk.
Bekasi – Indonesia

On Medical Prescription Only
Harus dengan resep dokter

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