Baxter

DIANEAL Low Calcium Peritoneal Dialysis Solution with 1.5%, 2.5% and 4.25% Dextrose

ULTRABAG System For Continuous Ambulatory Peritoneal Dialysis (CAPD)
For intraperitoneal administration only

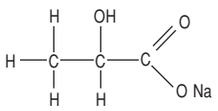
Description

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

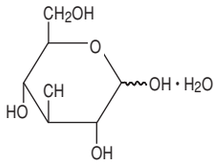
UltraBag containers are designed with an integrated "Y" set and drain container for infusion and drainage of Dianeal Low Calcium when disconnection of the "Y" set from the transfer set during dwell is desired.

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

	Composition/100 mL							Ionic Concentration (mEq/L)					How Supplied		
	Dextrose, Hydrous, USP	Sodium Chloride, USP (NaCl)	Sodium Lactate ($C_3H_5NaO_3$)	Calcium Chloride, USP ($CaCl_2 \cdot 2H_2O$)	Magnesium Chloride, USP ($MgCl_2 \cdot 6H_2O$)	**Osmolarity (mOsmol/L) (calc)**	pH	Sodium	Calcium	Magnesium	Chloride	Lactate	Fill Volume (mL)	Container Size (mL)	Code
DIANEAL Low Calcium (2.5mEq/L) 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	95	40	1500 2000 2500	2000 2000 3000	FNB9765 FNB9766 FNB9768
DIANEAL Low Calcium (2.5mEq/L) 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	95	40	1500 2000 2500	2000 2000 3000	FNB9775 FNB9776 FNB9778
DIANEAL Low Calcium (2.5mEq/L) 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	95	40	1500 2000 2500	2000 2000 3000	FNB9795 FNB9796 FNB9798



Sodium Lactate



Dextrose Hydrous, USP
(D-Glucopyranose monohydrate)

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. 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 indicated 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 ULTRABAG 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.

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 Low Calcium 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.

If the resealable rubber plug on the medication port is missing or partially removed, do not use product.

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.

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.

Precautions

DIANEAL 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 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.

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 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.

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 Low Calcium 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.

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.

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. 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, 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

Special Precaution for Storage

Store below 30°C.

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

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.

Management of Overdose:

- 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.
- Hyperglycemia in diabetic patients may be managed by adjusting the insulin dose or other treatments for hyperglycemia.

Dosage and Administration

The solution is used for dialysis therapy by instilling into the peritoneal cavity. DIANEAL 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.

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 per $1.73m^{2.}$

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.

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. 500 to 1000 USP units of heparin per liter of solution has been recommended for adults. For children, 50 USP units of heparin per 100 mL of dialysis fluid has been recommended.

Discard any unused remaining solution.

For single use only.

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 outlet port at the bottom of the container.
3. Attach administration set, according to the direction accompanying the set.
4. Suspend the container from eyelet support in the upper part of the bag.
5. Instill/drain the dialysis fluid in the ULTRABAG in the procedure described below.

Administration:

1. Remove the cap of the connection tube on the patient side.
2. Connect the connection tube connector of the ULTRABAG to the tip of connection tube on the patient side.
3. Drain intraperitoneal waste fluid via the waste fluid bag.
4. After drainage, clamp the connection tube on the patient side, and open the seal of the outlet on the fluid bag of the dialysis solution.
5. Wash the circuit with about 100 ml of a fresh dialysis fluid (for 10 seconds) and pour into the waste fluid tube.
6. Subsequently, clamp the waste fluid tube and release the clamp of the connection tube on the patient side to instill the fresh dialysis fluid intraperitoneally.
7. After infusion, detach the connection tube on the patient side from the connection tube connector of the ULTRABAG.
8. Attach the cap to the tip of the connection tube on the patient side to complete the replacement procedure.

MARKETING AUTHORISATION HOLDER

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