Baxter

DIANEAL PD-2 Peritoneal Dialysis Solution with 1.5%, 2.5% and 4.25% Dextrose

AMBU-FLEX Container For Peritoneal Dialysis

For intraperitoneal administration only

Description

DIANEAL PD-2 peritoneal dialysis solutions in AMBU-FLEX containers with a flanged port are sterile, nonpyrogenic solutions for intraperitoneal administration only. They contain no bacteriostatic or antimicrobial agents or added buffers.

Composition, calculated osmolarity, pH, and ionic concentrations are shown in Table 1.

The osmolarities shown in Table 1 are calculated values. As an example, measured osmolarity by freezing point depression determination of DIANEAL PD-2 peritoneal dialysis solution with 1.5% dextrose is approximately 334 mOsmol/L, compared with measured values in normal human serum of 280 mOsmol/L.

The plastic container is fabricated from a specially formulated polyvinyl chloride (PL-146 Plastic). The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g., di-2-ethylhexyl phthalate (DEHP), up to 5 parts per million; however, the safety of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.

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 to attempt to normalize plasma electrolyte concentrations resulting from osmosis and diffusion across the peritoneal membrane (between the plasma of the patient and the dialysis fluid). Toxic substances and metabolites, present in high concentrations 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.

Indications and Usage

Peritoneal dialysis is indicated for patients in acute or chronic renal failure when nondialytic medical therapy is judged to be inadequate. It may also be indicated in the treatment of certain fluid and electrolyte disturbances, and for patients intoxicated with certain poisons and drugs. However, for many substances other methods of detoxification have been reported to be more effective than peritoneal dialysis.

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 PD-2 peritoneal dialysis solutions. Infrequently, fatal outcomes of EPS have been reported with DIANEAL PD-2 peritoneal dialysis solutions.

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 PD-2 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.

In acute renal failure patients, plasma electrolyte concentrations should be monitored periodically during the procedure. 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.

Because average plasma magnesium levels in chronic CAPD patients have been observed to be elevated, the magnesium concentration of this formulation has been reduced to 0.5 mEq/L. Average plasma magnesium levels have not been reported for chronic IPD and APD patients. 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.

Because average serum bicarbonate levels in some chronic CAPD patients, some chronic IPD patients, and some chronic APD patients have been observed to be somewhat lower than normal values, the bicarbonate precursor (lactate) concentration of this formulation has been raised to 40 mEq/L. Serum bicarbonate levels should be monitored.

Potassium is omitted from DIANEAL PD-2 solutions due to 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. Addition of potassium chloride should be made after careful evaluation of serum and total body potassium and only under the direction of a physician.

The use of 5 liters of dialysis solution is not indicated in a single exchange.

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

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

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

Freezing of solution may occur at temperatures below 0°C (32°F). Do not flex or manipulate container when frozen. Allow container to thaw naturally in ambient conditions and thoroughly mix contents by shaking.

Precautions

DIANEAL PD-2 peritoneal dialysis solution 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.

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.

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

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 PD-2 peritoneal dialysis solutions volume into the peritoneal cavity may be characterized by abdominal distension/abdominal pain and/or shortness of breath.

Treatment of DIANEAL PD-2 peritoneal dialysis solutions 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.

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

Interactions with Other Medicinal Products and Other Forms of Interaction

No interaction studies have been conducted with DIANEAL PD-2 peritoneal dialysis solutions. The blood concentration of dialyzable drugs may be reduced by peritoneal dialysis.

Pregnancy and Lactation

Pregnancy Category C. There are no adequate data from the use of DIANEAL PD-2 peritoneal dialysis solutions in pregnant or lactating women. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing DIANEAL PD-2 peritoneal dialysis solutions.

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 PD-2 peritoneal dialysis solutions.

➢ 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 PD-2 peritoneal dialysis solution 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 PD-2 peritoneal dialysis solutions 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 PD-2 peritoneal dialysis solutions.

➢ 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.

Adverse Reactions

The adverse reactions within this section represent those adverse reactions that are thought to have an association with the use of DIANEAL PD-2 peritoneal dialysis solutions 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

DIANEAL PD-2 solutions are 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, if seals are not intact.

The mode of therapy (Intermittent Peritoneal Dialysis [IPD], Continuous Ambulatory Peritoneal Dialysis [CAPD], or Automated Peritoneal Dialysis [APD]), 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 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. 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.

Additives may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. If, in the informed judgement of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

Aseptic technique must be employed throughout the peritoneal dialysis procedure.

The drained fluid should be inspected for the presence of fibrin or cloudiness, which may indicate the presence of peritonitis.

Discard any unused remaining solutions.

For single use only.

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 the 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).

Continuous Ambulatory Peritoneal Dialysis (CAPD) and Automated Peritoneal Dialysis (APD)

For maintenance dialysis of chronic renal failure patients.

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.

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.

How Supplied

DIANEAL PD-2 peritoneal dialysis solutions in AMBU-FLEX containers are available in nominal size containers with fill volumes and dextrose concentrations as indicated in Table 1.

All DIANEAL PD-2 peritoneal dialysis solutions have overfills which are declared on container labeling. Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (30°C/86°F): brief exposure up to 40°C (104°F) does not adversely affect the product.

Directions for Use

Use aseptic technique.

For complete system preparation, see directions accompanying ancillary equipment.

Warming the DIANEAL PD-2 solution, if desired, should be done in the overwrap using dry heat only. For patient comfort, the solution should be at body temperature (37°C/98.6°F). 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 overwrap 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.

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.

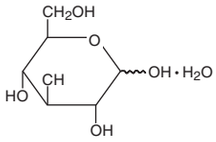
Preparation for Administration

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. Refer to complete directions in hardware manual and/or directions accompanying set.
4. Proceed as instructed by your healthcare professional.

Discard unused portion.

Table 1

	Composition/100 mL					Osmolarity (mOsmol/L) (calc)	pH	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 ($MgCl_2 \cdot 6H_2O$)			Sodium	Calcium	Magnesium	Chloride	Lactate	Fill Volume (mL)	Container Size (mL)	Code
DIANEAL PD-2 Peritoneal Dialysis Solution with 1.5% Dextrose	1.5 g	538 mg	448 mg	25.7 mg	5.08 mg	**346**	5.2 (4.0 to 6.5)	132	3.5	0.5	96	40	2000 2500 5000	2000 3000 5000	FNB5166 FNB5168 FNB5193
DIANEAL PD-2 Peritoneal Dialysis Solution with 2.5% Dextrose	2.5 g	538 mg	448 mg	25.7 mg	5.08 mg	**396**	5.2 (4.0 to 6.5)	132	3.5	0.5	96	40	2000 2500 5000	2000 3000 5000	FNB5177 FNB5178 FNB5194
DIANEAL PD-2 Peritoneal Dialysis Solution with 4.25% Dextrose	4.25 g	538 mg	448 mg	25.7 mg	5.08 mg	**485**	5.2 (4.0 to 6.5)	132	3.5	0.5	96	40	2000 2500 5000	3000 3000 5000	FNB5187 FNB5188 FNB5195



Dextrose Hydrous, USP
(D-Glucopyranose monohydrate)

MARKETING AUTHORISATION HOLDER

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