DIANEAL Peritoneal Dialysis Solution

DESCRIPTION

DIANEAL Peritoneal Dialysis Solutions are sterile, nonpyrogenic solutions in AMRO-FLEX and ULTRABAGS containers for intraperitoneal administration only. The peritoneal dialysis solutions contain no bacteriostatic or antimicrobial agents. Composition, calculated osmolarity, pH, and ionic concentrations are shown in Tables 1-4. DIANEAL is a hypertonic solution. The plastic container is fabricated from polyvinyl chloride (PL 146 Plastic). Exposure to temperatures above 65°C/149°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 overspill is insufficient to affect the solution significantly.

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 cell culture toxicity studies.

CLINICAL PHARMACOLOGY

Mechanism of Action

DIANEAL is a hypertonic peritoneal dialysis solution containing dextrose, a monosaccharide, as the primary or osmotic agent. An osmotic gradient must be created between the peritoneal membrane and the dialysis solution in order for ultrafiltration to occur. The hypertonic concentration of glucose in DIANEAL exerts an osmotic pressure across the peritoneal membrane resulting in transcapillary ultrafiltration. Like other peritoneal dialysis solutions, DIANEAL contains electrolytes to facilitate the correction of electrolyte abnormalities. DIANEAL contains a buffer, lactate, to help normalize acid-base abnormalities.

Pharmacokinetics of DIANEAL

Glucose content in DIANEAL is expressed as dextrose monohydrate and is available in three concentrations: 1.5%, 2.5% and 4.25%. Glucose is rapidly absorbed from the peritoneal cavity by diffusion and appears quickly in the circulation due to the high glucose concentration gradient between DIANEAL and blood capillary glucose level. Absorption per unit time will be the highest at the start of an exchange and decreases over time. The rate of glucose absorption will be dependent upon the transport characteristics of the patient's peritoneal membrane as determined by a peritoneal equilibration test (PET). Glucose absorption will also depend upon the concentration of glucose used for the exchange and the length of the dwell. Glucose is metabolized by normal cellular pathways (i.e. glycolysis) and provides a source of calories and may elevate blood glucose levels.

Transport of other molecules across the peritoneal membrane, such as lactate, will occur by diffusion. Metabolism of lactate occurs in the liver and results in the generation of the bicarbonate. Transport of other molecules will be dependent upon the molecular size of the solute, the concentration gradient, and the effective peritoneal surface area as determined by the PET.

INDICATIONS AND USAGE

DIANEAL peritoneal dialysis solutions are indicated for patients in acute or chronic renal failure when nondialytic medical therapy is judged to be inadequate.

CONTRAINDICATIONS

DIANEAL is contraindicated in patients with pre-existing severe lactic acidosis.

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. Intraprofusely, fatal outcomes of EPS have been reported with DIANEAL.

Patients with severe lactic acidosis should not be treated 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 levels should be monitored carefully in patients treated with cardiac glycosides. For example, rapid potassium removal may create arrhythmias in cardiac patients using digitalis or similar drugs; digitalis toxicity may be masked by hyperkalemia, hypermagnesemia, or 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 is high. Calcium requires careful monitoring of insulin requirements and other treatments for hyperglycemia during and following dialysis with dextrose-containing solutions.

PRECAUTIONS

General

Peritoneal-Dialysis Related

DIANEAL is intended for intraperitoneal administration only. Not for intravenous administration.

The following conditions may predispose to adverse reactions to peritoneal dialysis procedures: abdominal conditions, including incomplete mechanical defects that prevent effective peritoneal dialysis or increase the risk of infection, disruption of the peritoneal membrane and diaphragm by surgery, congenital anomalies or trauma prior to complete healing, abdominal tumors, abdominal wall infections, hernias, local fistula, colostomies or enterostomies, 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, such as documented loss of peritoneal function or extensive adhesions that compromise peritoneal function. Conditions that precipitate normal nutrient, impaired respiratory function, recent aortic graft placement, and potassium deficiency may also predispose to complications of peritoneal dialysis.

DIANEAL PD-2 Peritoneal Dialysis Solution With 1.5% Dextrose

DIANEAL PD-2 Peritoneal Dialysis Solution With 2.5% Dextrose

DIANEAL PD-2 Peritoneal Dialysis Solution With 4.25% Dextrose

DIANEAL Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution With 1.5% Dextrose

DIANEAL Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution With 2.5% Dextrose

DIANEAL Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution With 4.25% Dextrose
Aseptic technique must be employed throughout the peritoneal dialysis procedure to reduce the possibility of infection.

Following use, 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 used.

Overtreatment of peritoneal dialysis solution volume into the peritoneal cavity may be characterized by abdominal distention, feeling of fullness and/or shortness of breath. Treatment of overtreatment is to drain the peritoneal dialysis solution from the peritoneal cavity.

Need for Trained Physician

Treatment should be initiated and monitored under the supervision of a physician knowledgeable in the management of patients with renal failure.

A patient's volume status should be carefully monitored to avoid hypervolemia and hypotension. Significant losses of protein, amino acids, water-soluble vitamins and other medications may occur during peritoneal dialysis. The patient's nutritional status should be monitored and replacement therapy should be provided as necessary.

Information for Patients

Patients should be instructed not to use solutions if they are cloudy, discolored, contain visible particulate matter, or if they show evidence of leaking containers (see Dosage and Administration).

Aseptic technique must be employed throughout the procedure.

An improper clamping sequence may result in infusion of air into the peritoneum (see Dosage and Administration, Directions for Use).

To reduce possible discomfort during administration, patients should be instructed that solutions may be warmed to 37°C (98°F) prior to use. Only dry heat should be used. It is best to warm solutions within the overwrap using a heating pad. To avoid the formation of microbubbles, solutions should not be immersed in water for warming. Do not use a microwave oven to warm the solution (see Dosage and Administration, Directions for Use).

Laboratory Tests

Serum Electrolytes

DIANEAL does not contain potassium. Evaluate serum potassium prior to administering potassium chloride to the patient. In situations where there is a normal serum potassium level or hypokalemia, addition of potassium chloride (up to a concentration of 4 mEq/L) to the solution may be necessary to prevent severe hypokalemia. This should be made under careful evaluation of serum and total body potassium, and only under the direction of a physician.

Fluid, hematologic, blood chemistry, electrolyte concentrations, and bicarbonate should be monitored periodically. If serum magnesium levels are low, magnesium supplements may be used.

Patients receiving DIANEAL solutions should have their calcium levels monitored periodically. The use of DIANEAL during pregnancy has not been studied. Therefore, calcium supplements may be used.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies to evaluate the carcinogenic or mutagenic potential of this product, or its potential to affect fertility adversely, have not been performed.

Drug Interactions

No clinical drug interaction studies were performed. As with other dialysis solutions, coadministration of dialyzable drugs may be reduced by dialysis. Dosage adjustment of concomitant medications may be necessary. In patients using salicylates (aspirin and others), plasma levels of calcium, potassium and magnesium must be carefully monitored (see Warnings).

Use in Specific Population

Pregnancy

Pregnancy Category C. DIANEAL is a peritoneal dialysis solution of electrolytes, lactate and dextrose and is pharmacologically inactive. Animal reproduction studies have not been conducted with DIANEAL dialysis solution. While there are no adequate and well controlled studies in pregnant women, appropriate administration of DIANEAL with monitoring of fluid, electrolyte, acid-base balance, and glucose balance. Is not expected to cause fetal harm, or affect reproductive capacity. Maintenance of normal acid-base balance is important for fetal well being. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing DIANEAL.

Pediatric Use

Safety and effectiveness have been established based on published clinical data. No adequate and well-controlled studies have been conducted with DIANEAL solutions in pediatric patients.

Geriatric Use

Safety and effectiveness have been established based on published clinical data.

ADVERSE REACTIONS

The following adverse reactions have been identified during post approval use of DIANEAL. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship during drug exposure. Adverse 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, Hypokalemia, Fluid retention, Hypophosphatemia, Hypocalcemia, Hypomagnesemia, Hypoglycemia, Hypophosphatemia

ACUTE GASTROINTESTINAL DISORDERS: Hypokalemia, Hypophosphatemia, Fluid retention

SKIN AND SUBCUTANEOUS TISSUE DISORDERS: Erythema, Rash, Pruritus, Urticaria, Pyrexia, Malaise, Infusion site pain, Catheter related complication

DRUG ABUSE AND DEPENDENCE

There has been no observed potential of drug abuse or dependence with DIANEAL solution.

OVERDOSAGE

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

DIANEAL peritoneal dialysis solutions are intended for intraperitoneal administration only.

The mode of therapy, 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.
DIANEAL should be administered at a rate that is comfortable for the patient, generally over a period of 10-20 minutes for each exchange.

Patients on continuous ambulatory peritoneal dialysis (CAPD) 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 1.73m².

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 concentration of DIANEAL is recommended. DIANEAL 4.25% dextrose-containing solution has the highest osmolarity of the DIANEAL solutions and should be used only if the fluid removal requirements cannot be achieved with other DIANEAL solutions.

Solutions are cloudy, discolored, contain visible particulate matter, or show evidence of leakage should not be used. Following use, the drained fluid should be inspected for the presence of fibrin or cloudiness which may indicate the presence of fibrin or particulate matter. For single use only. Discard unused portion.

It is recommended that patients being placed on peritoneal dialysis and/or on chronic CAPD have DIANEAL solutions at home that is available for all exchanges. DIANEAL is not sterile and should not be infused into the bloodstream. Do not use for injection.

To open, tear the overwrap down at the slit and remove the container. To open, tear the overwrap down at the slit and remove the solution container. To open, tear the overwrap down at the slit and remove the solution container. To open, tear the overwrap down at the slit and remove the solution container.

Some opacity of the plastic, due to moisture absorption during the sterilization process, may be observed. This does not affect the solution quality or safety and may often have a slight amount of moisture within the overwrap. The opacity should diminish gradually.

Inspect for Container Integrity

Inspect the patient connector to ensure the pull ring is attached. Do not use if pull ring is not attached to the connector. Inspect the DIANEAL container for signs of leakage and check for minute leaks by squeezing the container firmly. If the container has frangible(s), inspect that they are positioned correctly and are not broken. Do not use DIANEAL if the frangible(s) are broken or leaks are suspected as sterility may be impaired.

For DIANEAL in UltraBag, inspect the tubing and drain container for presence of solution. Small droplets are acceptable, but if solution flows past the frangible prior to use, do not use and discard the units.

Adding Medications

Some drug additives may be incompatible with DIANEAL. See DOSAGE AND ADMINISTRATION section for additional information. If the reusable rubber plug on the medication port is missing or partly removed, do not use the product if medication is to be added:

1. Place DIANEAL on work surface.
2. Prepare medication port site using aseptic technique.
3. Using a syringe with a 1-inch long, 25- to 19-gauge needle, puncture the medication port and inject additive.
4. Place DIANEAL on work surface. Do not re-use the solution or container.
5. If the pull ring has been removed do not reuse the solution or container. Immediately attach the solution container to patient connector (transfer set) and add additive.
6. For Ambu Flex, continue with therapy as instructed in user manual or directions accompanying tubing sets for automated peritoneal dialysis.
7. For UltraBag, follow the below steps:
   • Clamp solution line and then break frangible near solution bag. Hang solution container and place the drainage container below the level of the abdomen.
   • Open transfer set to drain the solution from abdomen. If drainage cannot be established, contact your clinician. When drainage complete, close transfer set.
   • Remove clamp from solution line and flush new solution to flow into the drainage container for 5 seconds to prime the line. Clamp drain line after flush complete.
   • Open transfer set to fill. When 80% complete, close transfer set.
   • Disconnect UltraBag from transfer set and apply MiniCap.
8. Upon completion of therapy, discard any unused portion.

HOW SUPPLIED

DIANEAL peritoneal dialysis solutions are available in nominal size flexible containers as shown in Tables 1-4. All DIANEAL peritoneal dialysis solutions have overfills which are declared on container labeling.

The presence of solution may occur at temperatures below 6°C (43°F). Allow to thaw naturally in ambient conditions and thoroughly mix contents by shaking. Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (25°C/77°F); shelf exposure up to 40°C (104°F) does not adversely affect the product.
Table 1. DIANEAL PD-2 Peritoneal Dialysis Solution (AMBU-FLEX CONTAINER)

<table>
<thead>
<tr>
<th>Composition (10 mL)</th>
<th>Ionic Concentrations (mEq/L)</th>
<th>New Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calcium</td>
<td>Sodium</td>
</tr>
<tr>
<td>AMBU-FLEX II Container</td>
<td>2.5% Dextrose</td>
<td>448 mg</td>
</tr>
<tr>
<td>AMBU-FLEX III Container</td>
<td>1.5% Dextrose</td>
<td>25.7 mg</td>
</tr>
<tr>
<td>AMBU-FLEX III Container</td>
<td>4.25% Dextrose</td>
<td>6000 mg</td>
</tr>
<tr>
<td>AMBU-FLEX III Container</td>
<td>1.5% Dextrose</td>
<td>25.7 mg</td>
</tr>
<tr>
<td>AMBU-FLEX III Container</td>
<td>4.25% Dextrose</td>
<td>6000 mg</td>
</tr>
</tbody>
</table>

- Dextrose, Hydrous, USP
- Sodium Chloride, USP
- Sodium Lactate (C₃H₅NaO₃)
- Calcium
- Magnesium
- Chloride
- Lactate
Table 2. DIANEAL Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution (AMBU-FLEX CONTAINER)

<table>
<thead>
<tr>
<th>Container Size (mL)</th>
<th>Composition/10 mL</th>
<th>pH</th>
<th>Ionic Concentration (mEq/L)</th>
<th>How Supplied</th>
<th>Code</th>
<th>NDC</th>
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</thead>
<tbody>
<tr>
<td>3000 mL</td>
<td>2.5% Dextrose PDS</td>
<td>7.3</td>
<td>Calcium</td>
<td>4.25</td>
<td>152</td>
<td>2.5</td>
</tr>
<tr>
<td>5000 mL</td>
<td>2.5% Dextrose PDS</td>
<td>7.3</td>
<td>Calcium</td>
<td>4.25</td>
<td>152</td>
<td>2.5</td>
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<td>3000 mL</td>
<td>2.5% Dextrose PDS</td>
<td>7.3</td>
<td>Calcium</td>
<td>4.25</td>
<td>152</td>
<td>2.5</td>
</tr>
<tr>
<td>5000 mL</td>
<td>2.5% Dextrose PDS</td>
<td>7.3</td>
<td>Calcium</td>
<td>4.25</td>
<td>152</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Other Language: U.S. English

Table 2. DIANEAL Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution (AMBU-FLEX CONTAINER)
Table 3. DIANEAL PD-2 Peritoneal Dialysis Solution (ULTRABAG CONTAINER)

<table>
<thead>
<tr>
<th>Composition/10 mL</th>
<th>Ionic Concentration (mEq/L)</th>
<th>New Supplied</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>pH</td>
<td>Calcium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(mEq/L)</td>
</tr>
<tr>
<td>DIANEAL PD-2</td>
<td>448</td>
<td>5.3</td>
</tr>
<tr>
<td>Peritoneal Dialysis Solution with 3.5% Dextrose</td>
<td>5.0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>152</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>3000</td>
<td>2500</td>
</tr>
</tbody>
</table>

Table 4. DIANEAL Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution (ULTRABAG CONTAINER)

<table>
<thead>
<tr>
<th>Composition/10 mL</th>
<th>Ionic Concentration (mEq/L)</th>
<th>New Supplied</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>pH</td>
<td>Calcium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(mEq/L)</td>
</tr>
<tr>
<td>DIANEAL Low Calcium (2.5 mEq/L)</td>
<td>448</td>
<td>5.3</td>
</tr>
<tr>
<td>Peritoneal Dialysis Solution with 3.5% Dextrose</td>
<td>5.0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>152</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>3000</td>
<td>2500</td>
</tr>
</tbody>
</table>

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