

1. NAME OF THE MEDICINAL PRODUCT

Vantive Dianeal PD-2 Peritoneal Dialysis Solution with 1.5% Dextrose
Vantive Dianeal PD-2 Peritoneal Dialysis Solution with 2.5% Dextrose
Vantive Dianeal PD-2 Peritoneal Dialysis Solution with 4.25% Dextrose
Vantive Dianeal Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution with 1.5% Dextrose
Vantive Dianeal Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution with 2.5% Dextrose
Vantive Dianeal Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution with 4.25% Dextrose

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

	Composition/100 mL					Osmolarity (mOsmol/L) (calc)	pH	Ionic Concentration (mEq/L)				
	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
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
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
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
DIANEAL Low Calcium (2.5 mEq/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
DIANEAL Low Calcium (2.5 mEq/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
DIANEAL Low Calcium (2.5 mEq/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

3. PHARMACEUTICAL FORM AND PRODUCT DESCRIPTION

Solution for peritoneal dialysis.
 DIANEAL peritoneal dialysis solutions are sterile, clear, colourless and nonpyrogenic.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AMBUFLEX:

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.

Dianeal Low Calcium peritoneal dialysis solutions are indicated for use in chronic renal failure patients being maintained on peritoneal dialysis.

ULTRABAG:

Dianeal PD-2 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.

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

4.2 Posology and method of administration

DIANEAL peritoneal dialysis 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 osmolality 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 osmolality 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.

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.

It is recommended that adult patients being placed on 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.

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.

4.3 Contraindications

DIANEAL is contraindicated in patients with:

- hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- 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.

4.4 Special warnings and precautions for use

• 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 tumours, abdominal wall infection, hernias, faecal 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
- 2) other conditions including recent aortic graft replacement and severe pulmonary disease.

- 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 some patients using DIANEAL as part of their PD therapy. 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 may be indicated.
- Solutions containing glucose 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 severe lactic acidosis should not be treated with lactate-based peritoneal dialysis solutions. (See section 4.3) 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 metformin and 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.
- 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.
- Significant losses of protein, amino acids and water soluble vitamins may occur during peritoneal dialysis. Replacement therapy should be provided as necessary.
- Patients receiving low calcium solution should have their calcium levels monitored for the development of hypocalcaemia or worsening of hypercalcaemia. 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.
- Overinfusion of DIANEAL solutions into the peritoneal cavity may be characterised by abdominal distension/abdominal pain and/or shortness of breath.
- Treatment of DIANEAL overinfusion is to drain the solution 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.
- Excessive use of DIANEAL peritoneal dialysis solution with a higher glucose concentration 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 hyperkalaemia.
- In situations in which there is a normal serum potassium level or hypokalaemia, the addition of potassium chloride (up to a concentration of 4 mEq/L) may be indicated to prevent severe hypokalaemia 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 haematological parameters should be monitored periodically.
- Diabetics require careful monitoring of blood-glucose levels during and following dialysis with glucose-containing solutions. The dosage of insulin or other treatment for hyperglycaemia should be adjusted.

4.5 Interaction with other medicinal products and other forms of interaction

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

Plasma levels of potassium, calcium and magnesium in patients using cardiac glycosides must be carefully monitored, as there is a risk of digitalis intoxication. Potassium supplements may be necessary.

4.6 Pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of DIANEAL in pregnant women.

Animal studies are insufficient with respect to reproductive toxicity.

DIANEAL is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breastfeeding

It is unknown whether DIANEAL metabolites are excreted in human milk.

A risk to the newborns/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from DIANEAL therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility

There are no clinical data on fertility.

4.7 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 (e.g. Malaise, Hypovolaemia).

4.8 Undesirable effects

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

Undesirable effects which occurred in patients treated with DIANEAL from post marketing are listed below.

The adverse drug reactions listed in this section are given following the recommended frequency convention: very common, common, uncommon, very rare, not known (cannot be estimated from available data).

System Organ Class	Preferred term	Frequency
Metabolism And Nutritional Disorders	Hypokalaemia Fluid retention Hypervolaemia Hypovolaemia Hyponatraemia Dehydration Hypochloreaemia	Not known
Vascular Disorders	Hypertension Hypotension	Not known
Respiratory, Thoracic, And Mediastinal Disorders	Dyspnoea	Not known

System Organ Class	Preferred term	Frequency
Gastrointestinal Disorders	Sclerosing encapsulating peritonitis Peritonitis Peritoneal cloudy effluent Vomiting Diarrhoea Nausea Constipation Abdominal pain Abdominal distension Abdominal discomfort	Not known
Skin And Subcutaneous Disorders	Stevens-Johnson syndrome Urticaria Rash (including pruritic, erythematous and generalised) Pruritus	Not known
Musculoskeletal, Connective Tissue Disorders	Myalgia Muscle spasms Musculoskeletal pain	Not known
General Disorders And Administrative Site Conditions	Generalised oedema Pyrexia Malaise Infusion site pain	Not known

Other undesirable effects of peritoneal dialysis related to the procedure: Fungal peritonitis, bacterial peritonitis, catheter related infection, catheter related complication.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose

There is potential for overdose resulting in hypervolaemia, hypovolaemia, electrolyte disturbances or (in diabetic patients) hyperglycaemia.

Management of overdose:

Hypervolaemia may be managed by using hypertonic peritoneal dialysis solutions and fluid restriction.

Hypovolaemia may be managed by fluid replacement either orally or intravenously, depending on the degree of dehydration.

Electrolyte disturbances shall be managed according to the specific electrolyte disturbance verified by blood test. The most probable disturbance, hypokalaemia, 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.

Hyperglycaemia in diabetic patients shall be managed by adjusting the insulin dose or other oral medications according to the insulin scheme prescribed by the treating physician.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 hypersmolar 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.

5.2 Pharmacokinetic properties

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

5.3 Preclinical safety data

Not appropriate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections to 100% w/v

6.2 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 hyperkalaemia. In situations where there is a normal serum potassium level or hypokalaemia, the addition of potassium chloride (up to a concentration of 4 mEq/L) may be indicated to prevent severe hypokalaemia. 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. (See section 4.5). Appropriate monitoring of blood glucose should be performed when initiating DIANEAL in diabetic patients and insulin dosage adjusted if needed (See section 4.4).

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, deferaxamine, 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.

6.3 Shelf life

The shelf life of the product as packaged for sale is 24 months.

The product, once removed from its overpouch, should be used immediately.

6.4 Special precautions for storage

Do not store above 30°C.

Do not refrigerate or freeze.

6.5 Nature and contents of container

The fluid is hermetically sealed inside a bag manufactured from medical grade plasticised PVC, designated PL-146. The bag is fitted with a port for connection to a suitable administration set, or alternatively the bag may be connected to an integral administration set and empty drainage bag. The bag is also fitted with a resealable latex injection port for the addition of medication to the solution prior to administration, if appropriate.

The bag is then sealed inside an overpouch manufactured from high density polyethylene or polypropylene.

Container Sizes: 250ml, 500ml, 750ml, 1000ml, 1500ml, 2000ml, 2500ml, 3000ml, 5000ml.

Not all sizes are marketed.

6.6 Instructions for Use and Handling, and Disposal

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 (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 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.

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. If a continuous fluid flow is noted, discard container.
3. Attach appropriate solution set to container. Refer to complete directions in hardware manual and/or directions accompanying set.
4. Proceed as instructed by your healthcare professional.

Discard unused portion.

ULTRABAG

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.

7. MANUFACTURER

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8. DATE OF TEXT REVISION

October 2024