SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DIANEAL PD-4 Peritoneal Dialysis Solution with 1.36% w/v Glucose (13.6 mg/ml Glucose)
DIANEAL PD-4 Peritoneal Dialysis Solution with 2.27% w/v Glucose (22.7 mg/ml Glucose)
DIANEAL PD-4 Peritoneal Dialysis Solution with 3.86% w/v Glucose (38.6 mg/ml Glucose)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DIANEAL PD-4 Peritoneal Dialysis Solution with 1.36% w/v Glucose (13.6 mg/ml Glucose)

	Anhydrous Glucose	Ph.Eur.	1.36% w/v
or	Glucose Monohydrate	Ph.Eur.	1.50% w/v
	Sodium Chloride	Ph.Eur.	0.538% w/v
	Sodium Lactate	Ph.Fr.	0.448% w/v
	Calcium Chloride	Ph.Eur.	0.0184% w/v
	Magnesium Chloride	Ph.Eur.	0.0051% w/v

mmol/l	
Na^+	132.00
$Ca^{2}{}_+$	1.25
Mg^2+	0.25
Cl^-	95.00
$C_3H_5O_3^-$	40.00

Osmolarity: (mOsm/l) 344
pH at 25°C 5.5

For a full list of excipients, see section 6.1

DIANEAL PD-4 Peritoneal Dialysis Solution with 2.27% w/v Glucose (22.7 mg/ml Glucose)

	Anhydrous Glucose	Ph.Eur.	2.27% w/v
or	Glucose Monohydrate	Ph.Eur.	2.50% w/v
	Sodium Chloride	Ph.Eur.	0.538% w/v
	Sodium Lactate	Ph.Fr.	0.448% w/v
	Calcium Chloride	Ph.Eur.	0.0184% w/v
	Magnesium Chloride	Ph.Eur.	0.0051% w/v

mmol/l	
Na^+	132.00
$Ca^{2}{}_+$	1.25
Mg^2+	0.25
Cl^-	95.00
$C_3H_5O_3^-$	40.00

Osmolarity: (mOsm/l) 395
pH at 25°C 5.5

For a full list of excipients, see section 6.1

DIANEAL PD-4 Peritoneal Dialysis Solution with 3.86% w/v Glucose (38.6 mg/ml Glucose)

	Anhydrous Glucose	Ph.Eur.	3.86% w/v
or	Glucose Monohydrate	Ph.Eur.	4.25% w/v
	Sodium Chloride	Ph.Eur.	0.538% w/v
	Sodium Lactate	Ph.Fr.	0.448% w/v
	Calcium Chloride	Ph.Eur.	0.0184% w/v
	Magnesium Chloride	Ph.Eur.	0.0051% w/v

mmol/l	
Na^+	132.00
$Ca^{2}{}_+$	1.25
Mg^2+	0.25
Cl^-	95.00
$C_3H_5O_3^-$	40.00

Osmolarity: (mOsm/l) 483
pH at 25°C 5.5

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for peritoneal dialysis.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

DIANEAL PD4 is indicated whenever peritoneal dialysis is employed, including:
- Acute and chronic renal failure;
- Severe water retention;
- Electrolyte disorders;
- Drug intoxication.

Route of administration
Intraperitoneal administration only.

4.2. Posology and method of administration

Administration

DIANEAL PD4 is intended for intraperitoneal administration only. Not for intravenous administration.

Peritoneal dialysis solutions may be warmed to 37°C to enhance patient comfort. However, only dry heat (for example, heating pad, warming plate) should be used.

Solutions should not be heated in water due to an increased risk of contamination.

Solutions should not be heated in a microwave oven due to the potential for damage to the container and patient injury or discomfort.

Aseptic technique should be employed throughout the peritoneal dialysis procedure.

Do not administer if the solution is discoloured, 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.

For single use only.

Posology:
The mode of therapy, frequency of treatment, exchange volume, duration of dwell and length of dialysis should be selected by the attending physician.

Adults

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 litres.

Paediatric patients (i.e.:, newborn to 18 years of age)

800 to 1400 ml/m^2 per cycle up to a maximum amount of 2000 ml, as tolerated, is recommended. Fill volumes of 500 to 1000 ml/m^2 are recommended in children less than 2 years of age.

As the patient's body weight becomes closer to the ideal dry weight, lowering the glucose concentration of DIANEAL is recommended.

DIANEAL 3.86% glucose-containing solution is a high osmotic pressure fluid and using it alone may cause dehydration. (See section 4.4).

To avoid the risk of severe dehydration, hypovolaemia and to minimise the loss of proteins, it is advisable to select the peritoneal dialysis solution with the lowest osmolarity consistent with fluid removal requirements for each exchange.

4.3. 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.

4.4. Special warnings and special 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 tumors, abdominal wall infection, hernias, fecal fistula or colostomy or iliostomy, 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 PD4 as part of their PD therapy. Infrequently, fatal outcomes of EPS have been reported with DIANEAL PD4.

- 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.

- Patients with conditions known to increase the risk of lactic acidosis [e.g., acute renal failure, inborn errors of metabolism, treatment with drugs such as metformin and nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)] should 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 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 should be considered by the physician.

- The use of 5 or 6 litres of solution in a single CAPD or APD exchange is not recommended due to potential for overinfusion.

- Overinfusion of DIANEAL PD4 solutions into the peritoneal cavity may be characterised by abdominal distension/abdominal pain and/or shortness of breath.

- Treatment of DIANEAL PD4 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 PD4 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 PD4 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 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 medicaments and other forms of interaction

No interaction studies have been conducted with DIANEAL PD4. 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. Fertility, pregnancy and lactation

There is no clinical experience with DIANEAL PD4 during pregnancy and lactation. No data are available from animal studies. The risk-benefit must be assessed.
See section 4.4.

When assessing peritoneal dialysis as a mode of therapy during advanced pregnancy, the benefits to the patient must be weighed against the possible complications.

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.

Undesirables effects which occurred in patients treated with Dianeal from clinical trials and post marketing are listed below.

The adverse drug reactions listed in this section are given following the recommended frequency convention: very common: ≥10%; common: ≥1% and <10%; uncommon: ≥0.1% and <1%; very rare: <0.01%, 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 Hypochloraemia	Not known
VASCULAR DISORDERS	Hypertension Hypotension	Not known
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS	Dyspnoea	Not known
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.

4.9. Overdose

Possible consequences of overdose include 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 according to the insulin scheme prescribed by the treating physician.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group : Hypertonic solutions, ATC Code: B05DB

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 the 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 hyperosmolar to the plasma, creating an osmotic gradient which facilitates fluid removal from the plasma to the solution, necessary to compensate for the over hydration 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

Compatibilities should be checked when additives are used.

6.3. Shelf life after removal from pouch

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

6.4. Special precautions for storage

The product should not be stored above 25°C.

6.5. Nature and content of container

Primary packaging: plastic bag {plasticized poly (vinyl chloride)} and pouch.

Container sizes: 1500 ml, 2000 ml, 2500 ml, 3000 ml and 5000 ml.

6.6. Special precautions for disposal and other handling

For details on the conditions of administration see section 4.2.

Detailed instruction on the use of the product is given to patients by means of specialised training, and in the leaflet.

Discard any unused remaining solution.

7. REGISTRATION NUMBERS

DIANEAL PD-4 Peritoneal Dialysis Solution with 1.36% w/v Glucose (13.6 mg/ml Glucose) :
067.57.28213.00
DIANEAL PD-4 Peritoneal Dialysis Solution with 2.27% w/v Glucose(22.7 mg/ml Glucose) :
067.58.28214.00.
DIANEAL PD-4 Peritoneal Dialysis Solution with 3.86% w/v Glucose (38.6 mg/ml Glucose) :
067.59.28215.00.

8. MANUFACTURER

Baxter Healthcare, S.A.,
Ireland.

9. LICENCE HOLDER

Teva Medical Marketing Ltd.,
Haorgim St. 8, Ashdod 77100