

SUMMARY OF PRODUCT CHARACTERISTICS

Dianeal PD4 Peritoneal Dialysis Solution with 1.36% Glucose

Dianeal PD4 Peritoneal Dialysis Solution with 2.27% Glucose

Dianeal PD4 Peritoneal Dialysis Solution with 3.86% Glucose

1. NAME OF THE MEDICINAL PRODUCT

Dianeal PD4 Peritoneal Dialysis Solution with 1.36% Glucose

Dianeal PD4 Peritoneal Dialysis Solution with 2.27% Glucose

Dianeal PD4 Peritoneal Dialysis Solution with 3.86% Glucose

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dianeal PD4 Peritoneal Dialysis Solution with 1.36% w/v Glucose

Glucose (as monohydrate)	Ph.Eur.	1.36% w/v
Sodium Chloride	Ph.Eur.	0.538% w/v
Sodium Lactate	Ph.Fr. + internal specification	0.448% w/v
Calcium Chloride	Ph.Eur.	0.0184% w/v
Magnesium Chloride	Ph.Eur.	0.0051% w/v

Dianeal PD4 Peritoneal Dialysis Solution with 2.27% w/v Glucose

Glucose (as monohydrate)	Ph.Eur.	2.27% w/v
Sodium Chloride	Ph.Eur.	0.538% w/v
Sodium Lactate	Ph.Fr. + internal specification	0.448% w/v
Calcium Chloride	Ph.Eur.	0.0184% w/v
Magnesium Chloride	Ph.Eur.	0.0051% w/v

Dianeal PD4 Peritoneal Dialysis Solution with 3.86% w/v Glucose

Glucose (as monohydrate)	Ph.Eur.	3.86% w/v
Sodium Chloride	Ph.Eur.	0.538% w/v
Sodium Lactate	Ph.Fr. + internal specification	0.448% w/v
Calcium Chloride	Ph.Eur.	0.0184% w/v
Magnesium Chloride	Ph.Eur.	0.0051% w/v

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for peritoneal dialysis.

Clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Dianeal PD4 is indicated whenever peritoneal dialysis is employed, including:

1. Acute and chronic renal failure;
2. Severe water retention;
3. Electrolyte disorders;
4. Drug intoxication.

Route of administration

Intraperitoneal administration only.

4.2 Posology and method of administration

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 population (i.e., newborn to 18 years of age)

800 to 1400 ml/m² per cycle up to a maximum amount of 2000 ml, as tolerated, is recommended. Fill volumes of 500 to 1000 ml/m² 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 PD4 is recommended.

Dianeal PD4 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.

Method of Administration

Precautions to be taken before handling or administering the medicinal product

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 must 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.

4.3 Contraindications

Dianeal PD4 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 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.
- 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 with 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 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 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 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

Pregnancy

There are no or limited amount of data from the use of Dianeal PD4 in pregnant women.

Animal studies are insufficient with respect to reproductive toxicity.

Dianeal PD4 is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breastfeeding

It is unknown whether Dianeal PD4 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 PD4 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 PD4 or in conjunction with performing the peritoneal dialysis procedure.

Undesirable effects which occurred in patients treated with Dianeal PD4 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: $\geq 10\%$; common: $\geq 1\%$ and $< 10\%$; uncommon: $\geq 0.1\%$ and $< 1\%$; very rare: $< 0.01\%$, not known (cannot be estimated from available data).

System Organ Class	Preferred term	Frequency
METABOLISM AND NUTRITIONAL DISORDERS	<ul style="list-style-type: none"> • Hypokalaemia • Fluid retention • Hypervolaemia • Hypovolaemia • Hyponatraemia • Dehydration • Hypochloraemia 	Not known
VASCULAR DISORDERS	<ul style="list-style-type: none"> • Hypertension • Hypotension 	Not known
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS	<ul style="list-style-type: none"> • Dyspnoea 	Not known
GASTROINTESTINAL DISORDERS	<ul style="list-style-type: none"> • Sclerosing encapsulating peritonitis • Peritonitis • Peritoneal cloudy effluent • Vomiting • Diarrhoea • Nausea • Constipation • Abdominal pain • Abdominal distension • Abdominal discomfort 	Not known
SKIN AND SUBCUTANEOUS DISORDERS	<ul style="list-style-type: none"> • Stevens-Johnson syndrome • Urticaria • Rash (including pruritic, erythematous and generalised) • Pruritus 	Not known
MUSCULOSKELETAL, CONNECTIVE TISSUE DISORDERS	<ul style="list-style-type: none"> • Myalgia • Muscle spasms • Musculoskeletal pain 	Not known
GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS	<ul style="list-style-type: none"> • 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.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:

<https://sideeffects.health.gov.il>

4.9 Overdose

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

Excessive use of Dianeal PD4 with 3.86% glucose during a peritoneal dialysis treatment can result in significant removal of water from the patient.

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 hyperosmolar 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

Compatibilities should be checked when additives are used.

Addition of Potassium

Potassium is omitted from Dianeal PD4 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.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

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

6.4 Special precautions for storage

Do not store above 25°C.

Do not refrigerate or freeze.

6.5 Nature and contents 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.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. LICENCE HOLDER AND MANUFACTURER

Licence Holder:

Baxter HealthCare Distribution Ltd., 34 Jerusalem St., Ra'anana 4350110.

Manufacturer:

Baxter Healthcare, S.A., Castlebar, Ireland.

8. REGISTRATION NUMBERS

Dianeal PD4 Peritoneal Dialysis Solution with 1.36% Glucose: 067.57.28213

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