Baxter

NUTRINEAL PD-4 Peritoneal Dialysis Solution with 1.1% Amino Acids

For intraperitoneal administration only

PATIENT LEAFLET

COMPOSITION

Each 1000mL contains

– Amino Acids	
L-Serine	0.510 g
L-Isoleucine	0.850 g
L-Leucine	1.020 g
L-Lysine (as Hydrochloride)	0.955 g
L-Methionine	0.850 g
L-Phenylalanine	0.570 g
L-Threonine	0.646 g
L-Tryptophan	0.270 g
L-Valine	1.393 g
L-Alanine	0.951 g
L-Arginine	1.071 g
Glycine	0.510 g
L-Histidine	0.714 g
L-Proline	0.595 g
L-Tyrosine	0.300 g
– Sodium Chloride	5.380 g
– Calcium Chloride Dihydrate	0.184 g
– Magnesium Chloride Hexahydrate	0.051 g
– Sodium Lactate	4.48 g
– Hydrochloric Acid	q.s. pH = 6.3
– Water for Injections	q.s.

Osmolarity:	366 mOsmol/l (Calculated excluding HCl)
Ionic formula	
Sodium	132 mmol/l
Calcium	1.25 mmol/l
Magnesium	0.25 mmol/l
Lactate	40 mmol/l
Chlorides	105 mmol/l
Amino Acids	87 mmol/l

PHARMACEUTICAL FORM

Peritoneal dialysis solution contained in bags.

CLINICAL PARTICULARS

1. **Therapeutic Indications**

Nutritional supplement for malnourished renal failure patients (albumin concentration lower than 35g/litre) being maintained on peritoneal dialysis.

2. **Dosage and Method of Administration**

Administration:

- NUTRINEAL is intended for intraperitoneal administration only. Not for intravenous administration.
- The intraperitoneal administration route requires the use of a specific peritoneal dialysis catheter and an appropriate administration set which connects the solution container to the patient's catheter.
- NUTRINEAL should be administered at a rate that is comfortable for the patient. The volume administered is determined by the prescribing physician.
- The mode of therapy, frequency of treatment, exchange volume, duration of dwell and length of dialysis should be initiated and supervised by the prescribing physician.
- Treatment should be re-evaluated after 3 months if there is no clinical or biochemical improvement in the status of the patient.
- Do not remove unit from overpouch until ready for use.
- 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 should be employed through the peritoneal dialysis procedure.
- Do not administer unless the solution is clear and free of particulate matter.
- In case of damage, the container should be discarded.
- Discard any unused remaining solution
- For single use only

Dosage :

- Dosage schedule, frequency of treatment and duration of dwell should be selected by the prescribing physician according to the patient's clinical status.
- Recommended dietary allowance of protein is approximately 1.2–1.3 g/kg for dialysed adults and 2–3 g/kg for infants. Higher amounts may be necessary in several catabolic states.
- For information, a 2-litre bag of Nutrineal with 1.1% amino acids provides 22g of amino acids which are equivalent to 0.30g/kg/day for a 70kg adult.
- Safety and effectiveness in pediatric patients has not been established.

3. **Contraindication**

NUTRINEAL is contraindicated in patients with:

- known hypersensitivity to any amino acids in the product or to any of the excipients
- Serum urea level above 38mmol/L
- uremic symptoms
- metabolic acidosis
- inborn errors of amino acid metabolism
- liver insufficiency
- severe hypokalemia
- 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. **Special Warnings and Special Precautions for Use**

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 NUTRINEAL.
- 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.
- If any signs or symptoms of a suspected hypersensitivity reaction develop, intraperitoneal administration of NUTRINEAL must be stopped immediately. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Precautions:

- 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.
- Caution is recommended in cases of uncorrected acidosis, severe hepatic failure, hyperammonaemia, hypersensitivity to one or several amino acids. Metabolic acidosis should be corrected before and during NUTRINEAL treatment.
- The safety and efficacy of this solution have not been assessed in children.
- Home patients on continuous ambulatory peritoneal dialysis and automated peritoneal dialysis should be trained in specialized centres.
- Protein, amino acids, water-soluble vitamins, and other medicines may be lost during peritoneal dialysis and may require replacement.
- In patients using cardiac glycosides, plasma level of potassium, calcium, and magnesium must be carefully monitored.
- 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, 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; and
  2) other conditions including aortic graft placement and severe pulmonary disease
- Overinfusion of a peritoneal dialysis solution into the peritoneal cavity may be characterized by abdominal distension/abdominal pain and/or shortness of breath.
- Treatment of peritoneal dialysis solution overinfusion is to drain the solution from the peritoneal cavity.
- Patients should be carefully monitored to avoid over-and underhydration. An accurate fluid balance record must be kept and the body weight of the patient must carefully be monitored.
- Potassium is omitted from NUTRINEAL solutions due to the 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 4mEq/L) may be indicated to prevent severe hypokalemia 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 hematological parameters should be evaluated periodically.
- In patients with diabetes, blood glucose levels should be monitored and the dosage

of insulin or other treatment for hyperglycemia should be adjusted.

- A portion of the amino acids in NUTRINEAL is converted to metabolic nitrogenous waste, such as urea. If dialysis is insufficient, the additional metabolic waste generated by the use of NUTRINEAL may lead to the appearance of uremic symptoms such as anorexia or vomiting. Symptoms can be managed by discontinuation of NUTRINEAL or an increased dialysis dose with a non amino acid based solution.
- In case of medicinal product admixture, compatibilities must be checked before use and the admixed solution must be used immediately. (See Interactions With Other Medicinal Products and Other Forms of Interaction).

5. Interactions With Other Medicinal Products and Other Forms of Interaction

No interaction studies have been conducted with NUTRINEAL. Blood concentration of other dialyzable medicinal products may be reduced during dialysis.

6. Pregnancy and Lactation

There are no adequate data from the use of NUTRINEAL in pregnant or lactating women. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing NUTRINEAL.

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.

8. Adverse Reactions

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

9. Adverse Reactions from Clinical Trials

In clinical trials the following Adverse Events were observed in ≥ 5% of patients receiving NUTRINEAL. Adverse events are presented in the table if the incidence of the adverse event was ≥ 2% higher compared with the control group.

Clinical Trial Adverse Events			
System Organ Class (SOC)	**Preferred MedDRA Term**	**Frequency**	**Percentage of Patients**
INFECTIONS AND INFESTATIONS	**Catheter site infection** **Infection**	Common Common	8.9 5.1
BLOOD AND LYMPHATIC SYSTEM DISORDERS	**Anemia**	Common	6.3
METABOLISM AND NUTRITION DISORDERS	**Acidosis** **Hypervolemia** **Hypokalemia** **Hypovolemia**	Very Common Very Common Common Common	35.4 13.9 8.9 6.3
PSYCHIATRIC DISORDERS	**Depression**	Common	5.1
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	**Dyspnea**	Common	6.3
GASTROINTESTINAL DISORDERS	**Nausea/Vomiting*** **Anorexia** **Nausea** **Gastritis**	Very Common Very Common Very Common Common	19.0 15.2 15.2 5.1
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	**Asthenia**	Very Common	10.1
INVESTIGATIONS	**Blood urea increased**	Very Common	15.2

Frequency is based upon the following scale:
Very Common (≥ 1/10); Common (≥ 1/100 – <1/10), Uncommon (≥ 1/1,000 – <1/100), Rare (≥ 1/10,000 – <1/1,000), Very Rare (<1/10,000)
* The term nausea and vomiting is not available in MedDRA 11.0. The term has been retained to reflect the available source data.

10. 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: Peritonitis bacterial
IMMUNE SYSTEM DISORDERS: Hypersensitivity
METABOLISM AND NUTRITION DISORDERS: Anorexia
GASTROINTESTINAL DISORDERS: Abdominal pain, Peritonitis, Peritoneal cloudy effluent, Abdominal discomfort
SKIN AND SUBCUTANEOUS DISORDERS: Angioedema, Pruritus
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Catheter related complication, Pyrexia, Malaise
INVESTIGATIONS: Peritoneal fluid analysis abnormal

11. Overdose

There is potential for overdose resulting in hypervolemia and electrolyte disturbances.
Management of Overdose:

- Hypervolemia may be managed by using hypertonic peritoneal dialysis solutions and fluid restriction.
- 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. (See Incompatibilities)

PHARMACOLOGICAL PROPERTIES

1) Pharmacodynamic Properties

Sterile and nonpyrogenic solution which when used in peritoneal dialysis enables the removal of toxic substances produced by nitrogen metabolism and normally excreted by the kidneys, and facilitates the regulation of fluid and electrolytes as well as acid base balance. The concentration of electrolytes in the fluid is similar, except for lactate, to the electrolyte composition of normal extracellular fluid.
The osmolarity of the NUTRINEAL solution with 1.1% amino acids is 366mOsm/l.

2) Pharmacokinetic Properties

The solution is instilled in the peritoneal cavity, and then drained. The solution takes effect across the peritoneal membrane according to the principles of osmosis and diffusion : the exchange (dialysis) is made between the solution (dialysate) and the patient's plasma. Electrolytes follow the standard metabolism of each ion. Lactate is a biological precursor of bicarbonate. 70% to 80% of the amino acids infused are absorbed after 6 hours of dwell in the peritoneal cavity.

PHARMACEUTICAL PARTICULARS

1. Incompatibilities

- When additives are used, pH and compatibility with salts should be taken into account. There is no incompatibility between Nutrineal and the addition of Heparin, Insulin or Vancomycin.
- Check compatibilities before mixing additives.
- 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.

2. Shelf Life

2 years.

3. Special Precautions for Storage

Store at a temperature lower than 30ºC and protected from light.

4. Nature and Contents of Containers

Flexible poly(vinyl chloride) bags.

NAME AND ADDRESS OF MANUFACTURER

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MARKETING AUTHORIZATION HOLDER

Baxter Healthcare (Thailand) Co. Ltd
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Date of revision

PPD-25-185 Feb 2015