SUMMARY OF PRODUCT CHARACTERISTICS

Nutrineal PD4 with 1.1% Amino Acids
Solution for Peritoneal Dialysis

1. NAME OF THE MEDICINAL PRODUCT

Nutrineal PD4 with 1.1% Amino Acids
Solution for Peritoneal Dialysis

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

L-Tyrosine	300 mg/l
L-Trytophan	270 mg/l
L-Phenylalanine	570 mg/l
L-Threonine	646 mg/l
L-Serine	510 mg/l
L-Proline	595 mg/l
Glycine	510 mg/l
L-Alanine	951 mg/l
L-Valine	1393 mg/l
L-Methionine	850 mg/l
L-Isoleucine	850 mg/l
L-Leucine	1020 mg/l
L-Lysine, HCl	955 mg/l
L-Histidine	714 mg/l
L-Arginine	1071 mg/l
Calcium Chloride, $2H_20$	184 mg/l
Magnesium Chloride, $6H_20$	51 mg/l
Sodium-S- Lactate	4480 mg/l
Sodium Chloride	5380 mg/l

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Peritoneal Dialysis

A clear, colourless to pale yellow, sterile solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nutrineal is a supplement for malnourished renal failure patients (albumin concentration lower than 35 g/liter) being maintained on peritoneal dialysis.

4.2 Posology and method of administration

Administration
Nutrineal is intended for intraperitoneal administration only. Not for intravenous administration.

Peritoneal dialysis solutions may be warmed in the overpouch 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 solutions 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 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.

Adults: one peritoneal dialysis exchange per day of one 2.0 l or one 2.5 l bag is the recommended dose for a 70 kg body weight patient. In smaller patients the fill volume may need to be reduced depending on body size. In exceptional cases, a different posology may be indicated but the dose should not exceed two exchanges per day. Note that the recommended daily total intake of proteins is over or equal to 1.2 g/kg body weight for adult dialysis patients. A 2.0 l bag of Nutrineal contains 22 g of amino acids which corresponds to 0.30 g/kg body weight/24 h (approximately 25% of the daily protein requirements) for an adult dialysis patient of 70 kg body weight.

Elderly: as for adults.

Children and adolescents: The recommended posology is one peritoneal dialysis exchange per day. The risk/benefit ratio should be assessed and individual dialysis prescription is necessary which includes appropriate adaptation of fill volumes.

4.3 Contraindications

Nutrineal is contraindicated in patients with:

- known hypersensitivity to any amino acids in the product or to any of the excipients listed in section 6.1,

- serum urea level above 38 mmol/L,
- uraemic symptoms,
- metabolic acidosis,
- inborn errors of amino acid metabolism,
- liver insufficiency,
- severe hypokalaemia,
- 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

- 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 should be stopped immediately. Appropriate therapeutic measures should be instituted as clinically indicated.

- Metabolic acidosis should be corrected before and during Nutrineal treatment.

- Safety and effectiveness in paediatric patients has not been established.

- Significant losses of medicinal products (including water soluble vitamins) may occur during peritoneal dialysis. Replacement therapy should be provided as necessary.

- Dietary protein intake should be 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 tumours, abdominal wall infection, hernias, faecal fistula, 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; and 2) other conditions including aortic graft placement and severe pulmonary disease.

- Overinfusion of a peritoneal dialysis solution into the peritoneal cavity may be characterised 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 should be kept and the patient’s body weight monitored.

- Potassium is omitted from Nutrineal 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 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 haematological parameters should be monitored periodically.

- In diabetic patients, blood glucose levels should be regularly monitored and the dosage of insulin or other treatment for hyperglycaemia 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 uraemic symptoms such as anorexia or vomiting. Symptoms can be managed by reduction of the number of Nutrineal exchanges, or discontinuation of Nutrineal or an increased dialysis dose with a non amino acid based solution.

- In patients with secondary hyperparathyroidism, the benefits and risks of the use of dialysis solution with a low calcium content should be carefully considered as it might worsen hyperparathyroidism.

4.5 Interaction with other medicinal products and other forms of interaction

- No interaction studies have been conducted with Nutrineal. Blood concentration of other dialysable medicinal products may be reduced during 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

There are no clinical data on exposed pregnancies and lactation, and no animal studies are available. Nutrineal should not be used during pregnancy or lactation unless clearly necessary. See section 4.

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 Nutrineal or in conjunction with performing the peritoneal dialysis procedure.

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

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)

System Organ Class (SOC)	Preferred MedDRA Term	Frequency

INFECTIONS AND INFESTATIONS	Infection	Common
IMMUNE SYSTEM DISORDERS	Hypersensitivity	Not known
BLOOD AND LYMPHATIC SYSTEM DISORDERS	Anaemia	Common
METABOLISM AND NUTRITION DISORDERS	Acidosis Hypervolaemia Hypokalaemia Hypovolaemia Anorexia	Very Common Very Common Common Common Very common
PSYCHIATRIC DISORDERS	Depression	Common
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Dyspnoea	Common
GASTROINTESTINAL DISORDERS	Vomiting* Nausea Gastritis Abdominal pain Sclerosing encapsulating peritonitis Abdominal discomfort Peritonitis Peritoneal Cloudy effluent	Very Common Very Common Very Common Common Not known Not known Not known Not known
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Asthenia Pyrexia Malaise	Very Common Not known Not known
INVESTIGATIONS	Blood urea increased Peritoneal fluid analysis abnormal	Very Common Not known
SKIN AND SUBCUTANEOUS DISORDERS	Pruritis Angioedema	Not known Not known

*The term nausea and vomiting is not available in MedDRA 11.0. The term has been retained to reflect the available source data.

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 and electrolyte disturbances.

Management of Overdose:

- Hypervolaemia 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, 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 (see section 6.2).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Sterile and nonpyrogenic solution for extrarenal waste removal in continuous ambulatory peritoneal dialysis.

The concentration of electrolytes in the fluid is similar to the electrolyte composition of normal extracellular fluid (except for lactate).

Osmolarity of the Nutrineal PD4 solution with 1.1% amino acids: 365 mOsm/litre.

5.2. Pharmacokinetic properties

The solution is administered into 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.

Seventy to eighty percent of the amino acids infused are absorbed after 6 hours of dwell in the peritoneal cavity.

5.3. Preclinical safety data

Toxicity data on 1.1% amino acids solutions show predicted margins of safety in rats and dogs. There is no evidence of adverse effects in studies of foetal toxicity or fertility, mutagenic potential, carcinogenic potential, irritancy or sensitization potential, or risk of addiction or dependency.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Concentrated hydrochloric acid (for pH adjustment)
Water for Injections

6.2 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 or Insulin.

Currently, no information is available on the stability of Nutrineal with aminoglycosides.

Check compatibilities before mixing additives.

Check clarity and colour before use.

6.3. Shelf life

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

6.4. Special precautions for storage

Store below 30°C. Keep in the original container.

6.4. Nature and contents of container

Flexible poly(vinyl chloride) bags.
Container size: 2000 ml and 2500 ml.
Not all package sizes may be marketed.

6.5 Instructions for use, handling and disposal

Follow directions of attending physician and information gained from training program.

7 LICENCE HOLDER AND MANUFACTURER

Licence Holder
Teva Medical Marketing Ltd. Haorgim St. 8, Ashdod

Manufacturer
Baxter Healthcare, S.A. Castlebar, Ireland

8 REGISTRATION NUMBER

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