Baxter

EXTRANEAL Peritoneal Dialysis Solution with 7.5% Icodextrin

License No. 023687

BAR CODE LOCATION (FOR POSITION ONLY)
REFER TO PARA. 5.2 FOR ACTUAL LOCATION

PPD25369

Prescription drug only
For intraperitoneal administration only

Product name

EXTRANEAL Peritoneal Dialysis Solution with 7.5% Icodextrin

Composition

EXTRANEAL is a sterile solution for intraperitoneal administration.

Each 100 ml of EXTRANEAL contains:		Electrolyte solution content per 1000 ml:	
Icodextrin	7.5 g	Sodium	132 mmol
Sodium Chloride	538 mg	Calcium	1.75 mmol
Sodium Lactate	448 mg	Magnesium	0.25 mmol
Calcium Chloride	25.7 mg	Chloride	96 mmol
Magnesium Chloride	5.08 mg	Lactate	40 mmol

Theoretical osmolarity 284 (milliosmoles per litre).

Excipient

EXTRANEAL also contains: Water for injections.

Pharmaceutical form and Pharmacological Properties

EXTRANEAL is a sterile peritoneal dialysis fluid containing Icodextrin as the active ingredient at a concentration of 7.5%, in an electrolyte solution.
It should not be used for intravenous administration.

EXTRANEAL is presented in flexible PVC containers and is available in the following bag sizes:

Code	Fill Volume (mL)	Container Size (mL)	Product Configuration	Pack Size
FNB4974	2000	2000	AMBU-FLEX	6
FNB4982	1500	2000	ULTRABAG	8
FNB4984	2000	2000	ULTRABAG	6

Properties

Icodextrin is a starch-derived glucose polymer which acts as an osmotic agent when administered intraperitoneally for continuous ambulatory peritoneal dialysis (CAPD). EXTRANEAL produces sustained ultrafiltration over a period up to 12 hours in CAPD, with a reduction in caloric load compared to 4.25% Dextrose solutions, but with similar volume of ultra filtrate.

Therapeutic Indications

EXTRANEAL is recommended for the treatment of chronic renal failure.

Contraindications

EXTRANEAL is contraindicated in patients with

- a known allergy to starch-based polymers (e.g. corn starch) and/or icodextrin
- maltose or isomaltose intolerance
- glycogen storage disease
- 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

Precautions for Use

- EXTRANEAL is intended for intraperitoneal administration only. Not for intravenous administration.
- To change the dialysis bag, it is of vital importance that all the steps shown during training are carefully followed and to ensure that all the connecting parts remain completely clean to reduce the possibility of infection.
- 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.
- Safety and effectiveness in pediatric patients have not been established.
- Protein, amino acids, water-soluble vitamins, and other medicines may be lost during peritoneal dialysis and may require replacement.
- 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.
- An accurate fluid balance record should be kept and the patient's body weight monitored. Patients should be carefully monitored to avoid over- and underhydration.
- Overinfusion of an EXTRANEAL volume into the peritoneal cavity may be characterized by abdominal distension, feeling of fullness and/or shortness of breath.
- Treatment of EXTRANEAL overinfusion is to drain the EXTRANEAL from the peritoneal cavity.
- Potassium is omitted from EXTRANEAL 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 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.
- Fluid, hematology, blood chemistry, and electrolyte concentrations should be monitored periodically, including, magnesium and bicarbonate. If serum magnesium levels are low, oral magnesium supplements or peritoneal dialysis solutions containing higher magnesium concentrations may be used.
- In diabetic patients, blood glucose levels should be regularly monitored, and the dosage of insulin or other treatment for hyperglycemia should be adjusted following initiation of treatment with EXTRANEAL.
- Decreases in serum sodium and chloride have been observed in patients using EXTRANEAL.

Special Warnings

- Blood glucose measurement must be done with a glucose-specific method to prevent maltose interference.

  Glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO) – based methods must not be used.

  Also, the use of some glucose monitors and test strips using glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) methodology has resulted in falsely elevated glucose readings due to the presence of maltose. The manufacturer(s) of the monitor and test strips should be contacted to determine if icodextrin or maltose causes interference or falsely elevated glucose results.

  If GDH-PQQ, GDO, or GDH-FAD–based methods are used, using EXTRANEAL may cause a falsely high glucose reading, which could result in the administration of more insulin than needed. Administration of more insulin than needed has caused hypoglycemia, which has resulted in loss of consciousness, coma, neurological damage, and death.

  Additionally, falsely elevated blood glucose measurements due to maltose interference may mask true hypoglycemia and allow it to go untreated with similar consequences.

  Falsely elevated glucose levels may be measured up to two weeks following cessation of EXTRANEAL (icodextrin) therapy when GDH-PQQ, GDO, or GDH-FAD-based blood glucose monitors and test strips are used.

  Because GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors may be used in hospital settings, it is important that the health care providers of all peritoneal dialysis patients using EXTRANEAL (icodextrin) carefully review the product information of the blood glucose testing system, including that of test strips, to determine if the system is appropriate for use with EXTRANEAL (icodextrin).

  To avoid improper insulin administration, educate all patients on EXTRANEAL therapy to alert health care providers of this interaction whenever they are admitted to the hospital.
- 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 EXTRANEAL. Infrequently, fatal outcomes of EPS have been reported with EXTRANEAL.
- 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.
- Rarely, serious hypersensitivity reactions to EXTRANEAL have been reported such as toxic epidermal necrolysis, angioedema, serum sickness, erythema multiforme and vasculitis. 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 Contraindications) 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 levels should be monitored carefully in patients treated with cardiac glycosides.

Pregnancy and Lactation

There are no adequate data from the use of EXTRANEAL in pregnant or lactating women. EXTRANEAL is not recommended during pregnancy or while breast feeding. Women of childbearing potential should be treated with EXTRANEAL only when adequate contraceptive precautions have been taken. Potential effects on male and female fertility are unknown.

Interactions with other Medicaments and other forms of Interaction

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

Drug-Laboratory Test Interferences

- Blood glucose measurement must be done with a glucose-specific method to prevent maltose interference. Glucose dehydrogenase pyrroloquinolinequinone(GDH-PQQ), glucose-dye-oxidoreductase (GDO)– based methods must not be used. Also, the use of some glucose monitors and test strips using glucose dehydrogenase flavin-adenine dinucleotide (GDH -FAD) methodology has resulted in falsely elevated glucose readings due to the presence of maltose. See Special Warnings and Precautions for use.
- An apparent decrease in serum amylase activity has been observed in patients administered EXTRANEAL.

Patients using cardiac glycosides should carefully monitor blood electrolytes level, such as calcium, potassium, magnesium.

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.

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 EXTRANEAL.
  - ➢ Addition of Potassium
    Potassium is omitted from EXTRANEAL solutions because dialysis may be performed to correct hyperkalemia. In situations where there is a normal serum potassium level or hypokalemia, the addition of potassium chloride (up to a concentration of 4 mEq/L) may be indicated to prevent severe hypokalemia. 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 EXTRANEAL was evaluated in 6 insulin-dependent diabetic patients undergoing CAPD for end stage renal disease. No interference of EXTRANEAL with insulin absorption from the peritoneal cavity or with insulin's ability to control blood glucose was observed. (See Interactions With Other Medicinal Products and Other Forms of Interaction). Appropriate monitoring of blood glucose should be performed when initiating EXTRANEAL in diabetic patients and insulin dosage adjusted if needed (See Special Warnings and Precautions for Use).
  - ➢ Addition of Heparin
    No human drug interaction studies with heparin were conducted. In vitro studies demonstrated no evidence of incompatibility of heparin with EXTRANEAL.
  - ➢ Addition of Antibiotics
    No formal clinical drug interaction studies have been performed. In vitro compatibility studies with EXTRANEAL and the following antibiotics have demonstrated no effects with regard to minimum inhibitory concentration (MIC): vancomycin, cephazolin, ampicillin/flucoxacillin, ceftazidime, gentamicin, and amphotericin. However, aminoglycosides should not be mixed with penicillins due to chemical incompatibility.

Dosage and Method of Administration

Dosage

The volume to be instilled should be given over a period of approximately 10 to 20 minutes at a rate which patients find comfortable. For adult patients of normal body size the instilled volume should not exceed 2.0 litres. If this causes abdominal tension a 1.5 litre volume should be used. The recommended dwell time is between 6 and 12 hours in CAPD and 14-16 hours in APD.

Administration:

- EXTRANEAL is intended for intraperitoneal administration only. Not for intravenous administration.
- EXTRANEAL 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 physician.
- 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 throughout the peritoneal dialysis procedure.
- 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.
- Discard any unused remaining solution.
- For single use only.

Special Populations:

- Adults:
  Use is limited to a single daily exchange for the long dwell, as part of a peritoneal dialysis regimen.
- Elderly:
  As for adults.
- Pediatrics:
  EXTRANEAL is not recommended in children.
  Safety and effectiveness in pediatric patients have not been established.

Adverse Reactions

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

Adverse Reactions from Clinical Trials

Clinical Trial Adverse Reactions†			
System Organ Class (SOC)	Preferred MedDRA Term	Frequency*	Frequency Percentage or Ratio N=493
INFECTIONS AND INFESTATIONS	Influenza	Uncommon	0.6
	Furuncle	Uncommon	0.2
	Infection	Uncommon	0.2
BLOOD AND LYMPHATIC SYSTEM DISORDERS	Anemia	Uncommon	0.4
	Leukocytosis	Uncommon	0.6
	Eosinophilia	Uncommon	0.2
ENDOCRINE DISORDERS	Parathyroid disorder	–**	–**
METABOLISM AND NUTRITION DISORDERS	Dehydration	Common	2.0
	Hypovolemia	Common	1.0
	Hypoglycemia	Uncommon	0.4
	Hyponatremia	Uncommon	0.4
	Hyperglycemia	Uncommon	0.2
	Hypervolemia	Uncommon	0.8
	Anorexia	Uncommon	0.8
	Hypochloremia	Uncommon	0.8
	Hypomagnesemia	Uncommon	0.4
	Hypoproteinemia	Uncommon	0.4
PSYCHIATRIC DISORDERS	Thinking abnormal	Uncommon	0.2
	Anxiety	Uncommon	0.2
	Nervousness	Uncommon	0.2
NERVOUS SYSTEM DISORDERS	Dizziness	Common	1.8
	Headache	Common	1.4
	Hyperkinesia	Uncommon	0.2
	Paraesthesia	Uncommon	0.6
	Ageusia	Uncommon	0.2
EAR AND LABYRINTH DISORDERS	Tinnitus	Common	3.6
CARDIAC DISORDERS	Cardiovascular disorder	Uncommon	0.2
	Tachycardia	Uncommon	0.2
VASCULAR DISORDERS	Hypotension	Common	3.2
	Hypertension	Common	2.6
	Orthostatic hypotension	Uncommon	0.2
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Pulmonary edema	Uncommon	0.2
	Dyspnea	Uncommon	0.4
	Cough	Uncommon	0.2
	Hiccups	Uncommon	0.2
	Lung disorder	Uncommon	0.4

Clinical Trial Adverse Reactions†			
System Organ Class (SOC)	Preferred MedDRA Term	Frequency*	Frequency Percentage or Ratio N=493
GASTROINTESTINAL DISORDERS	Abdominal pain	Common	1.6
	Abdominal distension	–**	-**
	Intestinal obstruction	Uncommon	0.2
	Peritonitis	Uncommon	0.6
	Bloody peritoneal effluent	Uncommon	0.2
	Diarrhea	Uncommon	0.6
	Gastric ulcer	Uncommon	0.2
	Gastritis	Uncommon	0.2
	Gastrointestinal disorder	Uncommon	0.4
	Vomiting	Uncommon	0.2
	Constipation	Uncommon	0.4
	Dyspepsia	Uncommon	0.6
	Nausea	Uncommon	0.2
	Dry Mouth	Uncommon	0.4
	Flatulence	Uncommon	0.2
SKIN AND SUBCUTANEOUS DISORDERS	Dermatitis exfoliative	Common	1.6
	Rash	Common	5.5
	Pruritus	Common	1.4
	Urticaria	Uncommon	0.2
	Dermatitis bullous	Uncommon	0.2
	Psoriasis	Uncommon	0.4
	Rash,macula-papular	Uncommon	0.2
	Skin ulcer	Uncommon	0.2
	Eczema	Uncommon	0.2
	Nail disorder	Uncommon	0.6
	Skin disorder	Uncommon	0.2
	Dry skin	Uncommon	0.2
	Skin discolouration	Uncommon	0.2
MUSCULOSKELETAL CONNECTIVE TISSUE DISORDERS	Bone pain	Uncommon	0.1
	Muscle spasms	Uncommon	0.4
	Myalgia	Uncommon	0.4
	Neck pain	Uncommon	0.4
RENAL AND URINARY DISORDERS	Renal pain	Uncommon	0.2
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Edema peripheral	Common	1.4
	Asthenia	Common	1.2
	Chest pain	Uncommon	0.4
	Catheter-related complication	Uncommon	0.2
	Face edema	Uncommon	0.2
	Edema	Uncommon	0.6
	Pain	Uncommon	0.2
INVESTIGATIONS	Urine output decreased	–**	–**
	Laboratory test abnormal	Common	2.6
	Alanine aminotransferase increased	Uncommon	0.4
	Aspartate aminotransferase increased	Uncommon	0.4
	Blood alkaline phosphatase increased	Uncommon	0.6
	Liver function test abnormal	Uncommon	0.6
	Weight decreased	Uncommon	0.2
	Weight increased	Uncommon	0.6
INJURY, POISONING, AND PROCEDURAL COMPLICATIONS	Injury	Uncommon	0.2

* Frequency has been evaluated using the following criteria: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

† This table represents an integration of safety data from the following clinical trials of 493 patients: RD-97-CA-130, RD-97-CA-131, ML/IB/001, PRO-Renal-Reg-035, ML/IB/020 (DELIA), ML/IB/011 (DIANA), ML/IB/004 (Midas-2), RD-99-CA-060, and ML/IB/014. The table also includes adverse events from clinical study BLR-PG21. Additionally, safety data from studies BLR-PG22, RD-00-CA-050 and RD-00-CA-022 were reviewed and did not require additions to the clinical trial data presented.

** Reported in 1 of 18 patients who were exposed to EXTRANEAL in clinical trial BLR-PG21. Therefore, estimation of frequency not presented due to limited patient population in clinical trial BLR-PG21.

Post-Marketing Adverse Reactions

In addition to the adverse reactions noted in clinical trials, 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: Fungal peritonitis, Peritonitis bacterial, Catheter site infection, Catheter related infection

BLOOD AND LYMPHATIC SYSTEM DISORDERS: Thrombocytopenia, Leukopenia

IMMUNE SYSTEM DISORDERS: Vasculitis, Serum sickness, Hypersensitivity

METABOLISM AND NUTRITION DISORDERS: Shock hypoglycemia, Fluid overload, Fluid imbalance

NERVOUS SYSTEM DISORDERS: Hypoglycemic coma, Burning sensation

EYE DISORDERS: Vision blurred

RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS: Bronchospasm, Stridor

GASTROINTESTINAL DISORDERS: Sclerosing encapsulating peritonitis, Aseptic peritonitis*, Peritoneal cloudy effluent, Ileus, Ascites, Inguinal hernia, Abdominal discomfort

SKIN AND SUBCUTANEOUS DISORDERS: Toxic epidermal necrolysis, Erythema multiforme, Angioedema, Urticaria generalized, Toxic skin eruption, Swelling face, Periorbital edema, Exfoliative rash, Skin exfoliation, Prurigo, Rash (including macular, papular, erythematous), Dermatitis (including allergic and contact), Drug eruption, Erythema, Onychomadesis, Skin chapped, Blister

MUSCULOSKELETAL, CONNECTIVE TISSUE DISORDERS: Arthralgia, Back pain, Musculoskeletal pain

REPRODUCTIVE SYSTEM AND BREAST DISORDERS: Penile edema, Scrotal edema

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Discomfort, Pyrexia, Chills, Malaise, Drug effect decreased, Drug ineffective, Catheter site erythema, Catheter site inflammation, Infusion related reaction (including Infusion site pain, Instillation site pain)

INJURY, POISONING AND PROCEDURAL COMPLICATIONS: Device interaction

*Lower level term

Overdose

Continuous administration of more than one bag of EXTRANEAL in 24 hours would increase plasma levels of carbohydrate metabolites and maltose. The effects of such an increase are unknown, but an increase in plasma osmolality may occur.

In the event of overdosage with EXTRANEAL continued peritoneal dialysis with glucose-based solutions should be provided.

Preclinical Safety Data

Carcinogenesis, Mutagenesis, Impairment of Fertility

Icodextrin did not demonstrate evidence of genotoxicity potential in in vitro bacterial cell reverse mutation assay (Ames test); in vitro mammalian cell chromosomal aberration assay (CHO cell assay); and in the in vivo micronucleus assay in mice. Long-term animal studies to evaluate the carcinogenic potential of EXTRANEAL or icodextrin have not been conducted. Icodextrin is derived from maltodextrin, a common food ingredient.

A fertility study in rats where males and females were treated for four and two weeks, respectively, prior to mating and until day 17 of gestation at up to 1.5 g/kg/day (1/3 the human exposure on a mg/m2 basis) revealed slightly low epididymal weights in parental males in the high dose group as compared to Control. Toxicological significance of this finding was not evident as no other reproductive organs were affected and all males were of proven fertility. The study demonstrated no effects of treatment with icodextrin on mating performance, fertility, litter response, embryo-fetal survival, or fetal growth and development.

Special Precautions for Storage

EXTRANEAL has a shelf life of 2 years. Do not use the product after expiry date shown on the carton and product label.

Store at temperature below 30°C. Do not use unless the solution is clear and the container undamaged.

Keep out of reach of children. Any unused portion of dialysis solution in a bag should be discarded.

Name and address of manufacturer

Baxter Healthcare SA, Singapore Branch
2 Woodlands Industrial Park D Street 2, Singapore 737778

Date of revision

PPD-25-369 Mar 2020

PPD-25-369
ATTACHMENT 4 OF 6
ISSUE DATE: SEE STAMP

“百特”愛多尼爾腹膜透析液

衛署藥輸字第023687號

EXTRANEAL Peritoneal Dialysis Solution with 7.5% Icodextrin

本藥限由醫師使用

僅供腹腔投予

產品名稱

EXTRANEAL Peritoneal Dialysis Solution with 7.5% Icodextrin

成份

EXTRANEAL 爲專供腹膜透析使用之無菌溶液。

每 100ml EXTRANEAL 含：

Icodextrin（澱粉類多糖）	7.5 g
Sodium Chloride（氯化鈉）	538 mg
Sodium Lactate（乳酸鈉）	448 mg
Calcium Chloride（氯化鈣）	25.7 mg
Magnesium Chloride（氯化鎂）	5.08 mg

每 1000 ml電解質溶液含：

Sodium（鈉）	132 mmol
Calcium（鈣）	1.75 mmol
Magnesium（鎂）	0.25 mmol
Chloride（氯）	96 mmol
Lactate（乳酸）	40 mmol

理論滲透壓爲 284（milliosmoles/公升）。

賦形劑

EXTRANEAL 亦含有：注射用水。

藥品包裝及藥品特性描述

EXTRANEAL 爲無菌腹膜透析液，主要含有 7.5% Icodextrin 之電解液。

EXTRANEAL 不可用於靜脈注射。

EXTRANEAL 儲存於具彈性的 PVC 材質中，有下列三種含量包裝：

產品碼	溶液含量 (mL)	包裝容量 (mL)	產品形式	包裝單位
FNB4974	2000	2000	AMBU-FLEX	6
FNB4982	1500	2000	雙連袋	8
FNB4984	2000	2000	雙連袋	6

特性

Icodextrin 爲澱粉類多醣聚合物，主要作用是在連續可活動式腹膜透析（CAPD）中產生滲透壓。EXTRANEAL 在長達 12 小時之連續可活動式腹膜透析（CAPD）中，仍可維持穩定脫水效能；相對於相似脫水效能之 4.25% 葡萄糖腹膜透析液，EXTRANEAL 可減輕病人由腹膜透析液中吸收熱量之負擔。

適應症

慢性腎功能衰竭。

禁忌

具有以下症狀病患不適合使用 EXTRANEAL：

- 對於澱粉類聚合物(例如玉米澱粉)和/或 Icodextrin 過敏
- 麥芽糖或異麥芽糖耐受不良
- 肝醣貯積症
- 曾患嚴重乳酸性酸中毒
- 無法矯正的機能性缺陷，使得 PD 不能有效進行，或使得感染的風險增加
- 記錄顯示腹膜功能缺失或因腹膜大範圍粘連致使腹膜功能受損

注意事項

- EXTRANEAL 僅用於腹腔投予，不可靜脈注射。
- 更換透析袋，在訓練中的所有步驟都要小心遵守是極為重要的，並確保所有連接部位完全保持清潔，以減少感染的可能性。
- 若出現變色、渾濁、含有微粒或有滲漏跡象，或密封不完整，不可使用該溶液。
- 檢查引流液是否存在纖維蛋白或渾濁現象，這可能是腹膜炎之前兆。
- 有關兒童患者的安全性和有效性尚未確定。
- 腹膜透析過程中可能會有蛋白質、氨基酸、水溶性維生素及其他藥物流失的情形，此時可做適當補充。
- 以下患者腹膜透析時，應謹慎操作：
  1) 腹部疾病：腹腔膜和橫膈膜因手術、先天性異常或創傷破損者，完全癒合前、腹部腫瘤、腹壁感染、疝氣、糞瘺、結腸造口或回腸造口、常發性憩室炎、腸道發炎或腸道缺血性疾病、多囊腎或其他能夠損害腹壁或腹部表面或腹內腔的疾病；和
  2) 其他疾病：包括主動脈移植、重度肺病。
- 應確實記錄體內液體平衡狀況，並隨時注意體重變化情形以免水份過多或過少。
- 過量的 EXTRANEAL 進入腹腔可引起腹脹、飽腹感和 / 或呼吸短促之症狀。
- 治療 EXTRANEAL 過量的措施爲將 EXTRANEAL 從腹膜腔引流出。
- EXTRANEAL 溶液不添加鉀是由於存在發生高血鉀症之危險性。
- 在正常的血鉀濃度或低血鉀的情況下，可能有必要添加氯化鉀（濃度最高爲 4mEq/L），以防止重度低血鉀。但應對血清鉀和總體鉀進行仔細評估後，謹遵醫師指導進行。
- 定期接受體液、血球分類、血液生化值及電解質的檢查，包括鎂、重碳酸鹽。若血清鎂濃度低，可口服鎂補充劑或者使用含有較高鎂濃度的腹膜透析液。
- EXTRANEAL 治療之初，糖尿病病人需定期監測血糖濃度，並調整胰島素劑量或其他治療高血糖症的藥物劑量。
- 在使用 EXTRANEAL 的患者中，曾觀察到血清鈉和氯的濃度下降。

特別警語：

- 必須採用葡萄糖專一性的檢測方法進行血糖檢測，以避免麥芽糖干擾。

  不可使用葡萄糖去氫酶吡咯喹啉醌（GDH-PQQ）或葡萄糖染色劑氧化還原酶（GDO）方法。

  同時應考量到，那些使用基於葡萄糖脫氫酶黃素腺嘌呤二核苷酸（GDH-FAD）方法的血糖檢測儀和測試試紙，會因麥芽糖而誤將血糖讀數判讀為高血糖，建議聯繫檢測儀和測試試紙製造商，以確定 Icodextrin 或麥芽糖是否會導致干擾或使血糖結果有誤。

  若使用 GDH-PQQ、GDO 或 GDH-FAD 方法，則 EXTRANEAL 可能導致錯誤的高血糖讀數，從而導致過量的胰島素給藥。胰島素給藥過量會導致低血糖，進而導致喪失意識、昏迷、神經損傷和死亡。

  此外，因麥芽糖干擾而造成錯誤的高血糖檢測結果可能掩蓋低血糖的實際病況，致使治療延誤從而導致類似上述之後果。

  在停用 EXTRANEAL（Icodextrin）治療的兩周內，使用基於 GDH-PQQ、GDO 或者 GDH-FAD 方法的血糖儀和測試試紙進行檢測，血糖濃度仍然可能出現假性升高。

  因為醫院會使用基於 GDH-PQQ、GDO 和 GDH-FAD 技術的血糖檢測儀，因此對於使用 EXTRANEAL（Icodextrin）進行腹膜透析的患者來說，重要的一點是醫療人員應仔細閱讀血糖檢測系統（包括測試試紙）的產品資料，從而確定該系統是否適合與 EXTRANEAL（Icodextrin）一起使用。

  為避免胰島素使用不當，應教導所有使用 EXTRANEAL 的患者，每當住院時，提醒醫療人員此類交互作用。
- 包囊性腹膜硬化症（EPS）被確認是一種罕見的腹膜透析治療併發症。已有報告稱，在使用腹膜透析液（包括 EXTRANEAL）的患者中出現過該病案。使用 EXTRANEAL 出現 EPS 的死亡案例亦曾有報告，但非常稀少。
- 如果發生腹膜炎，在條件允許之情況下，抗生素的選擇和用量應依據病原菌之鑒定及其敏感性結果來決定。在病原菌鑒定之前，可使用廣效型抗生素。
- 在關於 EXTRANEAL 的通報中，諸如中毒性表皮壞死、血管性水腫、血清病、多形性紅斑和血管炎等嚴重過敏反應較少出現。可能發生過敏性/類過敏性反應。如果出現疑似過敏反應的表徵或症狀，應立即停止輸注，並將腹腔內的液體引流出來。務必依照臨床表現制定因應的治療對策。
- 患有嚴重乳酸性酸中毒的病患不應使用以乳酸為基礎的腹膜透析液（見禁忌症）。建議已知有乳酸性酸中毒風險的病患（例如：可能伴隨急性腎衰竭的嚴重低血壓或敗血症、先天性代謝缺陷、使用某些藥物治療，如二甲雙胍 (metformin) 和核苷 / 核苷酸逆轉錄酶抑制劑 (NRTI) 者）在使用含乳酸的腹膜透析液進行治療前和治療期間，必須監測是否發生乳酸中毒。
- 給病患開具使用該溶液的處方時，應考量到透析治療和針對其它現有疾病的治療之間是否存在潛在之交互作用。要密切關注使用強心劑治療的患者的血鉀濃度。

妊娠及哺乳期

有關懷孕或哺乳婦女使用 EXTRANEAL 之注意事項尚無足夠訊息也尚未進行動物生殖試驗。不建議在懷孕或哺乳期間使用 EXTRANEAL。具生育能力的婦女，只有當已採取適當的避孕措施時才能接受 EXTRANEAL 的治療。對於男性或女性生育能力的潛在影響未知。

與其他藥物的交互作用以及其它形式的交互作用

有關 EXTRANEAL 交互作用的研究尚未進行。但可被透析的藥物的血液濃度可能由於腹膜透析而下降。

藥物－檢驗值干擾

- 血糖測定必須採用葡萄糖專一性之血糖測定方法，以避免麥芽糖干擾。不能使用採用 GDH-PQQ、GDO 技術的測量方法。此外，使用基於 GDH-FAD 技術的葡萄糖檢測儀和測試試紙可能會由於麥芽糖而導致葡萄糖讀數假性升高。請參見警語及注意事項部分。
- 使用 EXTRANEAL 的患者，可以觀察到血清澱粉酶活性明顯下降。

使用 cardiac glycosides 的病人，應小心監測鈣、鉀、鎂等離子之血中濃度。

對駕駛和機械操縱能力的影響

末期腎臟病（ESRD）患者接受腹膜透析時，可能會有不良影響，從而影響駕駛或操縱機械的能力。

不相容性

- 若有可能，請諮詢熟悉腹膜透析的藥師。若醫師確認需添加其它藥劑，務請採用無菌技術。
- 請參考藥物相容性使用指南，以獲得有關添加其他藥劑的詳細資訊。
- 某些藥物添加劑可能與 EXTRANEAL 不相容。

➢ 加鉀
EXTRANEAL 溶液中不添加鉀是因為透析可能是用來矯正高血鉀症的。在正常的血鉀濃度或低血鉀的情況下，可能有必要添加氯化鉀（濃度最高 4mEq/L），以防止重度低血鉀。但應對血清鉀和總體鉀進行仔細評估後，再在醫師指導下進行。

➢ 添加胰島素
在 6 名接受持續可活動式腹膜透析（CAPD）的胰島素依賴型糖尿病患者身上，進行了 EXTRANEAL 添加胰島素評估。據觀察，EXTRANEAL 沒有干擾腹腔內胰島素的吸收或者胰島素控制血糖的能力。（見與其他藥物的交互作用以及其他形式的交互作用）。當糖尿病患者進行 EXTRANEAL 治療時，應進行相應的血糖監測。如有必要，應調整胰島素劑量（見警語及注意事項）。

➢ 添加肝素
肝素的人體藥物交互作用研究尚未開展。體外研究未發現 EXTRANEAL 與肝素不相容的證據。

➢ 添加抗生素
正式的臨床藥物相容性研究尚未進行。EXTRANEAL 與下列抗生素的體外相容性研究顯示，對下列抗生素最低抑菌濃度（MIC）沒有影響：vancomycin、cephazolin、ampicillin/flucoxacillin、ceftazidime、gentamicin、及 amphotericin。但是，氨基糖苷類不能與盤尼西林混用，因爲兩者屬化學性不相容。

用量及用法

用量:

透析液在 10 至 20 分鐘的時間內，藉由病人覺得舒適的速度，注入腹腔。中等體型的成年病人，注入量不可超過 2 公升。如果誘發腹壓遽增時，改注入 1.5 公升。連續可活動式腹膜透析（CAPD）病人之建議留置期為 6 至 12 小時。而全自動腹膜透析（APO）病人建議留置期為 14-16 小時。

用法：

- EXTRANEAL 僅用於腹腔投予，不可靜脈注射。
- 應以令患者舒適的速度注入 EXTRANEAL。使用劑量由處方醫師決定。
- 治療方式、治療頻率、換液量、留置持續時間和透析時間，均應由醫師施行和監督。
- 爲減少患者的不舒服，可將腹膜透析液加熱到 37°C（98.6°F）。爲避免造成患者傷害或不適，只能採用乾熱方式（例如電熱毯、保溫板），不可在水中或在微波爐中加熱。
- 整個腹膜透析過程中，應採用無菌技術。
- 若出現變色、渾濁、含有微粒或有滲漏跡象，或密封不完整，不可使用該溶液。
- 檢查引流液是否存在纖維蛋白或渾濁現象，這可能是腹膜炎之前兆。
- 丟棄未使用完的剩餘溶液。
- 一次性使用。

特殊族群：

- 成人
  作為腹膜透析療法的一部分，本產品每日僅限使用一次，並用於長留置期。
- 老人
  同成人。
- 兒童
  不建議兒童使用 EXTRANEAL。
  有關兒童患者的安全性和有效性尚未建立。

不良反應

本節中的不良反應，是指與使用 EXTRANEAL 相關或與腹膜透析操作過程相關的不適反應。

臨床試驗中的不良反應

臨床試驗不良反應

分類 (SOC)	MedDRA 選用詞	出現頻率	頻率百分比或比例 N=493
感染與寄生蟲感染	流感	不常見	0.6
	疔	不常見	0.2
	感染	不常見	0.2
血液和淋巴系統疾病	貧血	不常見	0.4
	白血球增多	不常見	0.6
	嗜酸細胞增多	不常見	0.2
內分泌疾病	副甲狀腺疾病	_**	_**
代謝及營養障礙	脫水	常見	2.0
	低血容量	常見	1.0
	低血糖	不常見	0.4
	低鈉血症	不常見	0.4
	高血糖	不常見	0.2
	高血容量	不常見	0.8
	厭食	不常見	0.8
	低血氯	不常見	0.8
	低鎂血症	不常見	0.4
	低蛋白血症	不常見	0.4

臨床試驗不良反應

分類 (SOC)	MedDRA 選用詞	出現頻率	頻率百分比或比例 N=493
精神障礙	思維異常	不常見	0.2
	焦慮	不常見	0.2
	神經緊張	不常見	0.2
神經系統疾病	頭暈	常見	1.8
	頭痛	常見	1.4
	運動機能亢進	不常見	0.2
	感覺異常	不常見	0.6
	味覺缺失	不常見	0.2
耳朵和內耳迷路部分疾病	耳鳴	常見	3.6
心臟疾病	心血管疾病	不常見	0.2
	心搏過速	不常見	0.2
血管疾病	低血壓	常見	3.2
	高血壓	常見	2.6
	體位性低血壓	不常見	0.2
呼吸，胸及縱隔部位疾病	肺水腫	不常見	0.2
	呼吸困難	不常見	0.4
	咳嗽	不常見	0.2
	打嗝	不常見	0.2
	肺病	不常見	0.4
胃腸性疾病	腹痛	常見	1.6
	腹脹	_**	_**
	腸梗塞	不常見	0.2
	腹膜炎	不常見	0.6
	含血腹膜引流液	不常見	0.2
	腹瀉	不常見	0.6
	胃潰瘍	不常見	0.2
	胃炎	不常見	0.2
	胃腸道疾病	不常見	0.4
	嘔吐	不常見	0.2
	便秘	不常見	0.4
	消化不良	不常見	0.6
	噁心	不常見	0.2
	口乾	不常見	0.4
	脹氣	不常見	0.2
皮膚和皮下性疾病	剝落性皮膚炎	常見	1.6
	皮疹	常見	5.5
	瘙癢症	常見	1.4
	蕁麻疹	不常見	0.2
	大皰性皮膚炎	不常見	0.2
	乾癬	不常見	0.4
	皮疹、斑疹、丘疹	不常見	0.2
	瘡	不常見	0.2
	濕疹	不常見	0.2
	指甲疾病	不常見	0.6
	皮膚疾病	不常見	0.2
	皮膚乾燥	不常見	0.2
	皮膚變色	不常見	0.2
骨骼肌肉結締組織性疾病	骨痛	不常見	0.1
	肌痙攣	不常見	0.4
	肌肉酸痛	不常見	0.4
	頸部疼痛	不常見	0.4
腎臟和泌尿道疾病	腎臟痛	不常見	0.2
一般性疾病和給藥部位狀況	周圍水腫	常見	1.4
	虛弱	常見	1.2
	胸痛	不常見	0.4
	導管相關併發症	不常見	0.2
	臉部浮腫	不常見	0.2
	浮腫	不常見	0.6
	疼痛	不常見	0.2
調查	尿量減少	_**	_**
	實驗室檢測異常	常見	2.6
	丙氨酸轉氨酶 (ALT) 升高	不常見	0.4
	天門冬氨酸轉氨酶 (AST) 升高	不常見	0.4
	血液鹼性磷酸酶 (ALP) 增加	不常見	0.6
	肝功能檢查異常	不常見	0.6
	體重下降	不常見	0.2
	體重增加	不常見	0.6
損傷、中毒、併發症	損傷	不常見	0.2

* 表中頻率之評估標準：很常見（≥1/10），常見（≥1/100 to <1/10），不常見（≥1/1,000 to <1/100），罕見（≥1/10,000 to <1/1,000），非常罕見（<1 / 10,000）。在每個頻率組內，不良反應均按降序排列。

† 本表是依照如下 493 例臨床安全試驗的資訊集合而成：RD-97-CA-130、RD-97-CA-131、ML/IB/001、PRO-Renal-Reg-035、ML/IB/020 (DELIA)、ML/IB/011 (DIANA)、ML/IB/004 (Midas-2)、RD-99-CA-060 和 ML/IB/014。表中還包括來自臨床研究 BLR-PG22 的不良反應事件。此外，我們還審查了來自 BLR-PG22、RD-00-CA-050 和 RD-00-CA-022 的安全性研究資訊，但無需再添加目前提供的臨床試驗數據。

** 此報告是在臨床試驗 BLR-PG21 中使用EXTRANEAL 的 18 名患者中，其中 1 人發生的。由於在臨床試驗 BLR-PG21 中患者人數有限，因此尚未提出頻率估計。

上市後報告的不良反應

除上述臨床試驗之不良反應外，上市後已得到如下不良反應報告。不良反應依照系統器官分類、疾病嚴重程度之順序排列如下。

感染和寄生蟲感染：真菌性腹膜炎、細菌性腹膜炎、導管部位感染、導管相關性感染。

血液和淋巴系統疾病：血小板減少、白血球低下症。

免疫系統疾病：血管炎、血清病、過敏症。

代謝和營養障礙：低血糖休克、液體超負荷、液體不平衡。

神經系統疾病：低血糖昏迷、燒灼感。

眼疾：視覺模糊。

呼吸、胸、縱隔疾病：支氣管痙攣、喘鳴。

胃腸病：包囊性腹膜硬化症、無菌腹膜炎*、腹膜渾濁排出物、腸梗塞、腹水、腹股溝疝氣、腹部不適。

皮膚和皮下組織疾病：毒性表皮壞死、多形性紅斑、血管性水腫、全身性蕁麻疹、毒性皮膚疹、臉部浮腫、眶周水腫、剝落性皮疹、皮膚脫落、癢疹、皮疹（包括黃斑、丘疹、丘疹性紅斑）、皮炎（包括過敏性和接觸性皮炎）、藥疹、紅斑、脫甲病、皮膚乾裂、水皰。

肌肉骨骼、結締組織疾病：關節痛、背痛、肌肉骨骼疼痛。

生殖系統和乳腺疾病：陰莖水腫、陰囊水腫。

一般失調和因用藥位置情況所致的症狀：不適、發熱、畏寒、倦怠、藥物效果下降、藥物無效、導管部位紅斑、導管部位發炎、輸液相關反應（包括輸液部位疼痛、滴注部位疼痛）。

損傷、中毒和併發症：器械設備交互作用。

* 低發事件

過量

24 小時內，EXTRANEAL 持續用藥量超過 1 包，碳水化合物代謝產物和麥芽糖的血中濃度會增加。這種增長之影響尚未知，但可能導致血漿滲透壓升高。

若出現 EXTRANEAL 過量之情形，持續的腹膜透析應採用以葡萄糖為基礎的腹膜透析液。

臨床前安全資訊

致癌、致突變、生殖功能受損

Icodextrin 在體外細菌細胞回復突變試驗（Ames 試驗）、體外哺乳動物細胞染色體異常分析（CHO 細胞試驗）、以及老鼠體外微核試驗中沒有出現可能遺傳毒性的證據。對 EXTRANEAL 或Icodextrin 有關致癌性的長期動物研究尚未進行評估。Icodextrin 衍生自一種常見食物成分－麥芽糊精。

在對老鼠進行的一項生育能力研究中，雄鼠和雌鼠分別於交配前 4 周和 2 周開始藥物治療直到懷孕後第 17 天，接受 1.5g/kg/天（在 mg/m^2 基礎上，為 1/3 的人體使用劑量）。研究顯示，相較於控制組，高劑量給藥組中親代雄鼠附睾重量略有減輕。因為其它器官未受影響，所有雄鼠均具有交配能力，所以該研究的毒理學意義並不明顯。研究證明使用 Icodextrin 治療對交配能力、生育能力、仔畜反應、胚胎－胎兒存活率或胎兒生長發育均無影響。

儲存之注意事項

EXTRANEAL 效期 2 年。不可使用超過效期（標示於外箱及產品包裝上）之產品。儲存於低於 30°C 的環境。若非透析液清澈及包裝完整，則不可使用。

置於兒童不可及處。若袋內透析液出現任何不正常現象，應立即丟棄。

藥商名稱：百特醫療產品股份有限公司

藥商地址：台北市敦化南路二段 95 號 28 樓

製造廠名：Baxter Healthcare S.A., Singapore Branch

製造廠址：2 Woodlands Industrial Park D Street 2, Singapore 737778

最近一次修改仿單的時間

2020 年 3 月