PRESCRIBING INFORMATION

This abbreviated summary of product characteristics is intended for international use. Please note that it may differ from the licensed SPC in the country where you are practicing. Therefore, please always consult your country-specific SPC or package leaflet.

NAME OF THE MEDICINAL PRODUCT

EXTRANEAL (Icodextrin 7.5%)

Solution for peritoneal dialysis

QUALITATIVE AND QUANTITATIVE COMPOSITION

A sterile peritoneal dialysis fluid containing Icodextrin at a concentration of 7.5% w/v in an electrolyte solution.

Icodextrin	75,0	g/L
Sodium Chloride	5.4	g/L
Sodium S-Lactate	4.5	g/L
Calcium Chloride	0.257	g/L
Magnesium Chloride	0.051	g/L

The pH of the solution is 5,0 to 6,0

Composition of the solution	Concentration in mmol/l
Sodium	133mmol/L
Calcium	1.75mmol/L
Magnesium	0.25mmol/L
Chloride	96mmol/L
Lactate	40mmol/L
Theoretical osmolarity	284 (milliosmoles per litre) 301 (milliosmoles per kg)

List of excipients: Water for injections, Sodium Hydroxide or Hydrochloric acid q.s to required pH.

CLINICAL PARTICULARS

Therapeutic Indications

Extraneal is recommended as a once daily replacement for a single glucose exchange as part of an automated peritoneal dialysis (APD) regimen for the treatment of chronic renal failure, particularly for patients who have lost ultrafiltration on glucose solutions, because it can extend time on APD therapy in such patients.

Contra-indications

Extraneal should not be used in patients with: a known allergy to starch based polymers/or icodextrin, maltose or isomaltose intolerance, glycogen storage disease, pre-existing severe lactic acidocis, uncorrectable mechanical defects that prevent effective PD or increase the risk of infection or documented loss of peritoneal function or extensive adhesions that compromise peritoneal function

Special Warnings and Precautions for Use

Patients with diabetes mellitus often need additional insulin in order to maintain glycaemic control during Peritoneal Dialysis (PD). Transfer from glucose based PD solution to Extraneal may necessitate an adjustment of the usual insulin dosage. Initial results show that insulin is minimally absorbed from Extraneal in Clear Flex bags compared with PVC bags, so dosage adjustments may be also necessary and special attention is advised in this situation. Insulin can be administered intraperitoneally. 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 should 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 hypoglycaemia, 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 hypoglycaemia 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- or GDH-FAD-based blood glucose monitors may be used in hospital settings, it is important that the health care providers of peritoneal dialysis patients using Extraneal (icodextrin) carefully review the product information of the blood glucose testing system, including the information of test strips, to determine if the system is appropriate for use with Extraneal (icodextrin). To avoid improper insulin administration, educate patients to alert health care providers of this interaction, whenever they are admitted to the hospital. 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 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 Extraneal as part of their PD therapy. Infrequently, fatal outcomes have been reported with Extraneal. Patients with conditions known to increase the risk of lactic acidosis (e.g. severe hypotension, sepsis, 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. Peritoneal reactions, including abdominal pain, cloudy effluents with or without bacteria (aseptic peritonitis) have been associated with Extraneal. In case of peritoneal reactions, the patient should keep the icodextrin drained fluid bag along with its batch number, and contact the medical team for analysis of the drained fluid bag. The drained fluid should be inspected for the presence of fibrin or cloudiness, which may indicate the presence of infection or aseptic peritonitis. Patients should be asked to inform their physician if this occurs and appropriate microbiological samples should be drawn. The initiation of antibiotic treatment should be a clinical decision based on whether or

not infection is suspected. If other possible reasons for cloudy fluid have been excluded, Extraneal should be stopped and the result of this action evaluated. If Extraneal is stopped and the fluid becomes clear afterwards, Extraneal should not be reintroduced unless under close supervision. If by re-challenging with Extraneal, the cloudy fluid recurs then this patient should not be prescribed Extraneal again. Alternative peritoneal dialysis therapy should be initiated and the patient should be kept under close supervision. 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. Rarely, serious hypersensitivity reactions to Extraneal have been reported such as toxic epidermal necrolysis, angioedema, 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. Extraneal is not recommended in patients with acute renal failure. Protein, amino acids, water-soluble vitamins and other medicines may be lost during peritoneal dialysis and may require replacement. Patients should be carefully monitored to avoid overhydration or underhydration. Enhanced ultra-filtration, particularly in elderly patients, may lead to dehydration, resulting in hypotension and possibly neurological symptoms. An accurate fluid balance record should be kept and the patient's body weight monitored. Overinfusion of an Extraneal volume into the peritoneal cavity may be characterised by abdominal distension, feeling of fullness and/or shortness of breath. Treatment of Extraneal overinfusion is to drain Extraneal from the peritoneal cavity. In common with other peritoneal dialysis fluids, Icodextrin should be used with caution, after careful evaluation of its potential risks and benefits, in patients with conditions which preclude normal nutrition, with impaired respiratory function or with potassium deficiency. Fluid, haematology, 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. A decrease in the serum sodium and chloride level has been observed in some patients. Though these decreases have been regarded as clinically non-significant, it is recommended that serum electrolyte levels are monitored regularly. A decrease in serum amylase levels has also been noticed as a common finding in PD patients on long term treatment. The decrease has not been reported to be accompanied with any side effects. However, it is not known whether subnormal amylase level may mask the rise in serum amylase, commonly seen during acute pancreatitis. An increase in serum alkaline phosphatase of approximately 20 IU/L was seen during clinical trials. There were individual cases where increased alkaline phosphatase was associated with elevated SGOT- (ASAT-) levels.

Paediatric population: Extraneal is not recommended in children

Fertility, pregnancy and lactation

Pregnancy: There are no or limited amount of data from the use of Extraneal in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. In pregnant women or women of childbearing potential the benefit/risk should be assessed before using the product. Breastfeeding It is unknown whether Extraneal 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 Extraneal 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.

Undesirable Effects

Undesirable effects which occurred in patients with Extraneal from the clinical trials are:

Common undesirable effects: Dehydration, Hypovolaemia, Dizziness, Headache, Tinnitus, Hypotension, Hypertension, Abdominal Pain, Rash (including macular, papular, erythematous), Pruritus, Skin exfoliation, Oedema peripheral, Asthenia.
Uncommon undesirable effects: Flu syndrome, Furuncle, Anaemia, Leukocytosis, Eosinophilia, Hypoglycaemia, Hyponatraemia, Hyperglycaemia, Hypervolaemia, Anorexia, Hypochloraemia, Hypomagnesaemia, Hypoproteinaemia, Thinking Abnormal, Anxiety, Nervousness, Paraesthesia, Hyperkynesia, Ageusia, Cardiovascular disorder, Tachycardia, Orthostatic hypotension, Pulmonary oedema, Dyspnoea, Cough, Hiccups, Ileus, Peritonitis, Bloody peritoneal effluent, Diarrhoea, Gastric ulcer, Gastritis, Vomiting, Constipation, Dyspepsia, Nausea, Dry mouth, Flatulence, Urticaria, Dermatitis bullous, Psoriasis, Skin ulcer, Eczema, Nail disorder, Dry skin, Skin discolouration, Bone pain , Muscle spasms , Myalgia , Neck pain, Renal pain, Chest pain, Face oedema, Oedema, Pain, Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood alkaline phosphatase increased, Liver function test abnormal, Weight decreased, Weight increased
Not known undesirable effects: Thrombocytopenia, Leucopenia, Vasculitis, Hypersensitivity (Hypersensitivity-type reactions have been reported in patients using Extraneal including bronchospasm, hypotension, rash, pruritus and urticaria), Shock hypoglycaemia, Fluid imbalance, Hypoglycaemic coma, Burning sensation,Vision blurred, Bronchospasm, Ascites, Inguinal hernia, Abdominal discomfort, Toxic epidermal necrolysis, Erythema multiform, Angiodema, Urticaria generalised,Toxic skin eruption, Periorbital oedema, Dermatitis (including allergic and contact), Erythema, Blister, Arthralgia, Back pain, Musculoskeletal pain, Pyrexia, Chills, Malaise, Catheter site erythema, Catheter site inflammation, Infusion related reaction (including infusion site pain, instillation site pain), Device interaction (Icodextrin interferes with blood glucose measurement devices).

Other undesirable effects of peritoneal dialysis related to the procedure: fungal peritonitis, bacterial peritonitis, catheter site infection, catheter related infection and catheter related complication. Enhanced ultrafiltration, particularly in the elderly patients, may lead to dehydration, resulting in hypotension, dizziness and possibly neurological symptoms, Hypoglycaemic episodes in diabetic patients, Increase in serum alkaline phosphatases and electrolyte disturbances (e.g. hypokalaemia, hypocalcaemia and hypercalcaemia).
Peritoneal reactions, including abdominal pain, cloudy effluents with or without bacteria, aseptic peritonitis.
Fatigue was often reported spontaneously and in literature as an undesirable effect related to the procedure.

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. Healthcare professionals are asked to report any suspected adverse reactions via their national procedure.

For posology, incompabilities, interactions, pharmacological properties and pharmaceutical particulars, please refer to the full SPC.
Medicinal product subject to medical prescription.

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