

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Polithera Solution for peritoneal dialysis

2 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	mg/ml (75 g/L)
Sodium Chloride	5.4	mg/ml (5.4 g/L)
Sodium S-Lactate	4.5	mg/ml (4.5 g/L)
Calcium Chloride Dihydrate	0.257	mg/ml (0.257 g/L)
Magnesium Chloride Hexahydrate	0.051	mg/ml (0.051 g/L)

Theoretical osmolarity: 284 (milliosmoles per litre) Theoretical osmolality: 301 (milliosmoles per kg) Electrolyte solution content per 1000 ml (1 L)

Sodium	133	mmol/L
Calcium	1.75	mmol/L
Magnesium	0.25	mmol/L
Chloride	96	mmol/L
Lactate	40	mmol/L
pH = 5 to 6		

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for peritoneal dialysis.

Polithera Solution for peritoneal dialysis is a sterile, colourless or slightly yellowish solution.

Free from visible particles.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Polithera Solution for peritoneal dialysis is recommended as a once daily replacement for a single glucose exchange as part of a continuous ambulatory peritoneal dialysis (CAPD) or 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 CAPD therapy in such patients.

4.2 Posology and method of administration

Posology:

Polithera Solution for peritoneal dialysis is recommended for use during the longest dwell period, i.e. in CAPD usually overnight and in APD for the long daytime dwell.

The mode of therapy, frequency of treatment, exchange volume, duration of dwell and length of dialysis should be initiated and supervised by the physician.

Adults

By intraperitoneal administration limited to a single exchange in each 24 hour-period, as part of a CAPD or APD regimen.

The volume to be instilled should be given over a period of approximately 10 to 20 minutes at a rate which the patient finds comfortable. For adult patients of normal body size, the instilled volume should not exceed 2.0 L. For larger patients (more than 70-75 kg), a fill volume of 2.5 L may be used.

If the instilled volume causes discomfort due to abdominal tension, the instilled volume should be reduced. The recommended dwell time is between 6 and 12 hours in CAPD and 14-16 hours in APD. Drainage of the fluid is by gravity at a rate comfortable for the patient.

Older people

As for adults.

Paediatric population

The safety and efficacy of Polithera Solution for peritoneal dialysis in children aged less than 18 years has not been established. No data are available.

Method of administration

Precautions to be taken before handling or administering the medicinal product

- Polithera Solution for peritoneal dialysis is intended for intraperitoneal administration only. Not for intravenous injection
- 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 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 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 infection or aseptic peritonitis (see Section 4.4).
- For single use only

4.3 Contraindications

Polithera Solution for peritoneal dialysis should not be used in patients with:

- hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1
- a known allergy to starch based polymers (e.g. maize 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

4.4 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 Polithera Solution for peritoneal dialysis may necessitate an adjustment of the usual insulin dosage. Insulin can be administered intraperitoneally.
- Blood glucose measurement must be done with a glucose specific method to prevent maltose interference. Glucose dehydrogenase pyrroloquinoline quinone (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 Polithera Solution for peritoneal dialysis 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 Polithera Solution for peritoneal

dialysis (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 Polithera Solution for peritoneal dialysis (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 Polithera Solution for peritoneal dialysis (icodextrin).

To avoid improper insulin administration, educate patients to alert healthcare 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 tumors, 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; 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 Polithera Solution for peritoneal dialysis as part of their PD therapy. Infrequently, fatal outcomes have been reported with Polithera Solution for peritoneal dialysis.
- 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 Polithera Solution for peritoneal dialysis (see section 4.8). 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 infection is suspected. If other possible reasons for cloudy fluid have been excluded, Polithera Solution for peritoneal dialysis should be stopped and the result of this action evaluated. If Polithera Solution for peritoneal dialysis is stopped and the fluid becomes clear afterwards, Polithera Solution for peritoneal dialysis should not be reintroduced unless under close supervision. If by re-challenging with Polithera Solution for peritoneal dialysis, the cloudy fluid recurs then this patient should not be prescribed Polithera Solution for peritoneal dialysis 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 Polithera Solution for peritoneal dialysis 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.
- Polithera Solution for peritoneal dialysis 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 over or under hydration. 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.
- Over-infusion of an Polithera Solution for peritoneal dialysis volume into the peritoneal cavity may be characterized by abdominal distension, feeling of fullness and/or shortness of breath.
- Treatment of Polithera Solution for peritoneal dialysis over-infusion is to release the Polithera Solution for peritoneal dialysis from the peritoneal cavity by drainage of the Polithera Solution for peritoneal dialysis volume contained within 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 levels.

Paediatric population

Polithera Solution for peritoneal dialysis is not recommended in children

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been conducted with Polithera Solution for peritoneal dialysis. The blood concentrations of dialysable drugs may be reduced by dialysis. Corrective therapy should be instituted if necessary.

Blood glucose measurement must be done with a glucose-specific method to prevent maltose interference. Glucose dehydrogenase pyrroloquinoline quinone (GDH-PQQ)- or glucose-dye- oxidoreductase-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 section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of Polithera Solution for peritoneal dialysis in pregnant women.

Polithera Solution for peritoneal dialysis is not recommended during pregnancy unless the clinical condition of the woman clearly requires this treatment and only after a careful risk-benefit consideration.

Breastfeeding

Carbohydrates (icodextrin metabolites) and electrolytes Polithera Solution for peritoneal dialysis are excreted in human milk.

At therapeutic doses, no effects on the breastfed neonate/infant are expected. However, Polithera Solution for peritoneal dialysis should be used during lactation only after a careful risk-benefit consideration and only with caution. Nevertheless, breast-feeding is not recommended for mothers on peritoneal dialysis.

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.

4.8 Undesirable effects

Undesirable effects which occurred in patients treated with Polithera Solution for peritoneal dialysis from the clinical trials and post marketing are listed below.

Polithera Solution for peritoneal dialysis associated skin reactions, including rash and pruritus, are generally mild or moderate in severity. Occasionally, these rashes have been associated with exfoliation. In the event of this occurring and depending on the severity, Polithera Solution for peritoneal dialysis should be withdrawn at least temporarily.

Frequency is based upon the following scale: Very Common ($\geq 1/10$); Common ($\geq 1/100$ - $<1/10$), Uncommon ($\geq 1/1,000$ - $<1/100$), Rare ($\geq 1/10,000$ - $<1/1,000$), Very Rare ($<1/10,000$), not known (frequency cannot be estimated from the available data).

System (SOC)	Organ	Class	Preferred Term	MedDRA	Frequency
Infections and infestations			Flu syndrome		Uncommon
			Furuncle		Uncommon
Blood and lymphatic system disorders			Anaemia		Uncommon
			Leukocytosis		Uncommon
			Eosinophilia		Uncommon
			Thrombocytopenia		Not known
			Leucopenia		Not known
Immune system disorders			Vasculitis		Not known
			Hypersensitivity**		Not known
Metabolism and nutrition disorders			Dehydration		Common
			Hypovolaemia		Common
			Hypoglycaemia		Uncommon
			Hyponatraemia		Uncommon
			Hyperglycaemia		Uncommon
			Hypervolaemia		Uncommon
			Anorexia		Uncommon
			Hypochloraemia		Uncommon
			Hypomagnesaemia		Uncommon
			Hypoproteinaemia		Uncommon
			Shock hypoglycaemia		Not known
			Fluid imbalance		Not known
Psychiatric disorders			Thinking abnormal		Uncommon
			Anxiety		Uncommon
			Nervousness		Uncommon
Nervous system disorders			Dizziness		Common
			Headache		Common
			Hyperkinesia		Uncommon
			Paraesthesia		Uncommon
			Ageusia		Uncommon
			Hypoglycaemic coma		Not known
			Burning sensation		Not known

Eye disorders	Vision blurred	Not known
Ear and labyrinth disorders	Tinnitus	Common
Cardiac disorders	Cardiovascular disorder	Uncommon
	Tachycardia	Uncommon
Vascular disorders	Hypotension	Common
	Hypertension	Common
	Orthostatic hypotension	Uncommon
Respiratory, thoracic, and mediastinal disorders	Pulmonary oedema	Uncommon
	Dyspnoea	Uncommon
	Cough	Uncommon
	Hiccups	Uncommon
	Bronchospasm	Not known
Gastrointestinal disorders	Abdominal pain	Common
	Ileus	Uncommon
	Peritonitis	Uncommon
	Bloody peritoneal effluent	Uncommon
	Diarrhoea	Uncommon
	Gastric ulcer	Uncommon
	Gastritis	Uncommon
	Vomiting	Uncommon
	Constipation	Uncommon
	Dyspepsia	Uncommon
	Nausea	Uncommon
	Dry mouth	Uncommon
	Flatulence	Uncommon
	Ascites	Not known
	Inguinal hernia	Not known
	Abdominal discomfort	Not known
Skin and subcutaneous tissue disorders	Rash (including macular, papular, erythematous)	Common
	Pruritus	Common
	Skin exfoliation	Common
	Urticaria	Uncommon
	Dermatitis bullous	Uncommon
	Psoriasis	Uncommon
	Skin ulcer	Uncommon
	Eczema	Uncommon
	Nail disorder	Uncommon
	Dry skin	Uncommon
	Skin discolouration	Uncommon
	Toxic epidermal necrolysis	Not known
	Erythema multiform	Not known
	Angiodema	Not known
	Urticaria generalised	Not known

	Toxic skin eruption Periorbital oedema Dermatitis (including allergic and contact) Erythema Blister	Not known Not known Not known Not known Not known
Musculoskeletal and connective tissue disorders	Bone pain Muscle spasms Myalgia Neck pain Arthralgia Back pain Musculoskeletal pain	Uncommon Uncommon Uncommon Uncommon Not known Not known Not known
Renal and urinary disorders	Renal pain	Uncommon
General disorders and administrative site conditions	Oedema peripheral Asthenia Chest pain Face oedema Oedema Pain Pyrexia Chills Malaise Catheter site erythema Catheter site inflammation Infusion related reaction (including infusion site pain, instillation site pain)	Common Common Uncommon Uncommon Uncommon Uncommon Not known Not known Not known Not known Not known Not known
Investigations	Alanine aminotransferase increased Aspartate aminotransferase increased Blood alkaline phosphatase increased Liver function test abnormal Weight decreased Weight increased	Uncommon Uncommon Uncommon Uncommon Uncommon Uncommon Uncommon
Injury, poisoning, and procedural complications	Device interaction*	Not known

*Icodextrin interferes with blood glucose measurement devices (see section 4.4).

**** Hypersensitivity-type reactions** have been reported in patients using Polithera Solution for peritoneal dialysis including bronchospasm, hypotension, rash, pruritus and urticaria. 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 (see section 4.4).

Hypoglycaemic episodes in diabetic patients (see section 4.4).

Increase in serum alkaline phosphatases (see section 4.4) and electrolyte disturbances (e.g. hypokalaemia, hypocalcaemia and hypercalcaemia).

Peritoneal reactions, including abdominal pain, cloudy effluents with or without bacteria, aseptic peritonitis (see section 4.4).

Fatigue was often reported spontaneously and in literature as an undesirable effect related to the procedure.

4.9 Overdose

No data are available on the effects of overdosage. However, continuous administration of more than one bag of Polithera 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. Treatment could be managed by Icodextrin-free peritoneal dialysis or haemodialysis.

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 the Yellow Card Scheme. Website at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Peritoneal Dialytic, Isotonic solutions, ATC code: B05DA

Icodextrin is a starch-derived glucose polymer which acts as an osmotic agent when administered intraperitoneally for continuous ambulatory peritoneal dialysis. A 7.5% solution is approximately iso-osmolar to serum but produces sustained ultrafiltration over a period up to 12 hours in CAPD. There is a reduction in calorie load compared to hyperosmolar glucose solutions.

The volume of ultrafiltrate produced is comparable to that with 3.86% glucose when used in CAPD. Blood glucose and insulin levels remain unaffected.

Ultrafiltration is maintained during episodes of peritonitis.

The recommended posology is limited to a single exchange in each 24 hour-period, as part of a CAPD or APD regimen.

5.2 Pharmacokinetic properties

Carbohydrate polymer levels in blood reach steady state after about 7-10 days when used on a daily basis for overnight dialysis. The polymer is hydrolysed by amylase to smaller fragments which are cleared by peritoneal dialysis. Steady state plasma levels of 1.8 mg/ml have been measured for oligomers of glucose units greater than 9 (G9) and there is a rise in serum maltose (G2) to 1.1 mg/ml but there is no significant change in serum osmolality. When used for the long day time dwell in APD maltose levels of 1.4 mg/ml have been measured but with no significant change in serum osmolality.

The long-term effects of raised plasma levels of maltose and glucose polymer are unknown, but there is no reason to suppose these to be harmful.

5.3 Preclinical safety data

There are no non-clinical data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections
Sodium Hydroxide or
Hydrochloric acid (for pH adjustment).

6.2 Incompatibilities

Drug compatibility must be checked before admixture. In addition, the pH and salts of the solution must be taken into account.

In the absence of compatibility studies, the product must not be mixed or diluted with other medicinal products.

6.3 Shelf life

2 years.

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

6.4 Special precautions for storage

Do not refrigerate or freeze.

6.5 Nature and contents of container

Polithera Solution for peritoneal dialysis is a sterile solution.

Polithera is presented in the following two packaging:

2.0 litres polypropylene plastic bag containing the solution and 3.0 litres drainage empty polypropylene plastic bag with connection tubing.

Both bags and their connection are introduced into a protective two-layer film made of polypropylene and polyamide overpouch and supplied in carton boxes containing 4 bags.

2.0 litres polypropylene plastic bag containing the solution introduced into a protective two-layer film made of polypropylene and polyamide overpouch and supplied in carton boxes containing 4 bags.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

For details see section 6.2

In the absence of compatibility studies, the product must not be mixed or diluted with other medicinal products.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Vivisol S.r.l.

Via Gerolamo Borgazzi, 27 20900 Monza (MB)

Italy

8 MARKETING AUTHORISATION NUMBER(S)

PL 52631/0001

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

Date of first authorisation: 28/02/2023

Date of latest renewal: DD month YYYY

10 DATE OF REVISION OF THE TEXT

12/07/2024