Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Notecor solution for peritoneal dialysis

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Icodextrin 75 g/L
Sodium chloride 5.4 g/L
Sodium S-lactate 4.5 g/L
Calcium chloride dihydrate 0.257 g/L
Magnesium chloride hexahydrate 0.051 g/L

Electrolyte solution content per 1 L:

Sodium 133 mmol
Calcium 1.75 mmol
Magnesium 0.25 mmol
Chloride 96 mmol
Lactate 40 mmol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for peritoneal dialysis.

Notecor is clear, colorless to slightly yellow solution, free from visible particles.

Osmolality: 270 - 310 mOsm/kg
pH = 5.0 – 6.0

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Notecor 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. Notecor is especially recommended for patients who have lost ultrafiltration on glucose solutions because it can extend the time on CAPD therapy in such patients.

4.2 Posology and method of administration

Posology
Notecor 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 Notecor 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

- Notecor 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 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

Notecor should not be used in patients with:

- hypersensitivity to the active substance(s) or 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). Transferring from a glucose-based PD solution to Notecor 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 Notecor 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 Notecor (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 healthcare providers of peritoneal dialysis patients using Notecor (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 Notecor (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 tumours, 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 Notecor as part of their PD therapy. Infrequently, fatal outcomes have been reported with Notecor.

- 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 the 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 icodextrin peritoneal dialysis solution (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 or not infection is suspected. If other possible reasons for cloudy fluid have been excluded, Notecor should be stopped and the result of this action evaluated. If Notecor is stopped and the fluid becomes clear afterwards, Notecor should not be reintroduced unless under close supervision. If by re-challenging with Notecor, the cloudy fluid recurs then this patient should not be prescribed Notecor 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 the identification of the involved organism(s), broad-spectrum antibiotics may be indicated.

- Rarely, serious hypersensitivity reactions to icodextrin peritoneal dialysis solution 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.

- Notecor 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 dehydration. 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 Notecor volume into the peritoneal cavity may be characterised by abdominal distension, feeling of fullness and/or shortness of breath.

- Treatment of Notecor overinfusion is to release the Notecor from the peritoneal cavity by drainage of the Notecor 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 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 by any side effects. However, it is not known whether subnormal amylase levels 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

- Notecor is not recommended in children.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been conducted with Notecor. 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 data from the use of icodextrin peritoneal dialysis solution in pregnant women.
Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).
Notecor 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 are excreted in human milk.
At therapeutic doses, no effects on the breastfed neonate/infant are expected. However, Notecor should be used during lactation only after a careful risk-benefit consideration and only with caution.

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 their ability to drive or use machines.

4.8 Undesirable effects

Undesirable effects which occurred in patients treated with Notecor from the clinical trials and post-marketing are listed below.

Icodextrin peritoneal dialysis solution -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, icodextrin peritoneal dialysis solution should be withdrawn at least temporarily.

The undesirable effects listed are listed in order of frequency according to the MedDRA Convention: very common: ≥1/10, common: ≥1/100 to <1/10, uncommon: (≥1/1.000-<1/100), rare (≥1/10.000-<1/1.000), very rare (<1/10.000), not known (cannot be estimated from the available data).

System Organ Class (SOC)	Preferred MedDRA Term	Frequency
Infections and infestations	Flu syndrome Furuncle	Uncommon 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	Blurred vision	Not known
Ear and labyrinth disorders	Tinnitus	Common
Cardiac disorders	Cardiovascular disorder	Uncommon
	Tachycardia	Uncommon
Vascular disorders	Hypertension	Common
	Hypotension	Common
	Orthostatic hypotension	Uncommon
Respiratory, thoracic and mediastinal disorders	Pulmonary oedema	Uncommon
	Dyspnoea	Uncommon
	Cough	Uncommon
	Hiccups	Uncommon
	Bronchospasm	Not known
Gastrointestinal disorder	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	
	Skin exfoliation	Common

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

*Hypersensitivity-type reactions have been reported in patients using icodextrin peritoneal dialysis solution including bronchospasm, hypotension, rash, pruritus and urticaria.
**Icodextrin interferes with blood glucose measurement devices (see section 4.4).

Other undesirable effects of peritoneal dialysis related to the procedure: fungal peritonitis, bacterial peritonitis, catheter site infection, catheter related infection and catheter-related complications.

Enhanced ultrafiltration, particularly in 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.

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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

No data are available on the effects of overdosage. However, continuous administration of more than one bag of Notecor 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: blood substitutes and perfusion solutions, peritoneal dialytics .
ATC code: B05DA.

Icodextrin is a starch-derived glucose polymer which acts as an osmotic agent when administered intraperitoneally for continuous ambulatory peritoneal dialysis (CAPD). A 7.5% solution is approximately iso-osmolar to serum but produces sustained ultrafiltration over a period of 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 of 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 the blood reach a 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

Twice daily i.p. administration of 20% icodextrin solution for 28 days to rats and dogs revealed no target organ or tissue toxicity. The major effect was on the dynamics of fluid balance.

In vitro and *in vivo* studies on mutagenicity gave negative results.

A reproduction toxicity study in rats demonstrated no effect on fertility or embryofetal development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections
Sodium hydroxide (as pH adjusting agent)
Hydrochloric acid concentrated (as pH adjusting agent)

6.2 Incompatibilities

None known.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Unopened
2 years

Chemical and physical in use stability after removal from overpouch has been demonstrated for 24 hours at 25°C and 37°C.
From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately.
If not used immediately, in use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Do not refrigerate or freeze.
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

The chosen CAPD or APD systems comprise a polypropylene soft solution bag bearing 2 polypropylene tubes. One tube is sealed with a polycarbonate closure and the second tube, through a break off port, is connected with a delivering PVC tubing which ends up either in a three-way PVC tube (CAPD system) or in a single way tube (APD system). In both systems, the delivering tube is connected to a connect port which is sealed with a connect cap. Additionally, at the CAPD system, a drainage PVC bag is connected to a drainage PVC tubing which is connected to the three-way tube.

Both CAPD & APD systems are over-wrapped with a polypropylene overpouch and placed in a carton box.

Pack sizes:
Carton x 1 bag of 1.5 L solution x 1 delivery tubing
Carton x 1 bag of 1.5 L solution x 1 drainage bag x 1 delivery and drainage tubing

Carton x 2 bags of 1.5 L solution x 2 delivery tubings
Carton x 2 bags of 1.5 L solution x 2 drainage bags x 2 delivery and drainage tubings

Carton x 4 bags of 1.5 L solution x 4 delivery tubings
Carton x 4 bags of 1.5 L solution x 4 drainage bags x 4 delivery and drainage tubings

Carton x 1 bag of 2 L solution x 1 delivery tubing
Carton x 1 bag of 2 L solution x 1 drainage bag x 1 delivery and drainage tubing

Carton x 2 bags of 2 L solution x 2 delivery tubings
Carton x 2 bags of 2 L solution x 2 drainage bags x 2 delivery and drainage tubings

Carton x 4 bags of 2 L solution x 4 delivery tubings
Carton x 4 bags of 2 L solution x 4 drainage bags x 4 delivery and drainage tubings

Carton x 1 bag of 2.5 L solution x 1 delivery tubing

Carton x 1 bag of 2.5 L solution x 1 drainage bag x 1 delivery and drainage tubing

Carton x 2 bags of 2.5 L solution x 2 delivery tubings
Carton x 2 bags of 2.5 L solution x 2 drainage bags x 2 delivery and drainage tubings

Carton x 4 bags of 2.5 L solution x 4 delivery tubings
Carton x 4 bags of 2.5 L solution x 4 drainage bags x 4 delivery and drainage tubings

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Shelf-life after mixing
Chemical and physical in-use stability has been demonstrated at 37^{o}C, protected from light after admixing with the following parenteral antibiotics:
- Ampicillin concentration 333 mg/L for 8 hours
- Ampicillin concentration 800 mg/L for 4 hours
- Cefazolin between 667 mg/L and 800 mg/L for 8 hours
- Ceftazidime between 667 mg/L and 800 mg/L for 8 hours
- Flucloxacillin between 333 mg/L and 400 mg/L for 8 hours
- Gentamicin between 26.7 mg/L and 64 mg/L for 8 hours
- Vancomycin between 333 mg/L and 2000 mg/L for 8 hours

Note, aminoglycosides should not be mixed with penicillins due to chemical incompatibility..
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Noridem Enterprises Limited
Evagorou & Makariou
Mitsi Building 3, Office 115
1065 Nicosia
Cyprus

8 MARKETING AUTHORISATION NUMBER

PA1122/039/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th September 2025

10 DATE OF REVISION OF THE TEXT