

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Gambrosol trio 40, solution for peritoneal dialysis.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Gambrosol trio 40 is filled in a three-compartment bag.

Two smaller compartments (A and B) each contain 50% glucose solution and sodium chloride (NaCl) and a larger third compartment (C) the electrolyte solution. After breaking the frangible pin between compartments A and C and thoroughly mixing the two fluids a PD solution containing 1.5% glucose will be produced. Similarly mixing the contents of compartments B and C will produce a PD solution containing 2.5% glucose. Finally by breaking both frangible pins and mixing the contents of all three compartments will produce a solution containing 3.9% glucose.

BEFORE RECONSTITUTION

Each 1000 ml contains:

Glucose compartments A and B

Active ingredients:	
Glucose anhydrous	500.0 g
(as glucose monohydrate	550.0 g)
Sodium chloride	5.38 g

Electrolyte compartment C

Active ingredients:	
Sodium chloride	5.38 g
Sodium lactate S-(+) anhydrous	4.72 g
(as 60% m/m solution)	(7.87 g)
Calcium chloride dihydrate	0.209 g
Magnesium chloride hexahydrate	0.054 g

AFTER RECONSTITUTION

The glucose compartments A or/and B are mixed with the electrolyte compartment C to give the following reconstituted solutions:

Mix compartments A and C	Reconstituted solution 40L (Light)
Mix compartments B and C	Reconstituted solution 40M (Medium)
Mix compartments A, B and C	Reconstituted solution 40H (High)

Electrolyte content per each 1000 ml of reconstituted solution:

Reconstituted solution mmol/l	L	M	H
Sodium Na ⁺	133	132	131 mmol/l
Calcium Ca ⁺⁺	1.38	1.35	1.31 mmol/l
Magnesium Mg ⁺⁺	0.26	0.25	0.24 mmol/l
Chloride Cl ⁻	95.4	95.2	95.2 mmol/l
Lactate	41	40	39 mmol/l

Glucose	85	139	215 mmol/l
Calculated osmolarity mOsm/l	356	408	482
pH	5.5-6.5	5.5-6.5	5.5-6.5

Reconstituted solution mEq/l	L	M	H
Sodium Na ⁺	133	132	131 mEq/l
Calcium Ca ⁺⁺	2.76	2.70	2.62 mEq/l
Magnesium Mg ⁺⁺	0.52	0.50	0.48 mEq/l
Chloride Cl ⁻	95.4	95.2	95.2 mEq/l
Lactate	41	40	39 mEq/l

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solutions for peritoneal dialysis.

Clear and colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of acute and chronic renal failure. Treatment of excessive fluid retention and certain types of severe electrolyte imbalance (e.g. hyperkalemia) not amenable to other therapy. Treatment of intoxication with dialysable substances.

4.2 Posology and method of administration

For intraperitoneal administration

The mode of therapy, frequency of treatment, exchange volume, duration of dwell and length of dialysis are individually decided by the responsible physician.

The average frequency is 3 to 5 times a day. The fill volume depends on body size, usually from 2,0 to 2,5 litres for adults. There are no data from clinical studies in paediatric patients.

The glucose concentration in the solution is chosen according to the patient's ultrafiltration needs and should be kept as low as possible.

The intraperitoneal administration requires the use of a special catheter and a suitable administration set enabling the connection between the solution bag and the patient's catheter.

Mode of preparation

It is necessary to warm up the solution to body temperature before use using the special heater provided. Prior to preparing for administration ensure that all the solutions are clear and all the seals intact, wash the hands, clean the working area with a disinfectant and place the solution bag on the working area. To prepare solutions ready for use it is necessary to remove the overwrapping. Depending on the information provided by the physician then immediately the frangible pin(s) must be broken between the main electrolyte bag (compartment C) and one or both of the glucose solution compartments (compartment A and/or B). Allow the glucose solution to flow into the main electrolyte bag. Rinse the glucose compartment(s) by pressing the mixed solution back into the empty compartment(s). Allow it to finally run back again into the main compartment. The PD solution is now ready to use and must be used within 18 hours after admixture.

4.3 Contraindications

This solution must not be used in patients with lactic acidosis and severe hypokalaemia and severe hypocalcaemia. For peritoneal dialysis treatment in general.

A peritoneal dialysis treatment should not be commenced in the following circumstances:

- recent abdominal surgery or injury, a history of abdominal operations with fibrous adhesions, severe abdominal burns, abdominal perforation; extensive inflammation of the abdominal skin (dermatitis);
- inflammatory bowel diseases (Crohn's disease, ulcerative colitis, diverticulitis);
- localised peritonitis;
- internal or external abdominal fistula;
- umbilical, inguinal or other abdominal hernia;
- intra-abdominal tumours;
- ileus;
- pulmonary disease (especially pneumonia);
- sepsis;
- extreme hyperlipidemia;
- in rare cases of uremia, which cannot be managed by peritoneal dialysis;
- cachexia and severe weight loss, particularly in cases in which an adequate protein supplementation is not guaranteed;
- patients who are physically or mentally incapable of performing PD as instructed by the physician.

4.4 Special warnings and precautions for use

- It is generally not advisable to use peritoneal dialysis in advanced pregnancy.
- An accurate fluid balance record must be kept and the body weight of the patient should carefully be monitored to avoid over- or underhydration with severe consequences including congestive heart failure, volume depletion and shock.
- In renal failure patients, serum electrolyte concentrations (particularly bicarbonate, potassium, calcium, magnesium and phosphate), blood chemistry (including parathyroid hormone) and haematological parameters should be evaluated periodically.
- Replacement of proteins, amino acids and water-soluble vitamins may be necessary, as significant losses can take place during dialysis.
- In non-diabetic patients the degree of susceptibility to hyperglycaemia varies as a result of the combined effects of intolerance to glucose caused by uraemia and transperitoneal absorption of glucose.
- In patients with diabetes mellitus blood glucose levels should be monitored and the dosage of the insulin or other treatment for hyperglycaemia often need to be adjusted in order to maintain glycaemic control. Insulin can be administered intraperitoneally via the solution bag.
- In case of secondary hyperparathyroidism as Gambrosol trio 40 contains 1,35 mmol calcium per litre, serum parathormone and the other indicators of bone metabolism should be monitored periodically and the therapy should comprise the administration of calcium containing phosphate binders and/or active vitamin D metabolites to ensure adequate enteral calcium supply.
- Dehydration and hyperglycaemia may occur if the patient does not comply with the prescription and breaks both pins at every fluid exchange. Fluid retention may appear if the breaking of the pin(s) is unsuccessful and the intended mixture of the fluid volumes does not take place.
- Aseptic technique should be used throughout the procedure

4.5 Interaction with other medicinal products and other forms of interaction

The blood concentration of dialysable drugs may be reduced by dialysis. Corrective therapy should be instituted if necessary.

Plasma levels of potassium in patients using cardiac glucosides must be carefully monitored as there is a risk of digitalis intoxication. Potassium supplements may be necessary.

4.6 Fertility, pregnancy and lactation

Peritoneal dialysis during pregnancy and lactation is not advised, but the risks must be evaluated by the physician according to each patient's status.

4.7 Effects on ability to drive and use machines

Peritoneal dialysis has no reported effect on the ability to drive or use machinery.

4.8 Undesirable effects

Undesirable effects of peritoneal dialysis include procedure and solution related problems. The undesirable effects commonly observed are mentioned here below:

Frequencies are defined as follows:
Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1000, <1/100); rare (>1/10.000, <1/1000); very rare (<1/10.000).

	Undesirable effects	Frequency	Procedure-related	Solution-related
Metabolism and nutrition disorders	Hyperglycaemia	Common	Yes	Yes
	Hypocalcaemia	Common		Yes
	Hypokalaemia	Common		
	Ultrafiltration decrease	Common		
	Lactic acidosis	Uncommon		Yes
	Hypervolaemia	Uncommon		
Vascular disorders	Hypertension	Common	Yes	
General disorders and administration site conditions	Abdominal pain	Common	Yes	
	Aesthenia	Uncommon	Yes	
	Shivering	Uncommon	Yes	
	Headache	Uncommon	Yes	
	Peritonitis	Uncommon	Yes	
Nervous system disorders	Fainting	Uncommon	Yes	

Those which are related to the procedure include abdominal pain, bleeding, peritonitis (which is followed by abdominal pain, cloudy effluent and sometimes fever), infection around the catheter (signs of inflammation, redness and secretion), catheter blockage, ileus, shoulder pain, hernia of the abdominal cavity.

Those which are generally related to peritoneal dialysis solutions are seen less frequently than those related to the procedure and include weakness, fainting, tiredness, muscle cramping, headache, respiratory symptoms associated with pulmonary oedema and electrolyte disturbances (e.g.; hypokalaemia, hypomagnesaemia and hypocalcemia), diarrhoea and constipation.

Gambrosol trio 40 may cause or worsen hyperparathyroidism.

4.9 Overdose

Any excess of dialysis solution which has flown into the peritoneal cavity can easily be drained into the drainage bag. Possible consequences of overdose include hypovolaemia, electrolyte disturbances or (in diabetic patients) hyperglycaemia.

Management of overdose:

- Hypovolaemia may be managed by fluid replacement either orally or intravenously, depending on the degree of dehydration.
- Electrolyte disturbances shall be managed according to the specific electrolyte disturbance verified by blood test. The most probable disturbance, hypokalaemia, may be managed by the oral ingestion of potassium or by addition of potassiumchloride in the peritoneal dialysis solution prescribed by the treating physician.
- Hyperglycaemia (in diabetic patients) shall be managed by adjusting the insulin dose according to the insulin scheme prescribed by the treating physician.

Management when the patient has not used the correct solution:

- The electrolyte compartment C with no glucose concentration has been drained into the patient: the fluid should be drained out and a new bag prepared and infused. The glucose solution alone should never be infused to the patient.
- A lower glucose concentration than intended has been drained into the patient: at the next exchange the patient should use a higher glucose concentration.
- A higher glucose concentration than intended has been drained into the patient: at the next exchange the patient should use a lower glucose concentration.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic groups :

L: Peritoneal dialytics, Isotonic solutions, ATC code B 05D A00

M: Peritoneal dialytics, Hypertonic solutions, ATC code B 05D B00

H: Peritoneal dialytics, Hypertonic solutions, ATC code B 05D B00

The calcium dialysis concentration of Gambrosol trio 40 is set at 1.35 mmol/l which has been shown to reduce the risk of hypercalcaemia during the concomitant treatment with calcium-containing phosphate binders and/or vitamin D.

Sterile solution, free from bacterial endotoxins for intraperitoneal administration by peritoneal dialysis.

The level of electrolyte in the reconstituted solutions is similar to the physiological level in plasma except for potassium, lactate and magnesium.

The osmolarity of the reconstituted solutions is dependent on the glucose concentration.

Lactate is used as an alkalising buffer to correct and/or maintain the acid/base balance. The isomeric form of lactate in Gambrosol trio 40 is the S (+) which is the naturally present form in humans.

5.2 Pharmacokinetic properties

Intraperitoneally administered glucose, buffer, electrolytes and water are absorbed into the blood and metabolised by the usual pathways.

Glucose is metabolised (1 g of glucose = 4 calories) into CO₂ and H₂O.

Formal interaction studies have not been performed.

5.3 Preclinical safety data

There is no data of relevance to the prescriber that have not been included elsewhere in the Summary of the Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glucose compartment A and B:

Hydrochloric acid concentrated (37%) (for pH adjustment), water for injections.

Electrolyte compartment C:

Sodium hydroxide (for pH adjustment), water for injections.

6.2 Incompatibilities

Incompatibilities have not been studied.

Additives may be incompatible. When in doubt, a pharmacist should be consulted prior to the addition of drug. When introducing additives, use aseptic technique, mix thoroughly and use immediately.

6.3 Shelf life

As packed for sale: 18 months.

After reconstitution and before opening: 18 hours.

After opening: for immediate and single use.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Do not store below 4°C.

6.5 Nature and contents of container

The container made of Polyvinyl Chloride (PVC) is a three compartment bag. The electrolyte solution compartment (C) is fitted with an injection port for drug admixture after reconstitution at the topside and at the bottom an other port for the connection to the patient with a suitable set (tubing or connectors). The bag is overwrapped with a transparent overpouch made of multilayer copolymers.

Type of packaging

Single bag with connector: System 10

Single bag with tubing: System 100

Double bag with connector: Gemini 10

Double bag system: Gemini 100

Size of packaging

System 10	System 100	Gemini 10	Gemini 100
4 x 2000 ml	4 x 2000 ml	4 x 2000 ml	4 x 2000 ml
4 x 2500 ml	4 x 2500 ml	4 x 2500 ml	4 x 2500 ml
3 x 3000 ml	3 x 3000 ml	3 x 3000 ml	3 x 3000 ml
2 x 5000 ml			

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

Gambrosol trio peritoneal dialysis solutions are intended for intra-peritoneal administration only.

Prior to preparing for administration, inspect visually the bag for particulate matters, coloration or damage of container and ensure that all the solutions are clear and all the seals intact. Discard any solution presenting defects. Wash the hands, clean the working area with a specific disinfectant prescribed by the physician and place the solution bag on the working area.

To prepare solutions ready for use it is necessary to mix the contents of one or both of the smaller compartments containing glucose with the electrolyte solution in the larger compartment. The frangible pin(s) between the correct compartment(s) (A and/or B) must be broken and the glucose solution(s) allowed to flow into the electrolyte solution in compartment C. The glucose compartment(s) are then rinsed by pressing the mixed solution back into the smaller compartment(s) before being allowed to run back to the large compartment. The PD solution is then ready for use.

Recommendations how to break the frangible pin(s)

Break off a pin let it sink and settle in the bottom of the bag before opening the patient inflow tubing. The pin will remain there unless the bag is shaken.

The addition of any other medicine to Gambrosol trio 40 must only be *made to the final solution after mixing* when ready for use in peritoneal dialysis.

Aseptic technique must be applied during connection/disconnection of the lines.

When using the bag with the connector, it is recommended that, prior to disconnection, the external surfaces of the line/bag connector should be disinfected. After removing the protective cap on the new bag, disinfectant should also be applied to the interior of the connector.

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

Detailed instruction on the CAPD exchange procedure is given to patients by means of training, in a specialised training centre, prior to home use.

7 MARKETING AUTHORISATION HOLDER

Fresenius Medical Care Deutschland GmbH
61346 Bad Homburg v.d.H.
Germany

8 MARKETING AUTHORISATION NUMBER

PA 953/8/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 July 2000

Date of last renewal: 30 April 2009

10 DATE OF REVISION OF THE TEXT

July 2011