Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

CAPD/DPCA 18, Solution for Peritoneal Dialysis

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 litre contains:

Sodium chloride	5.786 g
Sodium-(S)-lactate solution equivalent to 3.925 g sodium-(S)-lactate	7.85 g
Calcium chloride x 2 H_2O	0.1838 g
Magnesium chloride x 6 H_2O	0.1017 g
Glucose monohydrate equivalent to 42.5 g/l anhydrous glucose and up to 2.1 g/l fructose	46.75 g

Na^+	134	mmol/l
Ca^{++}	1.25	mmol/l
Mg^{++}	0.50	mmol/l
Cl^-	102.50	mmol/l
(S)-lactate	35.00	mmol/l
Glucose	235.80	mmol/l

Theoretical osmolarity 509.00 mosm/l
pH ≈ 5.5

For excipients, *see Section 6.1*

3 PHARMACEUTICAL FORM

Solution for Peritoneal Dialysis.
Clear colourless to slightly yellow solution

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For use in patients with end-stage (decompensated) chronic renal failure of any origin which can be treated with peritoneal dialysis.

4.2 Posology and method of administration

Dosage

CAPD/DPCA 18 is exclusively indicated for intraperitoneal use.
The mode of therapy, frequency of administration, and dwell time required will be specified by the attending physician.

Continuous ambulatory peritoneal dialysis (CAPD)
Unless otherwise prescribed, patients will receive 2,000 ml solution per exchange four times a day (corresponding to a daily dose of 8,000 ml). After a dwell time between 2 and 10 hours the solution will be drained.

Adjustment of dosage will be necessary for individual patients.

If pain due to abdominal distension occurs at the commencement of peritoneal dialysis treatment, the solution volume per exchange should be reduced.

Children receive 500 and 1,500 ml (30 – 40 ml/kg body weight) of the solution per treatment, depending on weight.

In large adults and/or patients who tolerate higher volumes, and if residual renal function is lost, the volume to be administered is increased to 2,500 – 3,000 ml.

Automated peritoneal dialysis (APD)
If a machine (sleep.safe cycler) is used for intermittent or continuous cyclic peritoneal dialysis, larger volumes bags (5,000 ml) providing more than one solution exchange are used. The cycler performs the solution exchanges according to the medical prescription stored in the sleep.safe cycler.

Peritoneal dialysis is a long term therapy involving repeated administration by the same method.

Method and duration of administration

Patients should be proficient at performing peritoneal dialysis before performing it at home. The training should be performed by qualified personnel. The attending physician must ensure that the patient masters the handling techniques sufficiently before the patient performs peritoneal dialysis at home. In case of any problems or uncertainty the attending physician should be contacted.

Dialysis using the prescribed doses should be performed daily.
Peritoneal dialysis should be continued for as long as renal function substitution therapy is required.

Continuous ambulatory peritoneal dialysis (CAPD)
The ready-to-use solution is first warmed to body temperature. For bags with a volume up to 3,000 ml this should be done using an appropriate heater tray. The heating time for a 2,000 ml bag with a starting temperature of 22°C is approx. 120 min. The temperature control is done automatically and is set to 39°C ± 1°C. More detailed information can be obtained from the operating instructions of the bag warmer. Use of microwaves is not recommended due the risk of local overheating.

The appropriate dose is infused in the peritoneal cavity using a peritoneal catheter over 5 - 20 minutes. Depending on physician's instructions, the dose should dwell in the peritoneal cavity for 2 - 10 hours (equilibrium time), and then be drained. Depending on the required osmotic pressure, CAPD/DPCA 18 can be used sequentially with other peritoneal dialysis solutions with lower glucose content (i.e. with lower osmolarity).

Automated peritoneal dialysis (APD)
The connectors of the prescribed sleep safe solution bags are inserted in the free sleep.safe tray ports and then automatically connected to the sleep safe tubing set by the cycler. The cycler checks the bar codes of the solution bags and gives an alarm when the bags do not comply to the prescription stored in the cycler. After this check the tubing set can be connected to the patient’s catheter extension and the treatment be started. The sleep safe solution is automatically warmed up to body temperature by the sleep.safe cycler during the inflow into the abdominal cavity. Dwell times and selection of glucose concentrations are carried out according to the medical prescription stored in the cycler (for more details please refer to the operating instructions of the sleep.safe cycler).

4.3 Contraindications

For this specific peritoneal dialysis solution

CAPD/DPCA 18 must not be used in patients with lactic acidosis, severe hypokalaemia, severe hypocalcaemia, hypovolaemia and arterial hypotension.

Due to the content of fructose, this medicinal product is unsuitable for patients with fructose intolerance (hereditary fructose intolerance). A non-recognised hereditary fructose intolerance must be excluded prior to administration to babies and infants.

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 hyperlipidaemia,
- in rare cases of uraemia, 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

CAPD/DPCA 18 should only be administered after careful benefit-risk assessment in:

- loss of electrolytes due to vomiting and/or diarrhoea (a temporary change to a peritoneal dialysis solution containing potassium might then become necessary).
- hyperparathyroidism: The therapy should comprise the administration of calcium-containing phosphate binders and/or vitamin D to ensure adequate enteral calcium supply.
- hypocalcaemia: A change to a peritoneal dialysis solution with a higher calcium concentration must be considered in case an adequate enteral supply with calcium by calcium-containing phosphate binders and/or vitamin D is not possible.
- digitalis therapy: Regular monitoring of the serum potassium level is mandatory. Severe hypokalaemia may necessitate the use of a potassium-containing dialysis solution as well as dietary counseling.

Peritoneal dialysis solutions with a high glucose concentration (2.3 % or 4.25 %) should be used cautiously to treat the peritoneal membrane with care, to prevent dehydration and to reduce the glucose load.

A loss of proteins, amino acids, and vitamins (especially water-soluble vitamins) is unavoidable during peritoneal dialysis. To avoid deficiencies an adequate diet or supplementation should be ensured.

The transport characteristics of the peritoneal membrane may change during long-term peritoneal dialysis primarily indicated by a loss of ultrafiltration. In severe cases peritoneal dialysis must be stopped and haemodialysis commenced.

The monitoring of the following parameters is recommended:

- body weight for the early recognition of over-hydration and dehydration,
- serum sodium, potassium, calcium, magnesium, phosphate, acid base balance and blood proteins,
- serum creatinine and urea,
- blood sugar,
- parathyroid hormone and other indicators of bone metabolism,
- residual renal function in order to adapt the peritoneal dialysis treatment.

It is mandatory to monitor for turbidity of the effluent, decreased effluent volume, and abdominal pain as they may be indicators of peritonitis.

Addition of medication to the peritoneal dialysis solution:
The addition of medication to the peritoneal dialysis solution is generally not recommended because of the risk of contamination and of incompatibility between the peritoneal dialysis solution and the medication. It must be carried out under aseptic conditions. After thorough mixing and checking for the absence of any turbidity the peritoneal dialysis solution must be used immediately (no storage).

Handling
Plastic containers may occasionally be damaged during transport or storage. This can result in a contamination with growth of microorganisms in the dialysis solution. Thus all containers should be carefully inspected for damage prior to connection of the bag and prior to use of the peritoneal dialysis solution. Any damage, even minor, to connectors, at the closure, container welds and corners, must be noted because of possible contamination.

Damaged bags or bags with cloudy content should never be used!

Only use the peritoneal dialysis solution if container and seal are undamaged.

Aseptic conditions must be maintained during dialysate exchange in order to reduce the risk of infections.

4.5 Interaction with other medicinal products and other forms of interaction

The use of this peritoneal dialysis solution can yield to a loss of efficacy of other medication if these are dialysable through the peritoneal membrane. A dose adjustment might become necessary.

A distinct reduction of the serum potassium level can increase the frequency of digitalis-associated adverse reactions.

Special attention and monitoring is required in the case of hyperparathyroidism. Therapy should include the administration of calcium-containing phosphate binders and/or vitamin D to ensure adequate enteral calcium supply.

Use of diuretic agents may help maintain residual renal function, but may also result in water and electrolyte imbalances.

In diabetics the daily dose of blood sugar reducing medication must be adjusted to the increased glucose intake.

4.6 Pregnancy and lactation

No adequate or well-controlled studies with CAPD/DPCA 18 have been performed in pregnant or lactating women. No animal reproductive toxicity studies have been preformed. Peritoneal dialysis with CAPD/DPCA 18 is not recommended during pregnancy or breast feeding, unless in the opinion of the physician, its potential benefit outweighs

the likely risk to the mother or the child.

4.7 Effects on ability to drive and use machines

No effects on the ability to drive and use machines have been observed.

4.8 Undesirable effects

Possible side effects may result either from the technique of the peritoneal dialysis itself or may be induced by the dialysis solution.

Potential adverse reactions of the peritoneal dialysis solution are:

- hyperparathyroidism may develop or be aggravated,
- electrolyte disturbances, e.g. hypokalaemia, hypocalcaemia,
- disturbances in fluid balance. A rapid loss in body weight, drop in blood pressure and/or tachycardia might indicate dehydration; oedema, hypertension and possibly dyspnoea might indicate over-hydration,
- increased blood sugar levels,
- hyperlipidaemia or deterioration of pre-existing hyperlipidaemia,
- increase of body weight.

Potential side effects of the treatment mode are:

- peritonitis, indicated by cloudy dialysate. Later, abdominal pain, fever and malaise (generally feeling unwell) may develop or, in very rare cases, generalised blood poisoning (sepsis).
- skin exit site infection or tunnel infection of the catheter indicated by redness, swelling, pain, weeping or scabs. In case of any sign of infection the attending physician must be consulted immediately.
- in and outflow disturbances of the dialysis solution,
- diarrhoea or obstipation,
- dyspnoea caused by the elevated diaphragm,
- hernia,
- abdominal distension and feeling of fullness (abdominal pain),
- shoulder pain.

4.9 Overdose

Any excess of dialysis solution which has flowed into the peritoneal cavity can easily be drained into the drainage bag.

In case of too frequent or too rapid exchanges, dehydration and/or electrolyte disturbances might result which necessitates immediate emergency treatment.

If one or more of the daily exchanges have been forgotten or the administered volume of solution was too low, over-hydration and electrolyte disturbances may occur.

If the treatment is interrupted or stopped completely life threatening oedema and uraemia may develop.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group
Group: Solution for peritoneal dialysis
ATC: B05D B

CAPD/DPCA 18 represents a lactate-buffered, glucose-containing electrolyte solution indicated for intraperitoneal administration for the treatment of end-stage renal failure of any origin by continuous ambulatory peritoneal dialysis (CAPD). The calcium dialysis concentration of this peritoneal dialysis solution is set at 1.25 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.

The characteristic of continuous ambulatory peritoneal dialysis (CAPD) is the more or less continuous presence of usually 2 litres of dialysis solution in the peritoneal cavity which is replaced by fresh solution three to five times a day.

The basic principle behind every peritoneal dialysis technique is the use of the peritoneum as a semipermeable membrane allowing the exchange of solutes and water between the blood and the dialysis solution by diffusion and convection according to their physico-chemical properties.

The electrolyte profile of the solution is basically the same as that of physiological serum, although it has been adapted (e.g. the potassium content) for use in uraemic patients to enable renal function substitution therapy by means of intraperitoneal substance and fluid exchange. Substances which are normally eliminated with the urine, such as urea, creatinine, inorganic phosphate, uric acid, other solutes and water, are removed from the body into the dialysis solution. It should be borne in mind that medication may also be eliminated during dialysis, and that a dose adjustment may thus be necessary.

Individual parameters (such as patient size, body weight, laboratory parameters, residual renal function, ultrafiltration) must be used to determine the dose and combination of solutions required with differing osmolarity (glucose content), potassium, sodium, and calcium concentrations. The efficacy of therapy should be regularly monitored on the basis of these parameters.

Peritoneal dialysis solutions with a high glucose concentration (2.3% or 4.25%) are used when the body weight is above the desired dry weight. The withdrawal of fluid from the body increases in relation to the glucose concentration of the peritoneal dialysis solution.

5.2 Pharmacokinetic properties

Uraemic retention products such as urea, creatinine, and uric acid, inorganic phosphate, and electrolytes such as sodium, potassium, calcium and magnesium are removed from the body into the dialysis solution by diffusion and/or convection.

Dialysate glucose used as an osmotic agent in CAPD/DPCA 18 is slowly absorbed decreasing the diffusion gradient between dialysis solution and extracellular fluid. Ultrafiltration is maximal at the beginning of the dwell time reaching a peak after about 2 to 3 hours. Later absorption starts with a progressive loss of ultrafiltrate. After 4 hours the ultrafiltrate averages 100 ml with a 1.5 %, 400 ml with a 2.3 %, and 800 ml with a 4.25 % glucose solution. 60 to 80 % of dialysate glucose are absorbed.

L-lactate used as the buffering agent is almost completely absorbed after a 6-hour dwell time. In patients with a normal hepatic function L-lactate is rapidly metabolised demonstrated by normal values of intermediate metabolites.

Calcium mass transfer depends on the dialysis solution glucose concentration, the effluent volume, the serum ionised calcium, and the calcium concentration in the dialysis solution. The higher the glucose concentration, the effluent

volume and the serum ionised calcium concentration, and the lower the calcium concentration in the dialysis solution, the higher is the calcium transfer from the patient to the dialysate. It has been estimated that a typical CAPD schedule of three 1.5% and one 4.25% glucose-containing bags per day would remove up to 160 mg calcium per day enabling a higher intake of oral calcium containing drugs and vitamin D without the risk of hypercalcaemia.

5.3 Preclinical safety data

No preclinical toxicity studies with CAPD/DPCA 18 have been carried out, but clinical studies with comparable solutions for peritoneal dialysis have shown no major risk of toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid
Sodium hydroxide
Water for injections

6.2 Incompatibilities

Because of the risk of incompatibility and of contamination medicinal products must only be added when prescribed by a physician *(see also Section 4.4 under "Addition of medication to the peritoneal dialysis solution").*

6.3 Shelf Life

2 years

Shelf life after first opening: The content must be used immediately.

6.4 Special precautions for storage

Do not store above 25 °C. Do not refrigerate or freeze.

6.5 Nature and contents of container

stay safe:

The stay safe system is provided as a double bag system consisting of a non-PVC solution bag made of a multi layer polyolefine foil, a tubing system also made of polyolefines, a system connector (DISC, polypropylene), a drainage bag and an outer bag, also made of polyolefine multi layer film.

sleep safe:

The sleep safe system is provided as a single bag system consisting of a non-PVC solution bag made of a multi layer polyolefine foil, a tubing system, a bag connector both also made of polyolefines and an injection port made of polyolefine/synthetic rubber.

Pack sizes:

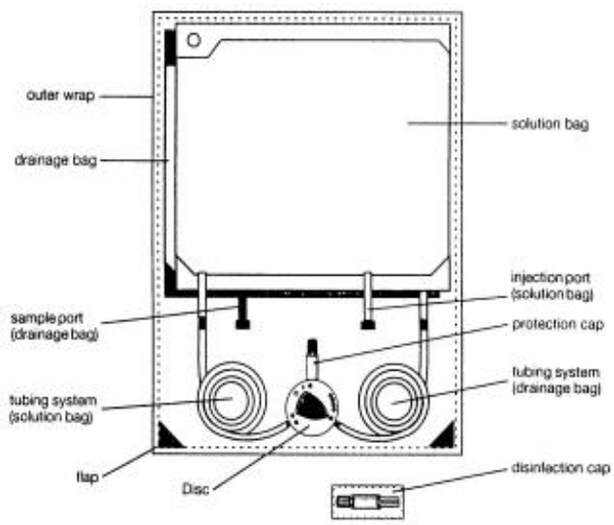
stay safe	sleep safe
6 bags of 1,500 ml each	2 bags of 5,000 ml each
4 bags of 2,000 ml each	
4 bags of 2,500 ml each	
4 bags of 3,000 ml each	

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

(see also Section 4.2 and 4.4)

Stay safe system:

1. Check the solution bag (label, the expiry date and ensure that the solution is clear) – open the outer wrap and package of the disinfection cap.
2. Clean hands with an antimicrobial washing solution.
3. Place the DISC into the organiser (suspend solution bag from the upper hole of the infusion pole – unroll the line "solution bag-DISC" – place the DISC into the organiser – afterwards place drainage bag into lower holder of the infusion pole).
4. Place catheter adapter into the organiser.
5. Disinfect your hands and remove protection cap of the DISC
6. Connect catheter adapter to the DISC:
7. Opening catheter clamp – position "●" – outflow procedure starts.
8. Flush-position "●●" -flush of fresh dialysate to the drainage bag (approx. 5 seconds)
9. Inflow – position "○◑●" – connection between solution bag and catheter.
10. Security step – position "●●●●" – automated closing of the catheter adapter with the PIN.
11. Disconnection (remove catheter adapter from DISC part) – screw catheter adapter to the new disinfection cap.
12. Close the DISC with the open end of the protection cap (which is placed in the right hole of the organiser)
13. Checking the drained dialysate and disposal.

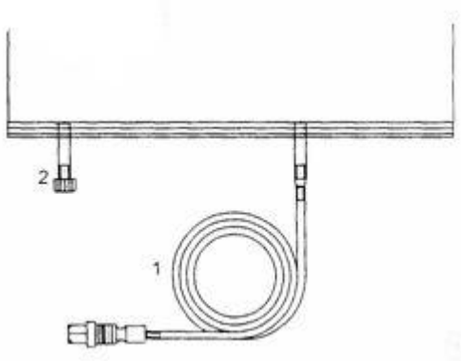


Sleep safe system (for the set up of the sleep.safe system please refer to its operating instructions):

1. Preparation of the solution
   - Check the solution bag (label, expiry date, clearness of the solution, bag, and overwrap not damaged).
   - Place the bag on a solid surface.
   - Open the overwrap of the bag.
   - Wash your hands with an antimicrobial washing lotion.

- Check whether the solution is clear and that the bag is not leaking.

2. Unroll tubing (1) of bag.
3. Remove the protection cap.
4. Insert connector in free sleep safe tray port.
5. The bag is now ready for use with the sleep safe set.



When adding drugs, use aseptic technique, mix thoroughly and after checking for the absence of any turbidity, which may occur due to incompatibilities, the peritoneal dialysis solution must be used immediately.

7 MARKETING AUTHORISATION HOLDER

Fresenius Medical Care Deutschland GmbH
D-61346 Bad Homburg
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8 MARKETING AUTHORISATION NUMBER

PA0953/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 June 2000

Date of last renewal: 24 June 2004