I.B.SUMMARY OF PRODUCT CHARACTERISTICS

1.Name of the medicinal product

CAPD/DPCA 2
CAPD/DPCA 3
CAPD/DPCA 4

2. Qualitative and quantitative composition

1 litre contains:

	CAPD/DPCA 2	CAPD/DPCA 3	CAPD/DPCA 4
Sodium chloride	5.786 g	5.786 g	5.786 g
Sodium (L)-lactate	3.925 g	3.925 g	3.925 g
Calcium chloride 2 H_2O	0.2573 g	0.2573 g	0.2573 g
Magnesium chloride 6 H_2O	0.1017 g	0.1017 g	0.1017 g
Glucose monohydrate	16.5 g	46.75 g	25.0 g
≙ anhydrous glucose	15.0 g	42.5 g	22.73 g
Na^+	134 mmol/l	134 mmol/l	134 mmol/l
Ca^{++}	1.75 mmol/l	1.75 mmol/l	1.75 mmol/l
Mg^{++}	0.5 mmol/l	0.5 mmol/l	0.5 mmol/l
Cl^-	103.5 mmol/l	103.5 mmol/l	103.5 mmol/l
Lactate	35 mmol/l	35 mmol/l	35 mmol/l
Theoretical osmolarity	358 mOsm/l	511 mOsm/l	401 mOsm/l
pH≈	5.5	5.5	5.5

3. Pharmaceutical form

Solution for peritoneal dialysis

4. Clinical particulars

4.1 Therapeutic indications

For use in patients with end-stage chronic renal failure of various genesis.

4.2 Posology and method of administration

Unless otherwise prescribed, 2000 ml of solution are infused per treatment. If at the beginning of treatment, pain due to abdominal distension occurs, the dose per treatment can be temporarily reduced to 500 - 1500 ml.

Children should be given doses between 500 and 1500 ml (30 – 40 ml/kg body weight) per treatment, depending on age, height and weight.

In large adults and/or patients who tolerate a larger filling volume, even 2500 or even 3000 ml may be used. If the dose is given by a machine as in intermittent or continuous cycling peritoneal dialysis, the use of larger volume bags is recommended.

Method and duration of use

Dwell times of 4 - 8 hours, a dose of 2000 ml of solution is used four times in every 24 hour period (total dose 8000 ml), or smaller or larger doses as appropriate (dose given merely as a guide, dosage must be adjusted for the individual patient).

Warm the ready-to-use solution to body temperature and then infuse into the peritoneal cavity through a peritoneal dialysis catheter, administration time per dose 5-20 minutes. The dose remains in the peritoneal cavity for 4-8 hours (equilibration time) and is then drained and replaced.

CAPD/DPCA 2	CAPD/DPCA 3	CAPD/DPCA 4
Depending on the fluid status and electrolyte concentration, CAPD/DPCA 2 is used in combination with another peritoneal dialysis solution of higher glucose concentration (i.e. of higher osmolarity) or other potassium or sodium concentrations.	Depending on the fluid status and electrolyte concentration, CAPD/DPCA 3 is used in combination with another peritoneal dialysis solution of lower glucose concentration (i.e. of lower osmolarity) or other potassium or sodium concentrations. To protect the peritoneum and to avoid the danger of dehydration, high glucose concentrations, as present in CAPD/DPCA 3, should be used as sparingly as possible. Generally, one or two exchanges with high glucose concentration are sufficient, other solutions of lower glucose concentration are used for the other exchanges.	Depending on the fluid status and electrolyte concentration, CAPD/DPCA 4 is used in combination with another peritoneal dialysis solution of lower or higher glucose concentration (i.e. of lower or higher osmolarity) or other potassium or sodium concentrations.

Treatment is carried out on a daily basis using the specified dosage. It is continued for as long as renal replacement therapy is required.

4.3 Contra-indications

For these specific solutions:
For CAPD/DPCA 2, 3 and 4: hypokalaemia, hypercalcaemia.
For CAPD/DPCA 3 additionally: hypovolaemia, arterial hypotension.

For peritoneal dialysis in general:
Peritoneal dialysis must not be commenced in the presence of one or more of the following diseases:

- Diseases which have an effect on the integrity of the abdominal wall or of the peritoneal cavity, such as: recent abdominal injury, abdominal burns, other extensive inflammatory conditions of the abdominal skin (dermatitis) in the region of catheter exit site, peritonitis; abdominal perforation; a history of abdominal operations with fibrous adhesions, inflammatory bowel diseases (Crohn's disease, ulcerative colitis, diverticulitis), intra-abdominal tumours, recent abdominal surgery, ileus, abdominal hernias; internal or external abdominal fistulae;
- Pulmonary diseases, especially pneumonia;
- Sepsis;
- Laktacidosis
- Cachexia and extreme weight loss, particularly when adequate nutrition is impossible;
- In rare cases of uraemia which can no longer be managed by peritoneal dialysis;
- Extreme hyperlipidaemia
- In patients who are physically or mentally incapable of performing peritoneal dialysis as instructed by the physician.

4.4 Special warnings and special precautions for use

Electrolyte imbalance, e.g. caused by vomiting or diarrhoea, may necessitate the temporary use of a potassium-containing peritoneal dialysis solution.

In hypercalcaemia, e.g. resulting from high doses of calcium-containing phosphate binders and/or vitamin D, a temporary or permanent change to a solution with a lower calcium content may be necessary.

The treatment volume should be reduced in children, according to age, height and body weight (see also Posology). In the elderly, the increased incidence of hernias should be considered before beginning treatment.

Exact records of fluid balance and body weight must be kept to avoid dehydration or hyperhydration with potentially life-threatening consequences. Regular monitoring of physical findings, electrolytes, creatinine and urea concentrations, serum protein, the level of blood sugar and if necessary, other laboratory parameters (e.g. blood gases, acid-base balance) is also essential.

In diabetics, the daily insulin dose must be adjusted to take account of the increased glucose uptake. Regular checks on blood glucose are therefore required.

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

Plastic containers may occasionally become damaged during transport from the manufacturer to the dialysis centre or during storage in the hospital. This can result in fungiform or bacterial contamination, with growth of micro-organisms in the dialysis solution. All containers should therefore be carefully inspected for damage prior to connection and use of the solution for peritoneal dialysis. Any damage, however minor, to the closure, container welds or corners, must be noted, because of possible contamination.

Bags with cloudy contents must never be used. Only use the peritoneal dialysis solution if the container and closure exhibit no signs of damage. The material should be set aside for examination, including a bacteriological investigation, if necessary.

Only use CAPD/DPCA 2, 3 and 4 if the solution is clear and the container is undamaged. Any unused portion of the solution is to be discarded. The peritoneal dialysis solution CAPD/DPCA 2, 3 and 4 is not to be used for intravenous infusion.

4.5 Interaction with other medicinal products and other forms of Interaction

As a general principle, it should be borne in mind that medication given concurrently might pass into the peritoneal dialysis solution and be lost from the body; hence its dosage may require adjustment.
The possibility of hypercalcaemia should be considered on concomitant administration of calcium compounds or vitamin D.

Simultaneous administration of diuretics may be worthwhile to support residual excretion by the kidneys, but can also cause disturbances of fluid and electrolyte balance. Potassium levels must be monitored particularly closely during concurrent digitalis therapy, as the sensitivity to these drugs is increased in patients with hypokalaemia.

4.6 Use during pregnancy and lactation

Peritoneal dialysis treatment should only be carried out in the later stages of pregnancy after careful weighing of the benefits and risks.

4.7 Effects on ability to drive and use machines

When CAPD/DPCA 2, 3 and 4 is used as directed, it does not impair driving ability or the operation of machines.

4.8 Undesirable effects

CAPD/DPCA 2, 3 and 4 is a solution of electrolytes whose composition is essentially similar to that found in human blood.

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

Undesirable effects of the procedure:
Very common complications of any peritoneal dialysis therapy, including CAPD/DPCA 2, 3 and 4, are peritonitis and infections of the catheter exit site and tunnel. Untreated peritonitis can lead to sepsis. Symptoms of an incipient peritonitis are cloudiness of the dialysate, abdominal pain, and fever.

Pathogens and white blood cell count in the dialysate must be determined; lack of any elevation in leukocytes does not necessarily exclude peritonitis if other symptoms are present. It is essential to institute treatment (intraperitoneal and/or systemic) without delay, being in accordance with the latest state of scientific knowledge and using agents effective against the presumed pathogen, even before culture results are available. Once these are known, therapy should be adjusted appropriately.

A relative loss of proteins (5 – 15 g/day) and amino acids (1.2 – 3.4 g/day) is unavoidable, likewise water-soluble vitamins may also be lost. A deficiency of these substances must be countered by adequate dietary intake. Hypoproteinaemia may occur if protein intake does not compensate for the protein loss.

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.

In addition, distension and a feeling of fullness (abdominal complaints), in- and outflow disturbances of the dialysis solution, hernia, pain in the shoulder, dyspnoea due to elevation of the diaphragm, diarrhoea, and constipation may occur.

Undesirable effects of the solution:

The dialysis solution may cause fluid and electrolyte imbalance, e.g. hypokalaemia.

Hypercalcaemia can occur if calcium intake is increased, e.g. through concomitant use of calcium-containing phosphate binders. These electrolyte disorders can be corrected by changing to other peritoneal dialysis solutions (hypercalcaemia) or a changed diet (hypokalaemia).

In terms of fluid balance, dehydration or hyperhydration may develop. Severe dehydration, (especially on treatment with solutions of higher glucose concentration) may take the form of low blood pressure, increased heart rate, dizziness and muscle cramps; the opposite, hyperhydration, may cause increased body weight, high blood pressure, swollen legs and shortness of breath.

Disorders of lipid metabolism (dyslipoproteinaemia and hyperlipidaemia) may occur or be exacerbated.

Because of the continuous uptake of glucose from the dialysis solution obesity might rarely occur if the diet of the patient is not adapted to the increased caloric load.

4.9 Overdose

To date, no emergency situations specific to this solution have been reported.

Excessive inflow of dialysis solution can be easily drained into an empty bag. If however, bag exchanges have been carried out too frequently, states of dehydration and/or disorders of blood electrolyte content (electrolyte imbalance) can occur.

If an exchange has been forgotten, then as a rule the dwell times of the next bags should be reduced in such a way that the total amount of dialysis solution required per day (e.g. 4 x 2000 ml) is still achieved. Incorrect balancing can lead to hyper- or dehydration and electrolyte disturbances.

The most likely consequence of an overdosage with CAPD/DPCA 2, 3 and 4 is dehydration. Underdosage or discontinuation of treatment can lead to life-threatening hyperhydration with peripheral oedema and cardiac decompensation and/or other symptoms of uraemia, which may endanger life.

The generally accepted rules of emergency and intensive medicine are applied. The patient may require urgent haemodialysis.

5. Pharmacological properties

5.1. Pharmacodynamic properties

CAPD/DPCA 2, 3 and 4 represents a lactate-buffered, glucose-containing electrolyte solution indicated for the intraperitoneal administration for the treatment of end-stage renal failure of any origin by e.g. peritoneal dialysis (PD).

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 uremic patients to enable renal function substitution therapy by means of intraperitoneal substance and fluid exchange. Substances which are normally eliminated with the urine, like uremic waste products, such as urea and creatinine, inorganic phosphate, uric acid, other solutes and water, are removed from the body into the dialysis solution.

The homeostasis of the hydration status can be maintained by the administration of different glucose-concentrations in the solution effecting the fluid removal (ultrafiltration).

Metabolic acidosis secondary to end-stage renal failure is counterbalanced by the presence of lactate in the solution.
The complete metabolism of lactate results in the generation of bicarbonate.

5.2 Pharmacokinetic properties

Uremic waste products (urea, creatinine, uric acid), inorganic phosphate, and electrolytes like sodium, potassium, calcium and magnesium are removed from the body to the dialysis solution by diffusion and/or convection.

Dialysate glucose used as an osmotic agent in CAPD/DPCA 2, 3 and 4 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 during a dwell time of 6 hours.

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.

5.3 Preclinical safety data

As all of the constituents are physiological substances, no toxicological investigations have been performed. Clinical use of solutions for peritoneal dialysis of similar composition has given no indications of a 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 drugs must only be added on prescription by a physician. After thorough mixing and checking for the absence of any turbidity the peritoneal dialysis solution must be used immediately (no storage).

6.3 Shelf-life

Two years

6.4 Special precautions for storage

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

CAPD/DPCA 2, 3 and 4 should be stored out of the reach of children!

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, system connector (DISC) with a rotable switch (polypropylene), and a drainage bag, also made of polyolefine multi layer film.

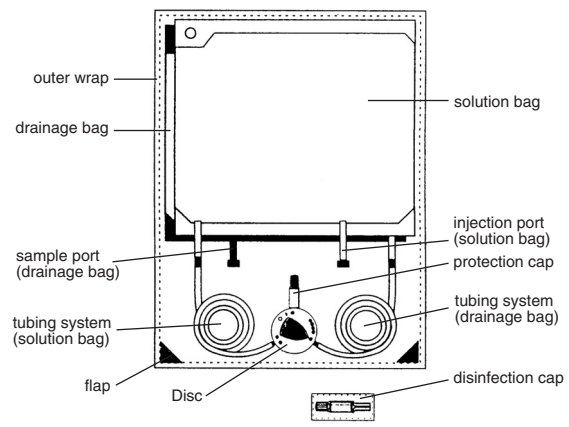
Sleep safe:
The sleep safe system is provided as a single bag system consisting of a non-PVC solution bag made of a multi layer polyolefine foil, a tubing system, a bag connector both also made of polyolefines and an injection port made of polyolefine/synthetic rubber.

6.6 Instructions for handling and disposal

See Section 4.2.

Instruction for use of the stay•safe system:

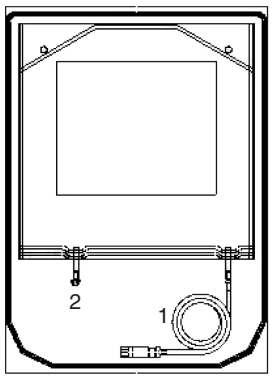
1. Check the solution bag (label, the expiry date and ensure that the solution is clear) – open the outer wrap and package of the disinfection cap.
2. Cleaning hands with an antimicrobial washing solution.
3. Place the DISC into the organiser (suspend solution bag from the upper hole of the infusion 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
    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.



Instruction for use of the sleep•safe system:

1. Unroll tubing (1) of bag.
2. Insert connector in free *sleep•safe*™ tray port.
3. The bag is now ready for use with the *sleep•safe*™ set.

A separate injection can be effected through the second injection port (2).



7. Marketing authorisation holder

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