SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium,
Solution for peritoneal dialysis

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium is delivered in a double chamber bag. One chamber contains the alkaline hydrogen carbonate solution, the other chamber contains the acidic glucose-based electrolyte solution. Mixing of both solutions by opening the median seam between the two chambers results in the ready-to-use solution.

BEFORE RECONSTITUTION

1 litre of acidic glucose based electrolyte solution contains:
active substances:

Calcium chloride dihydrate	0.5145	g
Sodium chloride	11.57	g
Magnesium chloride hexahydrate	0.2033	g
Glucose monohydrate	50.0	g
(equivalent to glucose)	45.46	g

This corresponds to

Ca^{2+}	3.5	mmol/l
Na^{+}	198.0	mmol/l
Mg^{2+}	1.0	mmol/l
Cl^{-}	209.0	mmol/l

1 litre of alkaline hydrogen carbonate solution contains:
active substances:

Sodium hydrogen carbonate	5.88	g

This corresponds to

Na^{+}	70.0	mmol/l
HCO_3^{-}	70.0	mmol/l

AFTER RECONSTITUTION

1 litre of the ready-to-use solution contains:
active substances:

Calcium chloride dihydrate	0.2573	g
Sodium chloride	5.786	g
Sodium hydrogen carbonate	2.940	g
Magnesium chloride hexahydrate	0.1017	g
Glucose monohydrate	25.0	g
(equivalent to glucose)	22.73	g

This corresponds to

Ca^{2+}	1.75	mmol/l
Na^{+}	134	mmol/l
Mg^{2+}	0.5	mmol/l
Cl^{-}	104.5	mmol/l
HCO_3^{-}	34	mmol/l
Glucose	126.1	mmol/l

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for peritoneal dialysis
Clear and colourless solution

Theoretical osmolarity: 401 mOsm/l
pH ≈ 7.40

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

End-stage (decompensated) chronic renal failure of any origin treated with peritoneal dialysis.

4.2 Posology and method of administration

Posology
bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium is exclusively indicated for the 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)
Adults:
Unless otherwise advised, patients will receive an infusion of 2000 ml solution per exchange four times a day. After a dwell time between 2 and 10 hours the solution will be drained.

Adjustment of dosage, volume and number of exchanges will be necessary for individual patients.

If dilation pain occurs at the commencement of peritoneal dialysis treatment, the solution volume per exchange should be temporarily reduced to 500-1500 ml.

In large patients, and if residual renal function is lost, an increased volume of dialysis solution will be necessary. In these patients, or patients who tolerate larger volumes, a dose of 2500 ml solution per exchange may be given.

Children:
In children the solution volume per exchange should be prescribed according to age and body surface area (BSA).
For initial prescription, the volume per exchange should be 600-800 ml/m^2 BSA with 4 (sometimes 3 or 5) exchanges per day. It can be increased up to 1000-1200 ml/m^2 BSA depending on tolerance, age and residual renal function.

Automated peritoneal dialysis (APD)
If a machine (sleep safe cycler) is used for intermittent or continuous cyclic peritoneal dialysis larger volume bags (3000 or 5000 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.

Adults:
Typically patients spend 8-10 hours a night cycling. Dwell volumes range from 1500 to 3000 ml and the number of cycles usually varies from 3 to 10 per night. The amount of fluid used is typically between 10 and 18 l but can range from 6 to 30 l. The cycler therapy at night is usually combined with 1 or 2 exchanges during the daytime.

Children:
The volume per exchange should be 800-1000 ml/m^2 BSA with 5-10 exchanges overnight. It can be increased up to 1400 ml/m^2 BSA depending on tolerance, age and residual renal function.

There are no special dosage recommendations for elderly patients.

Depending on the required osmotic pressure, bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium can be used sequentially with other peritoneal dialysis solutions with lower or higher glucose content (i.e. with lower or higher osmolarity).

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. These solutions should be used cautiously to protect the peritoneal membrane and to prevent dehydration and in order to keep the glucose burden as low as possible.

bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium contains 22.73 g glucose in 1000 ml solution. According to the dosage instruction up to 45.46 g glucose are supplied to the body with each bag.

Peritoneal dialysis is a long-term therapy involving repeated administrations of single solutions.

Method and duration of administration
Patients should 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.

For the step-by-step instruction for use please be referred to section 6.6.

Continuous ambulatory peritoneal dialysis (CAPD)
The solution bag is first warmed up to body temperature.
The heating will be performed with a heating plate. The time for heating is about 120 minutes for a 2000 ml bag at a temperature of 22º C. Details can be read in the instruction manual of the heating plate. A microwave oven must not be used due to the risk of local overheating.

Depending on physician's instructions, the dose should dwell in the peritoneal cavity for 2 to 10 hours (equilibrium time), and then be drained.

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 with 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
bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium must not be used in patients with severe hypokalaemia, severe hypercalcaemia, hypovolaemia and hypotension.

This peritoneal dialysis solution must not be used for intravenous infusion.

For peritoneal dialysis in general
Peritoneal dialysis should not be commenced in case of
- recent abdominal surgery or injury, a history of abdominal operations with fibrous adhesions, severe abdominal burns, bowel perforation,
- extensive inflammatory conditions of the abdominal skin (dermatitis),
- inflammatory bowel diseases (Crohn's disease, ulcerative colitis, diverticulitis),
- localized 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 the ingestion of adequate protein is not guaranteed,
- patients who are physically or mentally incapable of performing PD as instructed by the physician.

If any of the above mentioned disorders develops during the peritoneal dialysis treatment, the attending physician has to decide on how to proceed.

4.4 Special warnings and precautions for use

bicaVera may only be administered after careful benefit-risk assessment in:
- patients with loss of electrolytes due to vomiting and/or diarrhoea (a temporary change to a peritoneal dialysis solution containing potassium might then become necessary).
- patients with hypercalcaemia, e.g. due to the administration of calcium-containing phosphate binders: A transient or permanent change to a peritoneal dialysis solution with a lower calcium concentration should be considered.
- patients receiving digitalis therapy: Regular monitoring of the serum potassium level is mandatory. Severe hypokalaemia may necessitate the use of a potassium-containing dialysis solution besides dietary counselling.

The natural metabolic acidosis due to renal failure might not be totally compensated by the 34 mmol/l bicarbonate level of the final solution. Acidosis might be associated with undesirable effects e.g. malnutrition.

A loss of proteins, amino acids, and water-soluble vitamins occurs 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- and dehydration,
- serum sodium, potassium, calcium, magnesium, phosphate, acid base status and blood proteins
- serum creatinine and urea,
- parathormone and other indicators of bone metabolism,
- blood sugar,
- residual renal function in order to adapt the peritoneal dialysis

Elderly patients
The increased incidence of hernia should be considered in elderly patients prior to the start of peritoneal dialysis.

4.5 Interaction with other medicinal products and other forms of interaction

The use of this peritoneal dialysis solution can lead to a loss of efficacy of other medicinal products 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. Potassium levels must be monitored particularly closely during concurrent digitalis therapy.

The concomitant administration of calcium-containing drugs as well as vitamin D may cause hypercalcaemia.
The use of diuretic agents may help maintain residual diuresis, but may also result in water and electrolyte imbalances.
In diabetic patients the daily dose of blood sugar reducing medication must be adjusted to the increased glucose load.

4.6 Fertility, pregnancy and lactation

Fertility
No data available.

Pregnancy
There are no clinical data available from use of bicaVera solutions in pregnant women. Animal studies are insufficient with respect to reproductive and developmental toxicity (see section 5.3). bicaVera solution should only be used during pregnancy when the benefit to the mother clearly outweighs the potential risks to the fetus (see section 4.4).

Lactation
It is not known whether bicaVera solution ingredients are excreted in human milk.
bicaVera solution should only be used in lactating women, when the benefit to the mother clearly outweighs the potential risks to the infant.

4.7 Effects on ability to drive and use machines

bicaVera has no or negligible influence on the ability to drive and to use machines.

4.8 Undesirable effects

bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium is an electrolyte solution which composition is similar to blood.
In addition the physiological buffer bicarbonate is used.

Possible adverse reactions may result from the peritoneal dialysis itself or may be induced by the peritoneal dialysis solution.

The adverse drug reactions are ranked under the headings of reporting frequency, using the following convention:

very common	≥1/10
common	≥1/100 to <1/10
uncommon	≥1/1,000 to <1/100
rare	≥1/10,000 to <1/1,000
very rare	<1/10,000
not known	cannot be estimated from the available data

Potential adverse reactions of the peritoneal dialysis solution:

System Organ Class	Preferred Term	Frequency
Metabolism and nutrition disorders	Increased blood sugar levels	common
	Hyperlipidaemia	common
	Increase in body weight due to the continuous uptake of glucose from the peritoneal dialysis solution	common
Cardiac and vascular disorders	Hypotension	uncommon
	Tachycardia	uncommon
	Hypertension	uncommon
Respiratory, thoracic and mediastinal disorders	Dyspnoea	uncommon
Renal and urinary disorders	Electrolyte disturbances, e.g. Hypokalaemia	very common
	Electrolyte disturbances, e.g. Hypercalcaemia	uncommon
General disorders and administration site conditions	Dizziness	uncommon
	Oedema	uncommon
	Disturbances in hydration	uncommon

Potential adverse reactions of the treatment mode

System Organ Class	Preferred Term	Frequency
Infections and infestations	Peritonitis	very common
	Skin exit site and tunnel infections	very common
Respiratory, thoracic and mediastinal disorders	Dyspnoea caused by the elevated diaphragm	not known
Gastrointestinal disorders	Diarrhoea	uncommon
	Constipation	uncommon
	Hernia	very common
	Abdominal distension and sensation of fullness	common
Injury, poisoning and procedural complications	In- and outflow disturbances of the dialysis solution	common
	Shoulder pain	common

Peritonitis
is indicated by a cloudy effluent. Later abdominal pain, fever, and general malaise may develop or, in very rare cases, sepsis. The patient should seek medical advice immediately. The bag with the cloudy effluent should be closed with a sterile cap and assessed for microbiological contamination and white blood cell count.

Skin exit site and tunnel infections
are indicated by redness, oedema, exudations, crusts and pain at the catheter exit site. In case of skin exit site and tunnel infections the attending physician should be consulted as soon as possible.

Disturbances in hydration
is indicated by a rapid decrease (dehydration) or increase (overhydration) in body weight.
Severe dehydration might occur when using solutions of higher glucose concentration.

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 Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

Any excess of dialysis solution infused in the peritoneal cavity can easily be drained in the drainage bag. In case of too frequent exchanges dehydration and/or electrolyte disturbances might result which necessitate immediate medical attention.

If one or more of the daily exchanges are missed or a too small solution volume has been administered, overhydration and electrolyte disturbances may develop.

Interruption or discontinuation of treatment may result in life-threatening overhydration and uraemia.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:	Peritoneal dialytics, hypertonic solutions
ATC-code:	B05D B

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

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

bicaVera 2.3 % Glucose, 1.75 mmol/l Calcium contains bicarbonate - the physiological buffer - instead of lactate or acetate.

5.2 Pharmacokinetic properties

No animal studies have been performed with the intraperitoneal application of bicarbonate-containing bicaVera solutions. Clinical studies in patients on bica*Vera* have shown that dialysate bicarbonate equilibrates with blood bicarbonate within a two-hour dwell time.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, single dose toxicity and repeated dose toxicity.
The electrolytes and glucose included in bicaVera are physiological components in human plasma. According to the available data and the clinical experience with these substances no toxic effects are expected to occur as long as the indications, contraindications and dosage recommendations are adequately observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid
Sodium hydroxide
Carbon dioxide
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

Shelf life within the container: 2 years
Shelf life of the ready-to-use solution prepared as described in section 6.6 and without any additional drugs: 24 hours

6.4 Special precautions for storage

Do not store below 4°C.

6.5 Nature and contents of container

Double-chamber bag:
One chamber contains the alkaline hydrogen carbonate solution; the other chamber contains the acidic glucose-based electrolyte solution. Mixing of both solutions (ratio 1:1) by opening the median seam between the two chambers results in the ready-to-use solution.

stay safe:
The stay safe system is provided as a double bag system consisting of a double-chamber solution bag and a drainage bag, both with injection units, a transfer tubing system and a system connector. All components are based on polypropylene. The bags and tubings also contain synthetic elastomers. The solution bag is laminated in addition by polyester. The stay safe system is wrapped up in an outer bag made of polyolefins.

sleep safe:
The sleep safe system is provided as a single bag system consisting of a double-chamber solution bag with an injection unit, a transfer tubing system and a bag connector. All components are based on polypropylene. The bags and tubings also contain synthetic elastomers. Further materials of the solution bag are polyester and polyamide. The sleep safe system is wrapped up in an outer bag made of polyolefines.

Pack sizes:

stay safe :	sleep safe :
4 bags à 1500 ml	4 bags à 1500 ml
4 bags à 2000 ml	4 bags à 2000 ml
4 bags à 2500 ml	4 bags à 2500 ml
4 bags à 3000 ml	4 bags à 3000 ml
	2 bags à 5000 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Disposal
No special requirements for disposal

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. In case of doubt the attending physician should decide on the use of the solution.

The overwrap should only be removed before administration.

Do not use before the two solutions have been mixed.

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

Instruction for use of the stay safe system:
The solution bag is first warmed to body temperature. This should be done by using an appropriate heater tray. The heating time for a 2000 ml bag with a starting temperature of 22°C is approximately 120 min. More detailed information can be obtained from the operating instructions of the bag warmer. The use of microwaves to warm the solution is not recommended due to the risk of local overheating. After warming the solution you can start with the exchange of the bags.

1. Preparation of the solution
   - Place the bag on a solid ground
   - Open the overwrap of the bag and seal of the disinfection cap.
   - Control the solution bag (label, expiry date, clearness of the solution, integrity of the bag).
   - Wash your hands with an antimicrobial washing lotion.
   - Roll up the bag from one of the upper ends until the middle seam opens. The solutions in the two chambers are mixed automatically.
   - Then roll up the bag from the upper edge, until the peel seam of the lower triangle is completely opened.
   - The ready-to-use solution should be used immediately, but within a maximum of 24 hours after mixing!
2. Preparation of the bag exchange
   - Hang the solution bag on the upper hook of the infusion pole, unroll the tubing line of the solution bag, and place the DISC into the organizer. After unrolling the tubing line to the drainage bag, hang the drainage bag on the lower hook of the infusion pole and place the disinfection cap into the organizer.
   - Place catheter adapter into the organizer.
   - Disinfect your hands and remove the protection cap of the DISC.
   - Connect catheter adapter to the DISC.
3. Outflow
   - Open the catheter clamp. The outflow starts.

   ⇒ Position ●
4. Flush
   - Flush the drainage bag with fresh solution (approximately 5 seconds)

   ⇒ Position ●●
5. Inflow
   - Connect the solution bag with the catheter.

   ⇒ Position ○◑●
6. Security step

- Close the catheter adapter by putting in the PIN

⇒ Position ●●●●

7. Disconnection
   - Remove the catheter adapter from the DISC and screw the new disinfection cap to the catheter adapter
8. Closure of the DISC
   - Close the DISC with the open end of the protection cap of the used disinfection cap, which is placed in the right hole of the organizer.
9. Check the drained dialysate and dispose of it.

Instruction for use of the sleep safe system:
With the sleep safe system for automated peritoneal dialysis (APD) the solution is warmed automatically in the machine.

1. Preparation of the solution
   - Check the solution bag (label, expiry date, clearness of the solution, bag and overwrap are not damaged, peel seams are intact).
   - Place the bag on a solid surface.
   - Open the overwrap of the bag.
   - Wash your hands with an antimicrobial washing lotion.
   - Unfold middle seam and bag connector.
   - Roll up the bag, which is lying on the overwrap, from the diagonal end towards the bag connector. The middle peel seam will open.
   - Continue until the peel seam of the small chamber opens as well.
   - Check that all peel seams are completely open.
   - Check that the solution is clear and that the bag is not leaking.
2. Unroll tubing of bag.
3. Remove the protection cap and insert the bag connector in one of the free tray ports of the sleep safe cycler.
4. The bag is now ready for use with the sleep safe set.

Medicinal products must be added under aseptic conditions only when medically prescribed.
Because of the risk of incompatibility between the dialysis solution and the added medicinal products only the following medicinal products may be added up to the mentioned concentration if indicated by the attending physician: heparin 1000 I.U./l, insulin 20 I.U./l, vancomycin 1000 mg/l, teicoplanin 400 mg/l, cefazolin 500 mg/l, ceftazidime 250 mg/l, gentamycin 8 mg/l. After thorough mixing and checking for the absence of any turbidity the peritoneal dialysis solution must be used immediately (no storage).

7. MARKETING AUTHORISATION HOLDER

Fresenius Medical Care Deutschland GmbH
Else-Kröner-Straße 1
61352 Bad Homburg
Germany

8. MARKETING AUTHORISATION NUMBER

PL13689/0010

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Date of latest renewal: 14/05/2011

10. DATE OF REVISION OF THE TEXT

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