Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cifoban 136 mmol/l solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Cifoban is provided in a bag with 1500 ml ready-to-use solution.

1000 ml solution contains:

Sodium citrate 40.0 g
Na^+ 408 mmol
$Citrate^{3-}$ 136 mmol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion

Extracorporeal use. To be infused into the extracorporeal blood circuit only.

The solution is clear and colourless and practically free from particles.

Theoretical osmolarity: 544 mOsm/l
pH: 7.1 – 7.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cifoban is used for regional citrate anticoagulation (RCA) in continuous venovenous haemodialysis (CVVHD), continuous venovenous haemodiafiltration (CVVHDF), sustained low efficiency (daily) dialysis (SLEDD) and therapeutic plasma exchange (TPE) via membrane plasma separation.

Cifoban is indicated in adults and children of all age groups (except preterm newborn infants).

4.2 Posology and method of administration

Cifoban must be prescribed only by a physician competent in the application of RCA in the specific treatment mode of CVVHD, CVVHDF, SLEDD and/or TPE. For the paediatric population, Cifoban must be prescribed and monitored by physicians competent in the aforementioned treatment modes in children.

Posology

Adults
The pre-filter infusion rate of Cifoban is to be titrated proportional to the blood flow of the extracorporeal circuit to achieve a sufficient suppression of ionised calcium of the blood within the filter as per applied RCA protocol. Generally, a post-filter ionised calcium concentration below 0.3-0.35 mmol/l is to be targeted, which is usually achieved with dosing of 4-5 mmol of citrate per litre of treated blood. The required Cifoban flow (in ml/min) can be calculated by multiplying the intended citrate dosing with the blood flow (in ml/min) and dividing by 136 mmol/l (i.e., the citrate concentration of Cifoban). The patient's systemic ionised calcium concentration is to be maintained in the normal physiologic range, which commonly requires calcium supplementation.

The application volume of Cifoban in adult patients must not exceed 10.4 litre/day. The extracorporeal blood flow must be sufficient to reach the therapy targets but be kept low enough to avoid unnecessary citrate infusion and promote clearance of

citrate within the applied filter. This mitigates the risk of citrate overload and citrate accumulation (see section 4.4). Higher blood flows in combination with a lower dosing of Cifoban may unnecessarily reduce filter patency Ideally, the composition of the dialysis and substitution fluids within the indicated treatment protocol, calcium-free, low sodium and low-bicarbonate solutions need to be considered. This is recommended in view of Cifoban associated sodium and buffer supply per applied protocol.

A calcium-free dialysis solution is to be considered particularly for continuously applied therapies. A calcium-containing dialysis solution can be considered for SLEDD when a suitable calcium-free solution is not available. In this case, a higher post-filter ionised calcium concentration may be accepted in view of the relatively short duration of treatment or alternatively Cifoban may be dosed to a higher concentration per litre of treated blood. Accepting higher post-filter ionised calcium concentrations can likewise be appropriate in TPE, especially when the substitution fluid contains citrate (see section 4.4). Cifoban is then to be dosed to a lower concentration per litre of treated blood.

When used in combination with a calcium-free dialysis solution for CVVHD or CVVHDF having a sodium content of 133 mmol/l and bicarbonate content of 20 mmol/l, the citrate amount added to the blood before entering the dialysis filter is to be targeted to 3 to 5 mmol/l of blood during CVVHD and to 3 to 5.5 mmol/l blood during CVVHDF treatment modes, respectively. Similar dosing guidance may be applicable with other treatment protocols.

Special populations

Patients with impaired citrate metabolism
Cifoban can be applied in patients with a risk of having impaired citrate metabolism (e.g. shock with severe lactic acidosis, severe liver failure).

Treatment is to be initiated with a sufficiently low citrate dose.

When treated with CVVHD or CVVHDF at a blood flow not exceeding 100-120 ml/min, the citrate load generally is kept sufficiently low. The citrate dosing can be initiated at 4-5 mmol/l blood, as per protocol, and may only have to be reduced upon clear signs of citrate accumulation (please refer to section 4.4).

When treated with SLEDD at a blood flow not exceeding appr. 150-200 ml/min, an at least equal dialysate flow, and a treatment duration not extending beyond 12 hours, the patient citrate load generally is kept sufficiently low. When calcium-containing dialysate is applied, the citrate dosing can be initiated at up to 6-7 mmol/l blood, as per protocol, and may only have to be reduced upon clear signs of citrate accumulation (please refer to section 4.4).

In TPE, filter citrate clearance is generally limited, and comparatively lower, due to maximum acceptable filtration fractions. Citrate exposure may be further increased by using fresh frozen plasma (FFP) for the exchange. A blood flow not exceeding 100-120 ml/min is recommended when exchanging with FFP. The citrate dosing can be initiated at 3-4 mmol/l blood, as per protocol, and may only have to be reduced upon clear signs of citrate accumulation (please refer to section 4.4).

In all these therapies, intensified monitoring to prevent the development of citrate accumulation (see section 4.4) is recommended.

Geriatric population
Elderly patients may be at risk of impaired citrate metabolism. No dose reduction is required. Frequent monitoring to detect citrate accumulation (see section 4.4) is recommended.

Paediatric population

The safety and efficacy of Cifoban in preterm newborn infants has not yet been established. There are insufficient data available (see section 4.4).

Cifoban can be applied in children of all age groups (term neonates up to adolescents), when the patient citrate load remains sufficiently low. Of note, for the smallest patients, only scarce data is available. The used equipment must support paediatric application for the given weight, including the required low blood flows.

Blood flow and citrate dose guidance per age category

- Neonates up to toddlers (0 to 23 months): if a blood flow of 7-8 ml/kg/min (or higher) is required per used equipment, the citrate dosing is to be initiated at appr. 3 mmol/l blood.
- Children (2 to 11 years): the blood flow must not exceed 5-6 ml/kg/min; the citrate dosing can be initiated at appr. 4 mmol/l blood, as per protocol.
- Adolescents (12 to 17 years): the blood flow must be sufficient to reach the therapy targets, and generally not exceed blood flows in adults of similar weight. The citrate dosing can be initiated at appr. 4 mmol/l blood, as per protocol.

The citrate dosing may have to be reduced upon clear signs of citrate accumulation (please refer to section 4.4). When treated with CVVHD or CVVHDF a post-filter ionised calcium concentration below 0.3-0.35 mmol/l is preferably targeted, but this target depends on the feasible citrate dose.

Intensified monitoring to prevent the development of citrate overload and citrate accumulation (see section 4.4) is required in neonates up to toddlers and recommended in children and adolescents.

Furthermore, please refer to the posology considerations as given above for patients with impaired citrate metabolism. To limit the patient citrate load, a modest exchange rate is required when an exchange with fresh frozen plasma is indicated, along with a parallel calcium substitution recommended to maintain a normal systemic ionised calcium concentration.

Maximum infusion volumes for exemplary term neonatal up to adolescent weights are given in the table below. Of note, typical daily application volumes remain clearly below these limits consequent to the use of moderate blood flows as described above.

Body weight (kg)	Maximum application volume (litre/day)
2.5	1.6
3	1.9
5	2.2
10	3.2
20	4.9
30	6.4
40	8.5
50 and more	10.4

Method of administration

Extracorporeal use. To be infused into the extracorporeal blood circuit only.

Infusion only by an integrated pump within the extracorporeal blood purification device, which is intended by its manufacturer for the infusion of a concentrated citrate solution in the pre-pump segment of the access tubing system ("blood access line"), to mitigate the risk of any inadvertent overdose (see section 4.9). The device must also remove the volume provided by Cifoban into the effluent, to prevent fluid overload (see section 4.8).

The special warnings and precautions in section 4.4 must be considered, especially those concerning monitoring and the need for additional substitutions.

Additionally:

- Cifoban must only be used in accordance with an appropriate protocol for RCA. It shall only be used by, or under the direction of, a physician competent in the application of RCA and by health care professionals who are sufficiently trained in the indicated therapies and in the application of the involved products.
- Handling instructions of the used extracorporeal blood purification device and the tubing system provided by the manufacturer must be adhered to.
- Cifoban can be used for RCA in an intensive care unit or under similar conditions, where it must be used under close medical supervision and continuous monitoring.

For instructions on handling of the medicinal product before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substance
- Known severely impaired citrate metabolism (see section 4.4 Citrate accumulation due to impaired metabolism)

4.4 Special warnings and precautions for use

Warnings

Monitoring frequencies of impacted patient serum values

The indicated therapies call for the close monitoring of the patient's haemodynamic status, fluid balance, glucose level, electrolyte and acid-base balance before and during treatment. The exact frequency depends on the status of the patient and how rapidly the treatment can invoke changes to the blood volume and composition of the patient: e.g., TPE can invoke these changes more rapidly than CVVHD. The treatment- and RCA protocol must reflect this.

When using Cifoban, these may include the following monitoring frequencies and particulars:

- The patient's ionised calcium, pH and bicarbonate, sodium, and lactate levels according to clinical need, must be measured at baseline or at least within 1 hour upon start of the therapy. Further exemplary measurement frequencies are 1-hourly for TPE, 3-4 hourly for SLEDD, up to 6-8-hourly for CVVHD and CVVHDF.
- When balanced solutions are used, pre- and post-treatment measurements (TPE, SLEDD) or daily measurements (CVVHD, CVVHDF) of magnesium and total calcium may suffice.
- More intensified monitoring generally calls for a frequency that is 2-4 times higher.
- A blood gas analyzer shall directly be accessible.
- A separate arterial access is preferred as a sampling location. A sampling port in the access line is often available, however, its use can result in false measurement results in the case of recirculation at the catheter tip.

If circuit ionised calcium monitoring is part of the applied RCA protocol, a respective sampling port is required. The RCA protocol can request a first measurement within 20-30 minutes after treatment initiation to confirm the correct circuit set-up and subsequent measurements after each adaptation of the Cifoban dose (wait > 5 minutes after adjustment before taking the sample for the establishment of the new ionised calcium concentration).

Citrate accumulation due to impaired metabolism

In children and in adult patients with reduced citrate metabolism, as for example in patients with reduced hepatic function, hypoxia (hypoxemia) or a disturbed oxygen metabolism, RCA can lead to citrate accumulation. Signs are ionised hypocalcaemia, an increased need for calcium substitution, a ratio of total over ionised calcium above 2.25 and/or metabolic acidosis. Early signs may include decreased lactate clearance during therapy. It may then become necessary to increase the dialysate flow, reduce the blood flow, reduce the citrate dosing, or stop using Cifoban for anticoagulation. Intensified monitoring is recommended.

Citrate overload

Cifoban is hypernatraemic and, once metabolised, a source of bicarbonate. When deciding on the composition of other fluids within the RCA protocol, low-sodium and low-bicarbonate concentrations are preferable (please refer to section 4.2 Posology and method of administration). Iatrogenic metabolic alkalosis and hypernatraemia may nevertheless develop and can be managed by reducing blood flow or, when covered by the applied RCA protocol, by increasing dialysate flow. These interventions reduce the patient sodium citrate load. Furthermore, for metabolic alkalosis, the controlled infusion of e.g. 0.9% sodium chloride can be considered. Similarly, for hypernatraemia the controlled infusion of e.g. 5% glucose can be considered. In both cases, the additional volume load shall be considered by the treating physician.

Alternatively, filter clogging (i.e. reduced filter permeability) can result in a citrate overload. Filter clogging could reduce removal of calcium, citrate, sodium, and other substances, and result in hypercalcaemia, metabolic alkalosis, hypernatraemia, and other deviations from the expected therapy effect. In such a situation, it is likely no longer possible to correct the abnormalities via the interventions mentioned above. The filter then needs to be changed.

For an inadvertent overdose of the medicinal product, please refer to section 4.9.

Insufficient citrate load

If the other solutions used in the RCA protocol overcompensate for the sodium and bicarbonate buffer provision of Cifoban, iatrogenic metabolic acidosis and hyponatraemia may develop. These serum imbalances can be managed by increasing blood flow or, when covered by RCA protocol, by decreasing dialysate flow. These interventions increase the patient sodium citrate load. Furthermore, persisting metabolic acidosis and hyponatraemia can be managed by the controlled infusion of a sodium hydrogen carbonate solution.

Prolonged patient immobilisation

Under RCA, the early sign of an ionised hypercalcaemia may be masked by a decrease in the calcium infusion rate. Especially patients in a prolonged immobilised position may undergo bone remodelling/demineralisation, resulting in the release of calcium from the bones. This can ultimately lead to bone fractures. In patients under RCA for longer than 2 weeks continuously, or in whom the calcium infusion rate is progressively decreasing, bone turnover markers must be closely monitored.

Early clotting despite RCA

Early clotting can occur despite adequate RCA in patients that are in a (suspected) hypercoagulant state (e.g., heparin induced thrombocytopenia type II). An appropriately chosen systemic anticoagulant may then be required. RCA may be used in addition to further improve filter patency.

Precautions

Intoxications that result in mitochondrial dysfunction

Patients with a known severe mitochondrial dysfunction (e.g. paracetamol and metformin intoxications) may be preferably treated with an alternative anticoagulant protocol to mitigate the risk of citrate accumulation (see in this section 4.4 above). If treatment with Cifoban is initiated, the posology for special populations in section 4.2 must be observed.

Pre-existing hypocalcaemia

Critically ill patients may have hypocalcaemia. With RCA, there may be a drop in the systemic ionised calcium concentration during the first hours of treatment, which subsequently recovers. Therefore, a pre-existing hypocalcaemia is preferably treated before initiating the procedure to reduce the risk of suffering from any clinically relevant hypocalcaemia after treatment initiation.

Complexing and clearance of calcium and magnesium

Citrate chelates calcium and magnesium ions which, via subsequent elimination within the filter, could cause hypocalcaemia (see sections 4.8 and 4.9) and/or hypomagnesaemia (see section 4.8). Infusion of calcium for compensation of losses is often standard practice and supplementation with magnesium might also be necessary. The need for compensation must be part of the RCA protocol.

Blood product substitution (TPE)

Blood plasma products containing citrate, e.g. fresh frozen plasma, are regularly part of the exchange protocol for TPE in critically ill patients. In addition to providing a citrate load, blood products may also be hypernatraemic. Hence, the risk of both citrate accumulation and citrate overload is increased (see above). Management must be part of the RCA protocol.

4.5 Interaction with other medicinal products and other forms of interaction

Product-specific interactions

No pharmacodynamic drug interactions among the constituents of Cifoban are to be expected. Interactions could only be expected by inadequate or incorrect therapeutic use of the solution (see sections 4.4 and 4.9).

No interaction or compatibility studies with other medicinal products have been performed. Thus, no other substance or solution must be added to Cifoban (see also section 6.2).

Calcium containing solutions applied at the level of the filter (i.e. dialysis fluid) or upstream of the filter may reduce the effect of Cifoban.

Interactions are conceivable with sodium-enriched products, which may increase the risk of hypernatraemia (see section 4.8). Analogously, products containing hydrogen carbonate (or precursors metabolised yielding hydrogen carbonate, e.g. acetate) may increase the risk of a high concentration of hydrogen carbonate in the blood (metabolic alkalosis, see section 4.8). Analogously, blood products containing citrate may increase the risk of a higher citrate concentration in the blood (hypocalcaemia, metabolic acidosis, see section 4.8) and increase the risk of a high concentration of hydrogen carbonate in the blood (metabolic alkalosis, see section 4.8).

4.6 Fertility, pregnancy and lactation

Pregnancy and breast-feeding
There are no data from the use of Cifoban in pregnant or breast-feeding women.
Animal studies are insufficient with respect to reproductive toxicity.
Cifoban should not be used during pregnancy and breast-feeding unless the clinical condition of the woman requires treatment with RCA.

Fertility
No human data on the effect of sodium and citrate on fertility are available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Undesirable effects can result from the Cifoban solution or the dialysis treatment.

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

System Organ Class (SOC)	Frequency	Undesirable effects (Preferred Term)
Immune system disorders	*not known*	Hypersensitivity
Metabolism and nutrition disorders	*Very common*	Hypocalcaemia (<1.1 mmol/l) (see section 4.4)
		Hypernatraemia (>145 mmol/l) (see section 4.4)
		Metabolic alkalosis (pH >7.45) (see citrate overload in section 4.4)
	Common	Severe hypocalcaemia (<0.9 mmol/l) (see sections 4.4 and 4.9)
		Hypomagnesaemia (<0.7 mmol/l) (see citrate chelation in section 4.4)
		Severe hypernatraemia (>155 mmol/l) (see sections 4.4 and 4.9)
		Severe metabolic alkalosis (pH >7.55) (see citrate overload in section 4.4)
		Severe metabolic acidosis (pH <7.2) (see citrate accumulation in section 4.4)

	not known	Fluid overload (see method of administration in section 4.2)
Nervous system disorders	*not known*	Headache *
		Seizure *
		Coma *#
Cardiac disorders	*not known*	Arrhythmia *
		Cardiac arrest *#
		Pulmonary oedema (due to severe metabolic acidosis)
Vascular disorders	*not known*	Hypotension *
Respiratory, thoracic and mediastinal disorders	*not known*	Bronchospasm *
		Respiratory arrest *#
		Tachypnoea (Kussmaul breathing, due to severe metabolic acidosis)
Gastrointestinal disorders	*not known*	Vomiting *
Musculoskeletal and connective tissue disorders	*not known*	Muscle spasms *

* Due to (severe) electrolyte imbalance (e.g. hypocalcaemia, hypernatraemia, hypomagnesaemia) or metabolic alkalosis
# Potentially life-threatening

Undesirable events may also result from the equipment and other solutions used in the therapy. Please refer to the applicable product leaflet / instructions for use.

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

HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Inadvertent administration of too high of a volume of Cifoban may lead to an overdose, which can cause a life-threatening situation for the patient.

Inappropriate infusion of too large of an amount of citrate causes acute hypocalcaemia (and metabolic alkalosis, hypernatraemia) and may expose the patient to neurological and cardiac complications. This derangement needs to be corrected by immediately stopping/lowering the amount of Cifoban solution and by intravenous administration of calcium.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Haemodialytics and haemofiltrates, haemofiltrates
ATC code: B05ZB

Solution for RCA in CVVHD, CVVHDF, SLEDD and TPE.

RCA is a method to regionally anticoagulate blood in an extracorporeal circuit intended for blood purification, without having to use a systemic anticoagulant. RCA can be used in extracorporeal circuits that operate with low to moderate blood flows and where preferably a certain fraction of the citrate is removed by the blood purification treatment. Data from the scientific literature indicate that RCA may be used as a first-line anticoagulant in the indicated therapies; and may particularly benefit patients with active bleeding or at increased risk for bleeding. A higher degree of anticoagulation can usually be targeted compared to systemic anticoagulation, which benefits circuit patency and treatment efficacy.

Depending on the individual citrate-anticoagulated extracorporeal blood purification therapy, calcium is removed from the patient's blood in variable quantity, which makes calcium substitution necessary. Furthermore, a part of the citrate infused for RCA unavoidably enters the patient's systemic circulation with the re-transfused blood. This induces an increase in systemic

citrate concentration, which generally stabilises at a new level depending on the actual citrate infusion rate and the citrate metabolism in the liver and other tissues.

Calcium-citrate chelate complexes present in the patient's blood dissociate when more citrate is metabolised than systemically infused. As a net effect, free ionised calcium remains in the patient's blood and thereafter redistributes in the patient's body where it is essential for both bone remodelling and as an electrolyte with crucial cellular functions throughout the body (e.g. in muscle cells and neurons).

5.2 Pharmacokinetic properties

Citrate is a normal metabolite in the human body and an intermediate substrate in the Krebs cycle. This physiological pathway in conjunction with the respiratory chain is capable of processing high amounts of citrate in majority of patients. The Krebs cycle takes place in the mitochondria, and all cells that contain these cellular organelles can metabolise citrate. Tissues rich in mitochondria such as liver, skeletal muscles, and kidney therefore have a higher capacity for citrate generation and elimination.

Absorption and distribution
Absorption and distribution of sodium and citrate is determined by the patient's clinical condition, metabolic status, and residual renal function.

Biotransformation
In humans, citrate is an intermediate in the central metabolic pathway called Krebs cycle as mentioned above. Citrate is rapidly metabolised in several organs/tissues.

Elimination
A substantial part of citrate is removed with the effluent.
The amount of citrate being infused systemically is metabolised in most somatic cells.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections
Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

Shelf life after opening:
From a microbiological point of view, the product must 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.

Keep the bags in the outer carton in order to protect from light.

6.5 Nature and contents of container

The medicinal product is provided pairwise as two identical solution bags which can be separated by a tear seam in the protective bag.

The solution bag is made of polypropylene-elastomer-blends. Each bag is equipped with a connective tubing made of polypropylene-elastomer-blends, a connector made of polycarbonate and is covered by a polyolefine-based protective multilayer bag.

Pack sizes

SecuNect connector system:
8 bags of 1500 ml

Safe●Lock connector system:
8 bags of 1500 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Disposal
The solution is for single use only. Any unused solution and damaged container should be disposed of in accordance with local requirements.

Handling
The solution bags are equipped either with a **SecuNect connector** or with a **Safe●Lockconnector**.

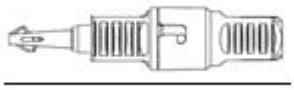
The following points prior to the use of the solution bag have to be considered:

Aseptic technique must be used throughout administration to the patient. The solution must be used immediately after opening to avoid microbiological contamination.

Extracorporeal use. To be infused into the extracorporeal blood circuit only.

The solution is not intended to be used for the addition of any drugs.

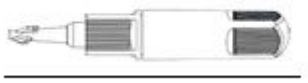
For solution bags equipped with a **SecuNect connector (transparent with a green ring)**:



1. Separate the two bags at the tear seam without damaging the integrity of the overwrap.
2. Remove the overwrap only immediately before using the solution. Check the solution bag (label, expiry date, clearness of the solution, bag and overwrap not damaged).Plastic containers may occasionally be damaged during transport from the manufacturer to the dialysis clinic or hospital clinic or within the clinic itself. This can lead to contamination and the growth of bacteria or fungi in the solution. Therefore, careful inspection of the bag and the solution before use is essential. Particular attention must be paid to even the slightest damage to the closure of the bag, the welding seams and the corners of the bag. The solution must only be used if colourless and clear and if the bag and connector are undamaged and intact.
3. Put the bag on the dedicated attachment by its hanger hole.
4. Remove the protection cap from the **SecuNect connector with its green ring** and attach the connector only to its corresponding counterpart with same colour to prevent misconnection. Do not touch any inner parts, especially do not touch on top of the connector. The inner part of the connector is delivered sterile and is not intended to be further treated with chemical disinfectants. Connect the bag connector with a twisting motion to the tubing line connector by hand, overcoming a guarding force until a "click" is audible and connection is established.
5. Before start of treatment and in case of bag changes break the frangible pin of the bag connector and make sure that the pin is completely broken.

6. Proceed with the further steps as indicated in the treatment applied RCA protocol.

For solution bags equipped with a **Safe●Lockconnector (transparent)**:



1. Separate the two bags at the tear seam without damaging the integrity of the overwrap.
2. Remove the overwrap only immediately before using the solution. Check the solution bag (label, expiry date, clearness of the solution, bag and overwrap not damaged).Plastic containers may occasionally be damaged during transport from the manufacturer to the dialysis clinic or hospital clinic or within the clinic itself. This can lead to contamination and the growth of bacteria or fungi in the solution. Therefore, careful inspection of the bag and the solution before use is essential. Particular attention must be paid to even the slightest damage to the closure of the bag, the welding seams and the corners of the bag. The solution must only be used if colourless and clear and if the bag and connector are undamaged and intact.
3. Put the bag on the dedicated attachment by its hanger hole.
4. Remove the protection cap from the **transparent Safe●Lock connector** and attach the connector only to its corresponding counterpart to prevent misconnection. Do not touch any inner parts especially do not touch on top of the connector. The inner part of the connector is delivered sterile and is not intended to be further treated with chemical disinfectants. Connect the bag connector with the appropriate counterpart and twist together.
5. Before start of treatment and in case of bag changes break the frangible pin of the bag connector and make sure that the pin is completely broken.
6. Proceed with the further steps as indicated in the treatment applied RCA protocol.

7 MARKETING AUTHORISATION HOLDER

Fresenius Medical Care Deutschland GmbH
Else-Kröner-Straße 1
61352 Bad Homburg v.d.H.
Germany

8 MARKETING AUTHORISATION NUMBER

PA1350/008/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/10/2023

10 DATE OF REVISION OF THE TEXT

November 2023