Package leaflet of the product

Citralysate K4 PLUS

Medical device IIb

1. Treatment indication

Citralysate K4 PLUS is a dialysis solution containing phosphate and is indicated for continuous methods of blood purification (CRRT – Continuous Renal Replacement Therapy) with regional citrate anticoagulation provided by 4% trisodium citrate. Concurrent calcium administration is mandatory. Citralysate K4 PLUS can be used only in combination with devices designed for continuous hemodialysis equipped with a module for citrate anticoagulation and with pumps for citrate and calcium infusion next to the standard pumps for regulation of blood, dialysis solution and filtrate flow.

2. Composition

Citralysate K4 PLUS is delivered as a double-chamber bag with a total volume of 5000 ml. Dialysis solution for an immediate use is made by mixing contents of both the chambers just before use. The smaller chamber contains 250 ml of an acid solution with 20 mmol/l Mg^{2+}, 80 mmol/l K^+,97 mmol/l Cl^-, 25 mmol/l $H_2PO_4^-$ with excess of 2 mmol/l (corresponding to pH around 3.1) and 111 mmol/l of glucose. The larger chamber contains 4750 ml of solution with 140 mmol/l Na^+, 118.84 mmol/l Cl^- and 21.16 mmol/l HCO_3^-.

Dialysis solution for an immediate use contains:

Sodium chloride	6.604	g/l
Sodium hydrogencarbonate	1.680	g/l
Potassium chloride	0.2055	g/l
Magnesium chloride hexahydrate	0.2033	g/l
Potassium dihydrogenphosphate	0.1701	g/l
Glucose monohydrate	1.100	g/l

Other components:

Water for injection
Hydrochloric acid 25%

Ions and glucose concentration in the dialysis fluid for immediate use are:

Na^+		133	mmol/l
K^+		4.00	mmol/l
Mg^{2+}		1.00	mmol/l
Cl^-		117.75	mmol/l
HCO_3^-		20	mmol/l
$H_2PO_4^-$		1.25	mmol/l
Anhydrous glucose		1.00	g/l
pH	~	7.4	
Theoretical osmolarity	≥	283	mosmol/l

3. Directions for use

User should be properly instructed by the manufacturer on the application of Citralysate K4 PLUS before its use. During the use other additional devices and solutions are needed and a 4% solution of trisodium citrate should be administered via infusion in pre-dilution. The ratio of the 4% solution of trisodium citrate to blood flow under the standard conditions should be 1:34, which corresponds to an infusion of 4 mmol of citrate per 1 liter of the treated blood. A solution of calcium with concentration within 50 and 500 mmol/l should be administered via system infusion or via venous CRRT blood set just before connecting to venous catheter's lumens. The volume of calcium administered via infusion should be set appropriately to regulate the concentration of system ionized calcium. Appropriate initial dose is routinely 1.7 mmol of calcium per 1 liter of applied dialysis solution. Dose 2 l/h of Citralysate K4 PLUS corresponds to 3.4 mmol/h of infused calcium.

Metabolic acid-base conditions of the patient can be controlled by the ratio of a buffer infusion to blood and citrate flow and by the buffer removal via a change of flow of the dialysis solution. Increased flow of the dialysis solution may result in acidosis, which should be taken into account. The previously mentioned distinguishes Citralysate K4 PLUS from other dialysis solutions used in CRRT combined with system anticoagulation (e.g. 35 mmol/l of bicarbonate). If rate of Citralysate K4 PLUS equals 2 l/h and rate of blood flow equals 100 ml/min, balanced metabolic conditions can be achieved. The previously mentioned applies only if a high-flux dialyzer with adequate dimensions and no limits for a transport of buffers is used.

Electrolytes (Na, K, inorganic phosphate) and glucose concentration levels in blood serum should be periodically monitored before and during the treatment. Concentration of potassium in Citralysate K4 PLUS is 4 mmol/l, which minimizes the need for its substitution during the CRRT. The solution is not suitable for patients suffering from uremia and severe hyperkalemia, because a high rate of decrease to standard levels of potassium is desirable. When the standard level of potassium is achieved, Citralysate K4 PLUS may be used also for previously mentioned patients. Citralysate K4 PLUS contains phosphate to use CRRT in patients without severe hyperphosphatemia. Concentration of phosphorus in the solution results in a regulated correction of an elevated level of phosphorus and concurrently it prevents from creation of severe hypophosphatemia in course of the treatment. Usually no additional substitution of phosphate related to the elimination method is necessary, unless there is another indication used.

4. Continuous hemodialysis dosage

If it is not clinically contraindicated, the required efficacy of the hemodialysis treatment is achieved by administering 1.5 – 2.5 l/h of the dialysis solution in adults, depending on the body weight. No experience with treatment in children has been obtained to date.

5. Bag connection to extracorporeal circuit

After mixing the contents of both the chambers, the bag with the dialysis solution is connected to the dialysate circuit according to instructions for devices designed for continuous renal replacement therapies. It is necessary to avoid a contamination of the dialysis solution and any parts being in contact with the dialysis solution. The bag with Citralysate K4 PLUS disconnected from the dialysate circuit have to be disposed of.

Citralysate K4 PLUS must not be administered intravenously or infused into extracorporeal circuit.

Before use Citralysate K4 PLUS should be warmed up closely to the patient's body temperature so its rapid decrease is avoided.

Notes

Dialysis solution for citrate CRRT in a double-chamber bag.

- **Do not use before mixing both the chambers.**
- **The solution is not indicated for an intravenous infusion.**
- **Use only if the fluid is pure and the packaging is not damageed.**
- **Dialysis solution must be used only in combination with citrate infusion (citrate anticoagulation).**
- **Dialysis calcium-free solution: a separate calcium infusion is necessary.**
- **Connection of system citrate CRRT must be carefully checked before the treatment initiation.**
- **Incorrect connection of the citrate and calcium infusion must be avoided above all. Correct connection must be approved by measuring a level of decrease of the ionized calcium induced by the citrate in extracorporeal circuit within 20-30 min after the therapy initiation, at the latest. If the level does not decrease, it is necessary to check the connection, because an exchange of citrate and calcium infusions may result in a serious electrolyte imbalance.**
- **Use a high-flux dialyzer with a minimal active area of 1.4 m^2 and change it at least every 72 hours.**
- **Citrate impaired metabolism, e.g. in patients with impaired liver functions may result in acidosis, hypocalcemia or in an increased need for calcium substitution. In this case citrate CRRT must be terminated and another therapy of renal replacement should be applied.**
- **An efficacious CRRT therapy may cause hypomagnesemia. Therefore, magnesium levels in blood serum should be monitored before and during the treatment and a relevant deficit should be compensated.**
- **Despite the contained level of phosphate in the solution, phosphate levels in serum should be monitored during the treatment a relevant deficit should be compensated.**
- **Steam sterilized.**
- **Free of bacterial endotoxins.**
- **Store at the temperature within 4°C and 25 °C.**
- **Expiry date: see information on the label.**
- **EXP 24 months**
- **Only for single use.**

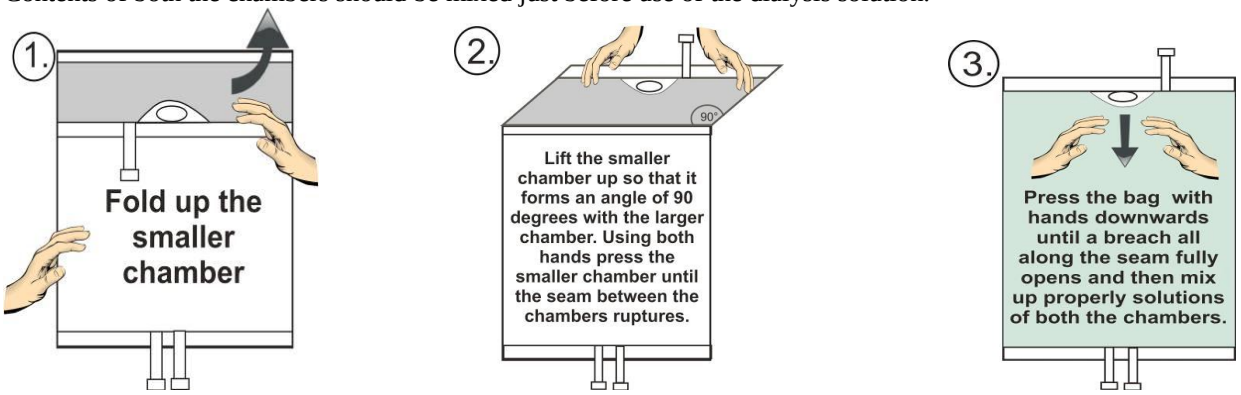
6. Handling

Container's opening:

Double-chamber bag containing dialysis solution should be taken out from the cardboard just before use. Before mixing the contents of both the chambers, check the composition, batch number and expiry date. Check the solution for its purity. Check the bag and outlet safety lock for their integrity. Solution should not be used if the bag or outlet safety lock is damaged. When unpacking the bag from the secondary packaging, do not grasp the tubes with connectors.

Instruction for mixing both the chambers:

Contents of both the chambers should be mixed just before use of the dialysis solution.



After mixing the contents of both the chambers check if the seam has been entirely opened, the solution is pure and no liquid is leaking.

Citralysate K4 PLUS must be used within 48 hours after mixing.

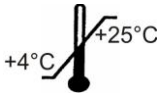
7. Information on disposal of the packaging

The product is recommended to be considered a potentially hazardous waste.

Symbols stated on the container:

Caution: Read instructions for use

Nonpyrogennous fluid (Apyrogenic)



Storage temperature: from +4 to +25°C

Do not re-use

Sterilized using steam

CE mark, notified person 1023

Producer: Biomedica, spol. s r.o., Pekařská 8, CZ 155 00 Praha 5

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0 mmol/l Ca^{2+}

In case of questions or reporting of undesirable effects please contact us on:

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