Package leaflet of the product

Natrium Citricum 4%

(Trisodium citrate 136 mM)

SOLUTION FOR APHERESIS AND EXTRACORPOREAL BLOOD PURIFICATION

Anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM)
Medical device IIb
Read carefully the following information for a safe usage of the solution.

1. Product information:
Product name:
Natrium Citricum 4%
Anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM)

Composition:
One liter of the solution contains trisodium citrate dihydrate Ph. Eur. 40 g (4% w/v).
(pH is adjusted with citric acid monohydrate Ph. Eur.).
Water for injection Ph. Eur. ad 1000 ml.
pH 6.4-7.5

Composition in mmol/l units:

Natrii citras	136	mmol/l
Na^+	408	mmol/l
$C_6H_5O_7^{3-}$	138.4	mmol/l
Theoretical osmolarity	554	mosmol/l

Pharmaceutical form:
Anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM) is a sterile, pyrogen-free, clear anticoagulation solution filled in transparent printed PP bags and packed in polypropylene or polyamide/polyethylene foil. It is delivered in bags of 250 ml, 1000 ml, 1500 ml and 2000 ml and in PVC bags of 250 ml.

Pharmaceutical group:
Anticoagulation solution for full blood.

2. Treatment indication:
Anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM) is used exclusively for full blood anticoagulation within apheresis procedures in transfusion medicine, continuous (CRRT – Continuous Renal Replacement Therapy), extended intermittent or intermittent methods of blood purification. The solution can be also used as a citrate lock of intravascular catheters. Citrate solution has anticoagulant properties and interferes with creation of biofilms in catheters. The citrate lock which is applied into the catheter, when no dialysis is performed, protects the catheter from thrombosis and limits creation of a catheter infection.

3. Important information:
Contraindications:
Severe liver failure and/or severe shock state with failure of citrate utilization in intermediate metabolism represent relative contraindications.

Precautions for use:
- Not to be administered intravenously
- Not to be used unless the solution is clear
- Check up the bag and safety locks on connection tubings if they are tamper-proof
- Solution shall not be used if the container or outlet safety lock has been tampered
- Residues of the solution shall not be reused and shall be disposed of

Interactions with medications and other types of interactions:
The anticoagulant solution of 4 % sodium citrate (Trisodium citrate 136 mM M) may not be added to any remedies.

Warning and precautions:
- Condition for use is a use of substitute Ca free solution
- Citrate which has not been removed directly via renal hemofiltration is metabolized in the body into bicarbonate. This shall be taken into account in compounding the prescribed substitution solution.
- If anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM) is used during continuous blood elimination procedures, it is necessary to monitor regularly all electrolytes' levels and acid base equilibrium of the patient blood.

4. Directions for use:
- Trisodium citrate in 4% solution is designed for anticoagulation of full blood as a part of automatized apheresis procedures, continuous blood elimination methods CRRT. The solution can be used also as a citrate stopper of intravascular catheters. The citrate lock which is applied into the catheter, when no dialysis is performed, protects the catheter from thrombosis and limits creation of a catheter infection.
- Citrate anticoagulation is considered to be a suitable method of anticoagulation mainly to use in patients with risk of hemorrhage and is also recommended to use in patients with critical conditions hospitalized in intensive care units.
- Trisodium citrate in 4% solution is administered via infusion in pre-dilution. The 4% solution-blood flow ratio should provide the final concentration of the citrate in blood 3-5 mmol/l per an hour. This concentration provides decrease of ionized calcium

level behind the filter under 0.4 mmol/l and sufficient anticoagulation. Around 35-50% of the citrate is, depending on the configuration of CRRT, administered in the patient´s system circulation. The concentration level of ionized calcium shall be monitored to keep the level in physiological limits. If necessary, solution of calcium (concentration of calcium 50-500 mmol/l) is administered by infusion to the system or to the return part of the blood set CRRT system, right before connection to the venous catheter. A suitable starting dose is 1.7 mmol of calcium per 1 liter of the applied dialysis solution and is further adjusted to the level of ionized calcium in arterial blood which should be higher than 0.85 mmol/l. The shift to acidosis and compensation of the possible alkalizing effect of the trisodium citrate resulting from increase of the dialysis solution flow should be taken into account. Vice versa, increase of the blood flow and related doses of the citrate result to increase of the citrate concentration and shift to alkalosis. Modality, next to the regular monitoring of ionized calcium in blood and behind the filter, requires administration of a special dialysis hyponatremic solution with a lowered level of alkali to avoid a metabolic alkalosis and hypernatremia.

- Remove the bag from the cover right before use.
- Check up the composition, production batch number and expiry date.
- Check up the solution for its clarity.
- Check up the bag and safety locks on connection tubings if tamper-proof. The solution shall not be used if container or outlet safety lock has been tampered.
- Carry out the apheresis procedure in line with detailed operating instructions of the manufacturer of apheresis machines. After anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM) bag has been connected to the apheresis machine, hang it on the relative infusion stand.
- Carry out the elimination method according to detailed operating instructions of the manufacturer of dialysis monitors. The amount of anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM) administered via the pre-dilution shall be included in the fluid balance and the ultrafiltration calculation.
- When unpacking the bag from the secondary packaging, do not grasp tubing with connectors.

5. Adverse reactions:
Main adverse reactions are: hypocalcemia connected with tetany, paresthesia and heart function disorders (QT interval, arrhythmia,hypocontractility of myocardium). Routine substitution of calcium chloratum during the dialysis should prevent mentioned effects. It is necessary to monitor the total to ionized calcium index and assume accumulation of the citrate in organism when the index is higher than 2.5. Another adverse reactions are: metabolic alkalosis, hypernatremia, hypomagnesemia.

6. Expiry date and way of storage:
Expiry date of anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM) is imprinted on the container's rear side.
The product shall not be used after this date.
EXP 24 months
Anticoagulation solution of trisodium citrate 4% (Trisodium citrate 136 mM) shall be protected from light and stored at the temperature from + 4°C to + 25°C.

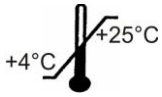
7. Packing: PP bag 250 ml, 1000 ml, 1500 ml, 2000 ml, PVC bag 250 ml

8. Information on packagings' disposal:
The product is recommended to be considered 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

Phtalates free

CE mark, notified person 1023

0 mmol/l Ca^{2+}

Producer: Biomedica, spol. s r.o., Pekařská 8, CZ 155 00 Praha 5
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In case of questions or reporting of undesirable effects please contact us on:
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