Package leaflet of the product

Natrium Citricum 14.7 %

(Trisodium Citrate 0,5 M)

SOLUTION FOR APHERESIS, EXTRACORPOREAL BLOOD PURIFICATION and THERAPEUTIC METHOD FPSA (FRACTIONED PLASMA SEPARATION AND ABSORPTION)

The anticoagulant solution of trisodium citrate 14.7% (Trisodium Citrate 0,5 M)
Medical device IIb
Please read the following information to use the solutions safely.

1. Product information:
Product Name:
Natrium Citricum 14.7%
The anticoagulant solution of 14.7 % sodium citrate (Trisodium citrate 0,5 M)

Product composition:
One liter of the solution contains sodium citrate dihydrate Ph. Eur. 147 g (14.7% w/v).
(pH is adjusted with citric acid monohydrate Ph. Eur.).
Water for injection Ph. Eur. 1000 ml.
pH 6.4-7.5

Composition in mmol units:

Natrii citras	500	mmol/l
Na^+	1500	mmol/l
$C_6H_5O_7^{3-}$	502.4	mmol/l
Theoretical osmolarity	2010	mosmol/l

Pharmaceutical form:
The anticoagulant solution of 14.7 % sodium citrate (Trisodium citrate 0,5 M) is a sterile, pyrogen-free, clear anticoagulant solution in transparent printed bags of PP and packed in polyamide/polyethylene or polypropylene/polyethylene foil. The product is supplied in bags of 500 ml.

Pharmaceutical group:
The anticoagulant solution for full blood.

2. Treatment indications:
The anticoagulant solution of 14.7 % sodium citrate (Trisodium citrate 0,5 M) - is exclusively designed for the use of anticoagulation for full blood within elimination continuous (CRRT – Continuous Renal Replacement Therapy), extended intermittent or intermittent methods of blood purification or in the systems of substitution function liver based on a method FPSA (fractionated plasma separation and adsorption). In all applications, assumes the use of devices with integral pumps for citrate and calcium. The solution may be used as a citrate lock in 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:
- Do not administer as an intravenous solution directly
- Use only if solution is clear
- Check the integrity of the bag and locks on trailers tubing
- The solution should not be used if the packaging or the fuse terminal is damaged
- 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 14.7 % sodium citrate (Trisodium citrate 0,5 M) shall not be mixed with any other remedies.

Warning and precautions:
- The condition of use is a substitution solution without calcium (Ca free)
- Citrate, which is not removed directly through renal hemofiltration, is metabolized to bicarbonate by the patient. The prescribed substitution solution must take this effect into account.
- When using anticoagulant solution of 14.7 % sodium citrate (Trisodium citrate 0,5 M), it is necessary to periodically check the concentration of electrolyte and acidobasic equlibrium in the patient's blood, especially plasma levels of sodium, calcium, magnesium and bicarbonate may be abnormal.

4. Directions for use:
- Trisodium citrate 14.7% is designed for use as an anticoagulant solution for citrate anticoagulation within elimination continuous methods (CRRT), in the systems of substitution function liver based on a method FPSA (fractionated plasma separation and adsorption). In all applications, assumes the use of devices with integral pumps for citrate and calcium. Even for apheresis procedures in transfusion medicine. The solution may be used as a citrate lock in 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 14.7% solution is administered via infusion in pre-dilution. The 14,7% 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 packaging until just before use.
- Check the composition, batch number and expiry date.
- Make sure the solution is clear.
- Check the bag and lock pin is not damaged. The solution should not be used if the packaging or fuse terminal is damaged.
- Perform the apheresis procedure according to the detailed operating instructions on use of the apheresis machine made by its manufacturer. After the bag with anticoagulant solution of 14.7% sodium citrate (Trisodium citrate 0,5 M) has been connected to the device, hang it on the appropriate infusion stand.
- Perform the elimination method according to the detailed operating instructions on use of the dialysis machine made by its manufacturer. The amount of anticoagulation solution of 14.7% sodium citrate (Trisodium citrate 0,5 M) administered via pre-dilution shall be included in the fluid balance and the ultrafiltration calculation.
- Perform the procedure according to the detailed operating instructions of machine made by its manufacturer which is base on the methods FPSA. After the bag has been with anticoagulant solution of 14.7% sodium citrate (Trisodium citrate 0,5 M) connected to the device. Hang it on the appropriate infusion stand.
- When unpacking the bag from the secondary packaging, do not grasp tubing with connectors.

5. Adverse effects:
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 performed procedure should prevent mentioned effects. It is necessary to monitor the total to ionized calcium index and to 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 the anticoagulant solution of 14.7 % sodium citrate (Trisodium citrate 0,5 M) is imprinted on the bag. After that date, the product must not be used.
EXP 24 months
The anticoagulant solution of 14.7 % sodium citrate (Trisodium citrate 0,5 M) must be protected from light and stored from +4 ° C to +25 ° C.

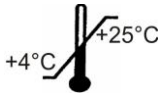
7. Package: PP bag 500 ml

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 steam

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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