

**ART**

Advanced Renal Technologies



# Citrasate®

## USERS MANUAL

“A Very Cost-Effective Answer for Patients with Bleeding or Clotting”

Concentrates from  
Neubrandenburg



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aus Verantwortung  
für die **DIALYSE...**

# Citrasate<sup>®</sup>

## USERS MANUAL

**“A Very Cost-Effective Answer for Patients with Bleeding or Clotting”**

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For full articles, posters and additional scientific information please visit ART's website at: [www.citrasate.com](http://www.citrasate.com) or MTN Neubrandenburg GmbH, Gustav-Kirchhoff-Str. 2, 17033 Neubrandenburg, Tel. +49 395 581000.

## 1. GENERAL INFORMATION

Health professionals responsible for the care of dialysis patients are well aware of the complex relationship between treatment variables and patient outcome. Much depends upon the interaction between the patient's blood and the extracorporeal circuit, especially within the hemodialyzer. Even with systemic heparin anticoagulation, clotting within the dialyzer reduces delivered "dose" of dialysis and increases blood loss. Dialyzer clotting is further accelerated in cases where heparin anticoagulation is contraindicated, for example, in patients with antibodies to this agent. These complications result in additional staff time required to treat the problems, as well as higher costs for additional supplies (dialyzers, blood lines, etc.).

Management of postsurgical and trauma patients with increased risk of bleeding limits the use of heparin, making the dialysis especially challenging. The alternatives to heparin therapy in this group are limited to periodic flushes of the circuit or to regional citrate anticoagulation. Although widely used, line flushing is relatively ineffective and increases fluid load to the patient. The alternative, regional citrate anticoagulation, is difficult to deliver properly and expensive to set up and monitor. Both methods involve significant additional effort on the part of the staff.

Furthermore, in patients receiving uncomplicated, "routine dialysis," the goal is to optimize treatment by increasing the dose of dialysis within the constraints of available time and cost. Advanced Renal Technologies (ART) has developed a new dialysate formulation that addresses these problems and brings treatment to a more effective level. Containing citric acid as the acidifying agent, it is the first major change in dialysate formulation in over three decades, shifting from traditional formulations that contain acetic acid. **Citrasate<sup>®</sup>** is cleared for clinical use by the FDA in the US and it has the CE mark for the European countries, it is already in use in many clinics around the world and available through Manufacturers and Distributors appointed by Advanced Renal Technologies.

Citrate dialysate is not to be confused with regional citrate anticoagulation, in which high concentrations of citrate are infused into the arterial blood line to bind calcium, and a corresponding infusion of calcium is delivered into the venous line or through the dialyzer to counteract hypocalcemia. Citrate dialysate has been used successfully in place of in-hospital regional citrate anticoagulation.

Citric acid content of both **Citrasate<sup>®</sup>** and **DRYalysate<sup>®</sup>** dialysates is only 0,8 mmol/l in the final diluted concentration within the dialyzer, well below the 2-5 mmol/l threshold of true anticoagulation. Calcium levels in the patient remain within the normal range when Citrasate dialysate is used, and no supplemental calcium replacement measures are usually needed.

Making the conversion from conventional dialysate to citrate dialysate is effortless. The conversion is "transparent" for both staff and dialysis equipment.

- No adjustment in the dialysis system is required; simply substitute citrate concentrate of equal concentration for the A-concentrate normally used.
- Additional staff training is unnecessary.
- There is no need to perform additional patient monitoring beyond ordinary measures. No extra blood tests are needed.

*NB: The dry form of citrate dialysate, **DRYalysate<sup>®</sup>** is not yet available in the EU*

**Clinical use:**

Compared with traditional acetic acid-containing dialysates, citrasate dialysate has the following documented benefits:

- Eliminates or Reduces Heparin need in RF patients <sup>(1)</sup>
- Increases dialysis dose Kt/V <sup>(2)</sup>
- Improves correction of Acidosis <sup>(3)</sup>
- Reduces post-dialysis Bleeding, if heparin is reduced <sup>(4)</sup>

**References:**

1. Heparin Free Slow Low Efficiency Dialysis (SLED) Using Citrate Dialysate (CD) Is Safe and Effective *S. Ahmad, A. Tu* March 7–10, 2007, San Diego, Calif.
2. Increased Dialysis Dose and Decreased Concentration of Beta-2 Microglobulin with Citrate Dialysate *Robert J Kossmann, MD, Robin Callan, LLM and Suhail Ahmad, MD.* ASN's 39th Annual Renal Week Meeting November 2006
3. Increased dialyzer efficiency using a dialysate containing citric acid in place of acetic acid. *Ahmad S, Callan R, Cole JJ, Blagg CR.* ASN, Miami, Fla., November 1999.
4. Fifty-five Percent Heparin Reduction is Safe with Citrate Dialysate in Chronic Dialysis Patients *Robert J Kossmann, MD, Robin Callan, LLM and Suhail Ahmad, MD* ASN's 39th Annual Renal Week Meeting November 2006

## 2. GUIDELINES FOR USE OF CITRASATE<sup>®</sup> DIALYSATE

### Introduction:

Citrasate<sup>®</sup> Dialysate contains a small amount of anticoagulant (Citrate) and thereby can provide some anticoagulation effect for the extracorporeal hemodialysis circuit in cases where heparin is contraindicated or is ineffective.

Citrasate<sup>®</sup> is particularly helpful for Acute and Chronic hemodialysis in patients with:

- Heparin Induced Thrombocytopenia, (HIT)
- Heparin Allergies
- Risk of bleeding, (post operative, GI bleeding or where heparin has proven to be ineffective in preventing clotting of the extracorporeal circuit)
- Low platelet count

### Protocol:

#### CITRASATE CAN ONLY BE PRESCRIBED BY OR ON ORDER OF A PHYSICIAN

- Verify physicians order and assure correct dialysate type (from the label on the A-component Citrasate<sup>®</sup> concentrate container) and check concentration, proportioning ratio and formulation.
- Replace the standard acetic A-component concentrate container with the appropriate Citrasate<sup>®</sup> concentrate container. The supply of sodium bicarbonate does not change. Use cartridge or fluid B-component concentrate as usual.
- Have verified that the dialysis machine delivers the composition as mentioned on the concentrate container label, use your standard laboratory dialysis fluid checks for approval.
- To have optimal effect of the anticoagulation is recommended that the dialysate flow is at least 1,75 times the blood flow [with a higher dialysate flow more citrate, in relation to the blood, passes through the dialyzer, thus providing more anticoagulation].
- Because anticoagulation from the dialysate is not available in the arterial bloodline, avoid a large volume and/or bubble traps
- Use the priming instructions given by the dialyser manufacturer, make sure no air (micro bubbles) are in the extracorporeal circuit before connecting the patient.
- Adjust the (Heparin) anticoagulation protocol down in steps, lower the dose by ~1/3 following each treatment while measuring ACT or aPTT at your regular intervals until lowest allowable clotting times are reached. In case of HIT or heparin allergy lower dose of heparin to zero from the first treatment and flush intermittently with saline as required.
- Pay special attention to the venous chamber during the treatment.
- If heparin adjustment is not needed or if patient is hypercoagulable, citrate dialysate can be used with the normal heparin dose.
- If the concentrate container is not empty after treatment, the remainder can be used for the next treatment, use your current protocol for that.
- You can add electrolytes like K<sup>+</sup> and Ca<sup>2+</sup> to the concentrate if you are used to doing so. Have in mind the concentration of the concentrate and the volume of the full container when calculating the amount to be added. If required, have dialysate tested in the lab and have the change signed off by authorized staff. Mark the concentrate container with new electrolyte level.

### DOCUMENTATION

Make note of the use and formula of Citrasate<sup>®</sup> dialysate and document the treatment according to your protocol in the patient's medical record

**CAUTIONS**


Although rarely occurring, be aware of patient's reaction to citrate or to low circulating  $Ca^{2+}$ . It has been reported (*Ahmad et al.*) that the use of Citrasate dialysate will temporarily, during dialysis only, decrease ionized Ca levels by approximately 10%. Assess the patient during treatment for signs of hypocalcemia: numbness/tingling around the mouth, unusual muscle cramps (in length and severity). If symptoms occur, place the hemodialysis machine in bypass and notify the physician. Symptoms should resolve in minutes as citrate is quickly metabolized in the body. Calcium can be supplemented per physician order.

**3. Sample Concentrate label (EU) MTN Neubrandenburg GmbH**

**Citrasate<sup>®</sup> 460**

**Acid Concentrate for Bicarbonate Dialysis 10 l e**

**$K^+$  2.00 mmol/l  $Ca^{2+}$  1.50 mmol/l Glucose 1.00 g/l**



Composition	g/l	mmol/l
1 l concentrate contains		
Natrii chloridum	263.00	Na <sup>+</sup> 451.00
Kalii chloridum	6.71	K <sup>+</sup> 90.00
Magnesi chloridum 6H <sub>2</sub> O	4.57	Mg <sup>2+</sup> 22.00
Calcii chloridum 2H <sub>2</sub> O	9.92	Ca <sup>2+</sup> 67.00
Acidum citricum	6.92	C <sub>6</sub> H <sub>5</sub> O <sub>7</sub> <sup>3-</sup> 36.00
Natrii acetatis 3H <sub>2</sub> O	1.84	CH <sub>3</sub> COO <sup>-</sup> 14.00
Glucosum anhydricum	45.00	Cl <sup>-</sup> 4770.00
Aqua purificata ad 1000 ml		Glucose 249.71


**EN** Preparation of the ready to use dialysis solution. 1 l type 460 + 42.225 l Aqua purificata + 1.775 NaHCO<sub>3</sub>-Sol. 8.4% results in the electrolyte concentrations shown as follows.

**Description for use:**  
This acid concentrate is formulated to be used with a three stream hemodialysis machine calibrated to an acid concentrated dilution ratio of 1:45. It must be used in conjunction with sodium bicarbonate solution providing the desired ionic composition of both sodium and bicarbonate. Final mix at time of dialysis will consist of 1 part acid concentrate liquid with 1.775 parts of bicarbonate concentrate and 42.225 parts purified water that meets standards for dialysis water acc. to Ph. Eur. monography 1167.


**Caution:**  
Review instructions that are provided by the manufacturer of the hemodialysis machine being used. Always check conductivity and approximate pH of dialysate just prior to dialysis treatment and each time new concentrate is supplied to the machine. Use only as directed. Mix thoroughly before use. Keep container sealed when not in use.

Citrasate<sup>®</sup> is registered trademark of Advanced Renal Technologies. U.S. Patents 5.252.213 and 6.610.206, European Patents 1124567, 479692 and others applied for.



Na <sup>+</sup> 139.75 mmol / l	Cl <sup>-</sup> 106.00 mmol / l
K <sup>+</sup> 2.90 mmol / l	HCO <sub>3</sub> <sup>-</sup> 37.04 mmol / l
Mg <sup>2+</sup> 0.50 mmol / l	Citrate <sup>-</sup> 0.80 mmol / l
Ca <sup>2+</sup> 1.50 mmol / l	Glucose 1.00 g / l
CH <sub>3</sub> COO <sup>-</sup> 0.30 mmol / l	Osmol. cal. / theor. 293 mOsm / l




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## 4. SAFETY DATA SHEET FOR CITRASATE®

Safety data sheet MTN Neubrandenburg GmbH

### 1. Identification of the preparation and of the company

<b>Productname</b>	Citrasate® Hemodialysis Concentrate A component
<b>Intended use</b>	A-Component for manufacturing of bicarbonate hemodialysis fluid
<b>Manufacturer</b>	MTN Neubrandenburg GmbH Gustav-Kirchhoff-Str. 2 17033 Neubrandenburg
<b>Telephone/Fax</b>	+49-(0)395-58 100-0/-99
<b>E-Mail</b>	<a href="mailto:info@mtn-nb.de">info@mtn-nb.de</a>
<b>In case of emergency</b>	Contact your local emergency response center

### 2. Hazards identification

Dialysis concentrate is not classified as a dangerous solution for health or environment. Dialysis concentrate may cause irritation when coming in contact with skin, eyes or mucous membranes.

### 3. Composition/Information on ingredients

Constituent	CAS-no.	EG-no.	content	symbols R-phrases
Citric acid	77-92-9	201-069-1	≤ 0.7%	Xi, R36
Sodium acetate	6131-90-4	204-823-8	≤ 0.2%	-
Calcium chloride	10035-04-8	233-140-8	≤ 1.0%	Xi, R36
Potassium chloride	7447-40-7	231-211-8	≤ 0.7%	-
Magnesium chloride	7791-18-6	232-094-6	≤ 0.5%	-
Glucose	50-99-7	200-075-1	≤ 9.0%	-
Sodium chloride	7647-14-5	231-598-3	≤ 26.3%	-

*The concentration of electrolytes will vary by formula, the highest concentrations are given in the table above. Explanation of the Symbols and R-Phrases are given under point 16. Content % given by weight.*

### 4. First-Aid Measures

<b>Eyes</b>	Rinse immediately with large amounts of water for 10-15 minutes. Keep eyes wide open. If irritation remains obtain medical assistance.
<b>Skin</b>	Remove contaminated clothing, wash with soap and water. If irritation remains obtain medical assistance.
<b>Ingestion</b>	Wash mouth with water and drink large amounts of water, do not induce vomiting. Obtain medical assistance.

### 5. Fire fighting measures

Hemodialysis concentrate is not flammable. Use fire-extinguishing media based on goods stored in surrounding area. Use water to cool nearby containers and structures. Move stored hemodialysis A-component to a safe place.

### 6. Accidental release measures

Use cleaning method on amount of released liquid. Handle used absorption materials as hazardous waste. In case of spillages, dilute with water and wash to drain. Avoid large quantities from entering drain undiluted.

### 7. Handling and storage

Store dry at normal temperatures (+5 to +30 degrees C).

### 8. Exposure control and personal protection

<b>Eye protection</b>	In case of contact with the active substances, flush with water under an eye shower.
<b>Skin protection</b>	Wear protective gloves when in risk of skin contact.

glove material	layer thickness	penetration time
Butylrubber	0.7 mm	≥ 8 h
nature latex	0.6 mm	≥ 8 h
polychloroprene	0.5 mm	≥ 8 h

The dates are reference values. Increased temperatures by warmed substances, body heat etc. and a reduction of the layer strength by stretching can lead to a reduction of the penetration time.

This recommendation only applies to the product mentioned in the safety data sheet. In case of dissolving into or mixing with other substances you must consult a supplier of CE approved gloves.

## 9. Physical and chemical properties

<b>Visual appearance</b>	colourless liquid
<b>Odor</b>	Smells of citric acid
<b>pH (20°C)</b>	~2
<b>Solubility</b>	In water soluble
<b>Density (g/cm<sup>3</sup>)</b>	1.2

## 10. Stability and reactivity

The dissolved salts in hemodialysis concentrate A-component may precipitate at approximately 0°C. Due to its citric properties the mixing hemodialysis concentrate A-component with sodium hypochlorite (bleach) causes formation of toxic chlorine gas.

## 11. Toxicological information

Health effects:

<b>Eyes contact</b>	splash and aerosol may irritate the eye
<b>Skin</b>	after long exposure, may cause irritation to the skin
<b>Ingestion</b>	cause gastrointestinal irritation, nausea and vomiting.

Toxicity:

<b>LD50</b> citric acid 100%	3,000 mg/kg (rat, oral)
<b>LD50</b> Sodium acetate 100%	3,310 mg/kg (rat, oral)
<b>LD50</b> CaCl <sub>2</sub>	1,000 mg/kg (rat, oral)
<b>LD50</b> MgCl <sub>2</sub>	8,100 mg/kg (rat, oral)
<b>LD50</b> KCl	2,600 mg/kg (rat, oral)
<b>LD50</b> NaCl	10,000 mg/kg (rat, oral)
<b>LD50</b> Glucose	25,800 mg/kg (rat, oral)

## 12. Ecological information

No ecological problems are expected when properly handled and used.

## 13. Disposal considerations

Dispose only if utilization is not possible. Small quantities can be discharged to drain (check national or regional regulations). Large amounts of solution are disposed off as chemical waste.

## 14. Transport information

Citratsate® Hemaodialysis Concentrate A-Component for manufacturing of bicarbonate hemodialysis fluid is not classified as a hazardous good.

## 15. Regulatory information

Citratsate® Hemaodialysis Concentrate A-Component for manufacturing of bicarbonate hemodialysis fluid is not classified as dangerous to health or environment.

## 16. Other information

This safety data sheet is compiled in accordance with Regulation (EC) No 1907/2006

symbol



<b>Indication of danger</b>	Irritant
<b>R-phrases</b>	Irritating to eyes

The information given in this safety data sheet are based on the present state of the knowledge and serve to describe the product with regard to the correct safety measures. They do not represent any assurance of characteristics of the described product.

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