

Fresenius Medical Care

***** Important Prescribing Information *****

NaturaLyte Liquid and Granuflo Acid Concentrate
Bicarbonate Alkalosis

DATE: March 29, 2012

SUBJECT: Risk of Alkalosis with acetate containing dialysis acid concentrates

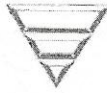
PRODUCT CODES: See Attached

Dear Unit Medical Director/Administrator/Director of Nursing/Home Therapies Manager/Customer,

Fresenius Medical Care North America (FMCNA) is issuing an urgent product notification involving the NaturaLyte Liquid and Granuflo powder product lines (Product Codes: See attached list). Both products contain acetate (NaturaLyte Liquid 4.0 mEq/L; Granuflo 8.0 mEq/L of acetate in the final dialysate); which in addition to bicarbonate, combine to yield the total prescribed buffer. Total buffer should be considered in addition to bicarbonate as part of writing the dialysis prescription.

Previous reports have identified an association between elevated pre-dialysis bicarbonate levels and an increased mortality risk.^{1,2,3,4} Recent analyses performed using FMCNA hemodialysis (HD) patient safety data confirms that alkalosis is a significant risk factor associated with cardiopulmonary (CP) arrest in the dialysis unit, independent of and additive to the risk of CP arrest associated with pre-dialysis hypokalemia. A major cause of metabolic alkalosis in dialysis patients is inappropriately high dialysate total buffer concentration.

NaturaLyte Liquid contributes 4.0 mEq/L of acetate and Granuflo contributes 8.0 mEq/L of acetate to the final dialysate; which in addition to bicarbonate, combine to the total buffer that the patient receives from the dialysate. Acetate is also contained in the dialysis acid concentrates produced by other manufacturers. Since acetate is rapidly converted into bicarbonate by the liver, the bicarbonate prescription entered into the dialysis machine underestimates the total buffer that the patient receives from the dialysate by ~8 mEq/L with dialysate prepared from Granuflo (powder) or by ~4 mEq/L with dialysate prepared from NaturaLyte (liquid).



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Fresenius recommends that clinicians exercise their best clinical judgment regarding the bicarbonate and total buffer base prescription for each patient. This includes individualizing dialysate prescriptions and reviewing them monthly with consideration of patient's pre-dialysis bicarbonate and dialysate total buffer.

Please complete and return the enclosed Reply Form, indicating receipt and understanding of this communication. If you have any additional questions, please contact Customer Service at 1-800-323-5188 or Medical Information at 1-855-616-2309.

Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting by:

- Linking to the MedWatch website at www.fda.gov/medwatch
- Calling 1-800-FDA-1088
- Faxing at 1-800-FDA-0178, or by
- Mailing to: MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787

The FDA has been advised of this product notification

Sincerely,

Jose Diaz-Buxo, MD, FACP
Senior Vice President
Chief Medical and Regulatory Affairs Officer
Fresenius Medical Care North America
Renal Therapies Group

Enclosure:
Reply Form

¹ Gennari FJ. Very low and high predialysis serum bicarbonate levels are risk factors for mortality: what are the Appropriate Interventions? *Semin Dial.* May-Jun;23(3):253-257 2010

² Wu DY, Shinaberger CS, Regidor DL, McAllister CJ, Kopple JD, Kalantar-Zadeh K: Association between serum bicarbonate and death in hemodialysis patients: is it better to be acidotic or alkalotic? *Clin J Am Soc Nephrol* 1:70 78, 2006

³ Bommer J, Locatelli F, Satayathum S, Keen MI., Goodkin DA, Saito A, Akiba T, Port FK, Young EW: Association of predialysis serum bicarbonate levels with risk of mortality and hospitalization in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Am J Kidney Dis* 44:661-671 2004

⁴ Lowrie EG, Lew NL: Death risk in hemodialysis patients: the predictive value of commonly measured variables and an evaluation of death rate differences between facilities. *Am J Kidney Dis* 15:458-482, 1990