

PEDIATRIC MULTI-TRACE ELEMENT AVAILABILITY

May 29, 2013

Dear Healthcare Professional,

Due to the critical shortage of pediatric multi-trace elements in the US market, Fresenius Kabi, USA LLC (Fresenius Kabi USA) is coordinating with the U.S. Food and Drug Administration (FDA) to provide an alternative treatment option during this critical shortage period.

At this time, FDA's regulatory discretion for the importation and distribution of Fresenius Kabi's Peditrace™ 10 mL Concentrate for Infusion Single Dose Plastic Vial is limited to Fresenius Kabi USA during the critical shortage of pediatric multi-trace elements. Importation or distribution of this product in the United States by any other entity is outside the scope of FDA's regulatory discretion, and FDA has not approved Fresenius Kabi's Peditrace™ 10 product for marketing in the U.S.

Effective immediately, and during this temporary period, Fresenius Kabi USA will offer the following presentation of pediatric multi-trace elements:

Peditrace 10 mL Concentrate for Solution for Infusion Single Dose Plastic Vial		
Trace Elements	Content of Trace Elements (per mL)	Active Ingredient (per mL)*
Zinc (Zn)	0.25 mg	Zinc Chloride 0.521 mg
Copper (Cu)	0.02 mg	Copper Chloride 0.054 mg
Manganese (Mn)	1 mcg	Manganese Chloride 3.60 mcg
Selenium (Se)	2 mcg	Sodium Selenite** 4.38 mcg
Iodine (I)	1 mcg	Potassium Iodide** 1.31 mcg
Fluorine (F)	57 mcg	Sodium Fluoride** 0.126 mg

***Active Ingredient content is information only and not to be used for dosing of the product. Use trace element content for dosing.**
 **The total Sodium and Potassium content in Peditrace corresponds to 0.07mg of Sodium (Na) and 0.00031mg of Potassium (K) per 1 mL.

It is important to note that there are some key differences in the formulation and labeling between the current U.S. marketed pediatric multi-trace element product and Peditrace that you need to be aware of which appear in the following table:

Property	Current U.S. neonate and pediatric multi-trace elements	Peditrace
Trace elements & active ingredient salt forms present	4 trace elements present <u>These include:</u> zinc sulfate, cupric sulfate, manganese sulfate, & chromic chloride	6 trace elements present <u>These include:</u> zinc chloride, copper chloride, manganese chloride, sodium selenite, potassium iodide, & sodium fluoride Chromium is not included
Dosing - differences in amount of trace elements present in each 1 mL	See Package insert	See Package insert
Package	10 mL multi-dose vials 3 mL single dose vials 2 mL single dose vials	10 mL single dose vial
Preservative	2 mL & 3 mL vials are preservative free 10 mL vial has preservative	10 mL vial is preservative free Strict Aseptic Technique must always be maintained during handling.
Barcode	Information not available	Any barcodes on Peditrace product will not be appropriately recognized by scanning systems used in the United States and should NOT be used. Institutions should manually input the product into their systems and confirm that barcode systems do not provide incorrect information when the product is scanned.
For questions regarding Peditrace in the United States, please contact Fresenius Kabi USA Vigilance and Medical Affairs at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail appmedicalinfo@APPpharma.com .		

Indications:

- Peditrace is indicated in premature and full-term infants and children needing intravenous nutrition to supply the basal requirements of trace elements. Before administering Peditrace, clinicians should assess the metabolic requirements for trace elements and disease state of the patient. Frequent determinations of serum levels of the various trace elements are suggested as a guideline for adjusting the dosage or completely omitting the solution.

Preparation / Administration:

- Peditrace must be diluted before administration and strict aseptic technique must always be maintained during handling.

- The trace elements present in the solution are physically compatible with the electrolytes and vitamins usually present in the amino acid/dextrose solution used for TPN.

Contraindications / Warnings:

- Peditrace is contraindicated in Wilson’s disease or known hypersensitivity to the active substance or to any of the excipients. In patients with impaired renal or biliary function, there is an increased risk for accumulation of trace elements.
- Peditrace is not tested for aluminum. Aluminum can be toxic and may reach toxic levels with prolonged parenteral administration if kidney function is impaired.
- Allergic reactions to iodine may occur following topical application. No adverse reactions are known to occur as a consequence of using the recommended intravenous iodide dosage levels
- The container closure is not made from natural rubber latex.

Refer to the Peditrace package insert for full prescribing information

This communication and product information is available on the APP web site www.APPpharma.com as well as on the FDA Drug Shortage web site. <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>.

To report adverse events or quality problems experienced with the use of this product, call Fresenius Kabi USA Vigilance and Medical Affairs at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail appmedicalinfo@APPpharma.com.

Fresenius Kabi USA CONTACT NUMBERS: Please use the following contact numbers as appropriate:

Reason To Call	Department	Number
ADE Reporting/Clinical/Technical Info.	Vigilance and Medical Affairs Dept.	1-800-551-7176
Product Availability & Ordering	Customer Service Department	1-888-386-1300

Adverse events may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- **Online:** www.fda.gov/medwatch/report.htm
- **Regular Mail:** use postage-paid FDA form 3500 available at: www.fda.gov/MedWatch/getforms.htm. Mail to MedWatch 5600 Fishers Lane, Rockville, MD 20852-9787
- **Fax:** 1-800-FDA-0178

Sincerely,



Melanie Power-Burns
Senior Director, U.S. Quality & Compliance

Neonate and Pediatric Multi-Trace Element Comparison Table (per mL)

Trace Elements	A.S.P.E.N. Neonates Recommended Dosage*	A.S.P.E.N. Infants Recommended Dosage*	A.S.P.E.N. Children Recommended Dosage*	Multitrace 4 Neonatal** (per mL)	Multitrace 4 Pediatric** (per mL)	Trace Elements 4 Pediatric** (per mL)	Peditrace (per mL)
Zinc (Zn)	Preterm: 400 mcg/kg/d Term: 250 mcg/kg/d	Premature: 450-500 mcg/kg/d Infants <3 mo: 250 mcg/kg/d Infants >3 mo: 50 mcg/kg/d (max 5,000 mcg/d)	50 mcg/kg/d (max 5,000 mcg/d)	1.5 mg (1,500 mcg)	1 mg (1,000 mcg)	0.5 mg (500 mcg)	0.25 mg (250 mcg)
Copper (Cu)	Preterm: 29 mcg/kg/d Term: 20 mcg/kg/d	20 mcg/kg/d (no max stated)	20 mcg/kg/d (500 mcg/d max)	0.1 mg (100 mcg)	0.1 mg (100 mcg)	0.1 mg (100 mcg)	0.02 mg (20 mcg)
Manganese (Mn)	1 mcg/kg/d	1 mcg/kg/d (max 50 mcg/d)	1 mcg/kg/d (max 50 mcg/d)	25 mcg	25 mcg	30 mcg	1 mcg
Chromium (Cr)	Preterm: 0.05-0.3 mcg/kg/d Term: 0.2 mcg/kg/d	0.2 mcg/kg/d (max 5 mcg/d)	0.2 mcg/kg/d (max 5 mcg/d)	0.85 mcg	1 mcg	1 mcg	-
Selenium (Se)	Preterm: 1.5-4.5 mcg/kg/d Term: 2 mcg/kg/d	Premature: 2-3 mcg/kg/d Infant: 1-3 mcg/kg/d	1-3 mcg/kg/d (100 mcg/d max)	-	-	-	2 mcg
Iodine (I)	1 mcg/kg/d	1 mcg/d	1 mcg/d	-	-	-	1 mcg
Fluorine (F)	No Recommendation	No Recommendation	No Recommendation	-	-	-	57 mcg



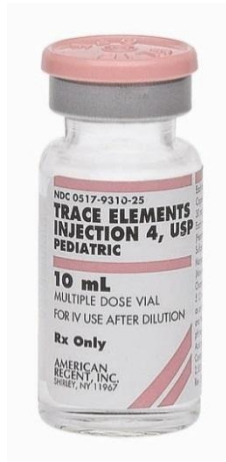

*Vaneek V, Borum P, Buchman A, et al. A.S.P.E.N. Position Paper: Recommendation for Changes in Commercially Available Parenteral Multivitamin and Multi-Trace Element Products. *Nutr Clin Pract.* 2012; June: 1-52. SDV = Single Dose Vial; MDV = Multidose vial

**Multitrace 4 Neonatal, Multitrace 4 Pediatric, Trace Element 4 Pediatric are registered products of American Regent.

Neonate and Pediatric Active Ingredient Comparison Table

Trace Elements	Multitrace 4 Neonatal & Multitrace 4 Pediatric	Trace Elements 4 Pediatric	Peditrace
Zinc (Zn)	Zinc Sulfate	Zinc Sulfate	Zinc Chloride
Copper (Cu)	Cupric Sulfate	Cupric Sulfate	Copper Chloride
Manganese (Mn)	Manganese Sulfate	Manganese Sulfate	Manganese Chloride
Chromium (Cr)	Chromic Chloride	Chromic Chloride	-
Selenium (Se)	-	-	Sodium Selenite
Iodine (I)	-	-	Potassium Iodide
Fluorine (F)	-	-	Sodium Fluoride

Neonate and Pediatric Label Product Comparison Table

	Multitrace 4 Neonatal	Multitrace 4 Pediatric	Trace Elements 4 Pediatric	Peditrace
				
NDC#	0517-6202-25	0517-9203-25	0517-9310-25	63323-147-10
Fill Volume	2 mL	3 mL	10 mL	10 mL
Description	Single Dose Vial	Single Dose Vial	Multiple Dose Vial	Single Dose Plastic Vial
Manufacturer	American Regent	American Regent	American Regent	Fresenius Kabi Norge A/S
Preservative Free	Yes	Yes	No	Yes