TRACE ELEMENTS 4- trace elements 4 injection, solution
American Regent, Inc.

Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.

TRACE ELEMENTS INJECTION 4, USP

PEDIATRIC

FOR IV USE AFTER DILUTION

Rx Only

DESCRIPTION

TRACE ELEMENTS INJECTION 4, USP PEDIATRIC is a sterile, nonpyrogenic solution containing four Trace Elements for use as an additive for Total Parenteral Nutrition (TPN).

Each mL provides: Zinc 0.5 mg, Copper 0.1 mg, Manganese 30 mcg, and Chromium 1 mcg. Each mL contains: Zinc Sulfate Heptahydrate 2.2 mg (equivalent to 0.5 mg Zinc), Cupric Sulfate Pentahydrate 0.4 mg (equivalent to 0.1 mg Copper), Manganese Sulfate Monohydrate 92.3 mcg (equivalent to 30 mcg Manganese), Chromic Chloride Hexahydrate 5.12 mcg (equivalent to 1 mcg Chromium), and Water for Injection q.s. pH may be adjusted with Sulfuric Acid and/or Sodium Hydroxide. 0.9% Benzyl Alcohol is added as an antimicrobial preservative.

CLINICAL PHARMACOLOGY

ZINC has been identified as a cofactor for over 70 different enzymes, including carbonic anhydrase, alkaline phosphatase, lactic dehydrogenase and both RNA and DNA polymerase. Zinc facilitates wound healing, helps maintain normal growth rates, normal skin hydration and senses of taste and smell.

Providing zinc during TPN prevents development of the following deficiency symptoms: Parakeratosis, hypogeusia, anorexia, dysosmia, geophagia, hypogonadism, growth retardation and hepatosplenomegaly. At plasma levels below 20 mcg zinc/100 mL, dermatitis followed by alopecia has been reported for TPN patients.

COPPER is essential as a cofactor for serum ceruloplasmin, an oxidase necessary for proper formation of the iron carrier protein, transferrin. Copper also helps maintain normal rates of red and white blood cell formation. Scorbutic type bone changes seen in infants fed exclusively with copper-poor cow’s milk are believed due to decreased activity of ascorbate oxidase, a cuproenzyme.

Providing copper during TPN prevents development of the following deficiency symptoms: leukopenia, neutropenia, anemia, depressed ceruloplasmin levels, impaired transferring formation and secondary iron deficiency.

MANGANESE is an activator for enzymes such as polysaccharide polymerase, liver arginase, cholinesterase and pyruvate carboxylase.

Providing manganese during TPN prevents development of the following deficiency symptoms: nausea and vomiting, weight loss, dermatitis, and changes in growth and color of hair.

CHROMIUM (trivalent) is part of glucose tolerance factor, an activator of insulin-mediated reactions. Chromium helps to maintain normal glucose metabolism and peripheral nerve function.

Providing chromium during TPN prevents development of the following deficiency symptoms: impaired glucose tolerance, ataxia, peripheral neuropathy, and a confusional state similar to mild/moderate

hepatic encephalopathy.

INDICATIONS AND USAGE

This formulation is indicated for use as a supplement to intravenous solutions given for TPN for children up to 11 years of age. Administration of the solution in TPN solutions helps to maintain plasma levels of zinc, copper, manganese, and chromium and to prevent depletion of endogenous stores of these trace elements and subsequent deficiency symptoms.

CONTRAINDICATIONS

TRACE ELEMENTS INJECTION 4, USP PEDIATRIC should not be given undiluted by direct injection into a peripheral vein because of the potential of infusion phlebitis.

WARNINGS

Copper and Manganese are eliminated via the bile. In patients with severe liver dysfunction and/or biliary tract obstruction, decreasing or omitting copper and manganese supplements entirely may be necessary.

This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

Before administering **TRACE ELEMENTS INJECTION 4, USP PEDIATRIC** in TPN solutions, the physician must 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. **ZINC** is eliminated via the intestine and kidneys. The possibility of retention should be considered in patients with malfunctioning excretory routes. **COPPER** and **MANGANESE** are eliminated via the bile, therefore, the possibility of the retention of these elements should be considered in patients with biliary obstruction. Ancillary routes of **MANGANESE** excretion, however, include pancreatic juice, or reabsorption into the lumen of duodenum, jejunum, or ileum.

In assessing the contribution of **CHROMIUM** supplements to maintenance of normal glucose homeostasis, consideration should be given to the possibility that the patient may be diabetic, in which case oral or intravenous antidiabetic medication may be indicated.

Pregnancy

Teratogenic Effects

Pregnancy Category C: Safety for use in pregnancy has not been established. Use of Multiple Trace Elements 4, USP in women of childbearing potential requires that anticipated benefits be weighed against possible hazards.

ADVERSE REACTIONS

The amounts of **ZINC, COPPER, MANGANESE, AND CHROMIUM** in the solution are very small and toxicity symptoms due to these trace elements at suggested dosage level are considered unlikely to occur.

OVERDOSAGE

Symptoms of **ZINC** overdose resulting from oral ingestion of Zinc Sulfate in large amounts have resulted in death. Symptoms included nausea, vomiting, dehydration, electrolyte imbalances, dizziness, abdominal pain, lethargy and incoordination. Single intravenous doses of 1 to 2 mg zinc/kg body weight have been given to adult leukemia patients without toxic manifestations. Normal plasma levels for Zinc vary from approximately 88 to 112 mcg/100 mL. Plasma levels sufficient to produce symptoms of toxic manifestations are not known. Calcium supplements may confer a protective effect against Zinc toxicity.

Symptoms of **COPPER** toxicity reported in literature include prostration, behavior change, diarrhea, progressive marasmus, hypotonia, photophobia and peripheral edema; such symptoms have been reported with a serum copper level of 286 mcg/dL. D-penicillamine has been reported effective as an antidote.

MANGANESE toxicity has not been reported in patients receiving TPN. Neither have reports of manganese toxicity from excessive intake in foods and/or beverages been published. Symptoms of **CHROMIUM** toxicity include nausea, vomiting, ulcers and gastrointestinal tract, renal and hepatic damage and abnormalities of the central nervous system culminating in convulsions and coma. Trivalent Chromium administered intravenously to TPN patients has been shown to be nontoxic when given at dosage levels up to 250 mcg/day for two consecutive weeks.

DOSAGE AND ADMINISTRATION

Do not use syringes, needles, or intravenous sets containing aluminum parts that may come in contact with **TRACE ELEMENTS INJECTION 4, USP PEDIATRIC,** for preparation or administration. Aluminum reacts and dissolves in acid media.

Each mL of the solution provides Zinc 0.5 mg, Copper 0.1 mg, Manganese 30 mcg, and Chromium 1 mcg, and is administered intravenously only after dilution to a minimum of 1:200. The suggested dosage ranges for the four trace elements are:

ZINC: For the metabolically stable adult receiving TPN, the suggested intravenous dosage level is 2.5 to 4 mg zinc/day. An additional 2 mg zinc/day is suggested for acute catabolic states. For the stable adult with fluid loss from the small bowel, an additional 12.2 mg zinc/liter of small bowel fluid lost, or an additional 17.1 mg zinc/kg of stool or ileostomy output is recommended. Frequent monitoring of zinc blood levels is suggested for patients receiving more than the usual maintenance dosage level of zinc. Normal plasma levels for zinc vary from approximately 88 to 112 mcg/100 mL.

For full term infants and children, 100 mcg zinc/kg/day is recommended. For premature infants (birth weight less than 1500 g) up to 3 kg in body weight, 300 mcg zinc/kg/day is suggested.

COPPER: For the metabolically stable adult receiving TPN, the suggested additive dosage level is 0.5 to 1.5 mg copper/day. For pediatric patients, the suggested additive dosage level is 20 mcg copper/kg/day. The normal plasma range for copper is approximately 80 to 160 mcg/100 mL.

MANGANESE: For the metabolically stable adult receiving TPN, the suggested additive dosage level for manganese is 0.15 to 0.8 mg/day. For pediatric patients, a dosage level of 2 to 10 mcg manganese/kg/day is recommended.

CHROMIUM: For the metabolically stable adult receiving TPN, the suggested additive dosage level is 10 to 15 mcg chromium/day. The metabolically stable adult with intestinal fluid loss may require 20 mcg chromium/day with frequent monitoring of blood levels as a guideline for subsequent administration. For pediatric patients, the suggested additive dosage level is 0.14 to 0.20 mcg/kg/day.

Periodic monitoring of plasma levels of Zinc, Copper, Manganese, and Chromium is suggested as a guideline for administration.

Aseptic addition of TRACE ELEMENTS® - 4 to parenteral nutrition solutions under a laminar flow hood is recommended. The trace elements present in TRACE ELEMENTS® - 4 are physically compatible with the electrolytes and vitamins usually present in parenteral nutrition formulations.

Do not directly mix ascorbic acid injection with copper or selenium containing parenteral products in the same syringe or vial, as this admixture may cause the formation of an insoluble precipitate.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) (See USP Controlled Room Temperature).

HOW SUPPLIED

TRACE ELEMENTS INJECTION 4, USP PEDIATRIC

Each mL provides: Zinc 0.5 mg, Copper 0.1 mg, Manganese 30 mcg, and Chromium 1 mcg.

NDC 0517-9310-25 10 mL Multiple Dose Vial* Packaged in boxes of 25

*Contains 0.9% Benzyl Alcohol as an antimicrobial preservative.

AMERICAN
REGENT, INC.
SHIRLEY, NY 11967

IN9310
Rev. 8/18

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Container

NDC 0517-9310-25

TRACE ELEMENTS INJECTION 4, USP
PEDIATRIC

10 mL
MULTIPLE DOSE VIAL

FOR IV USE AFTER DILUTION

Rx Only

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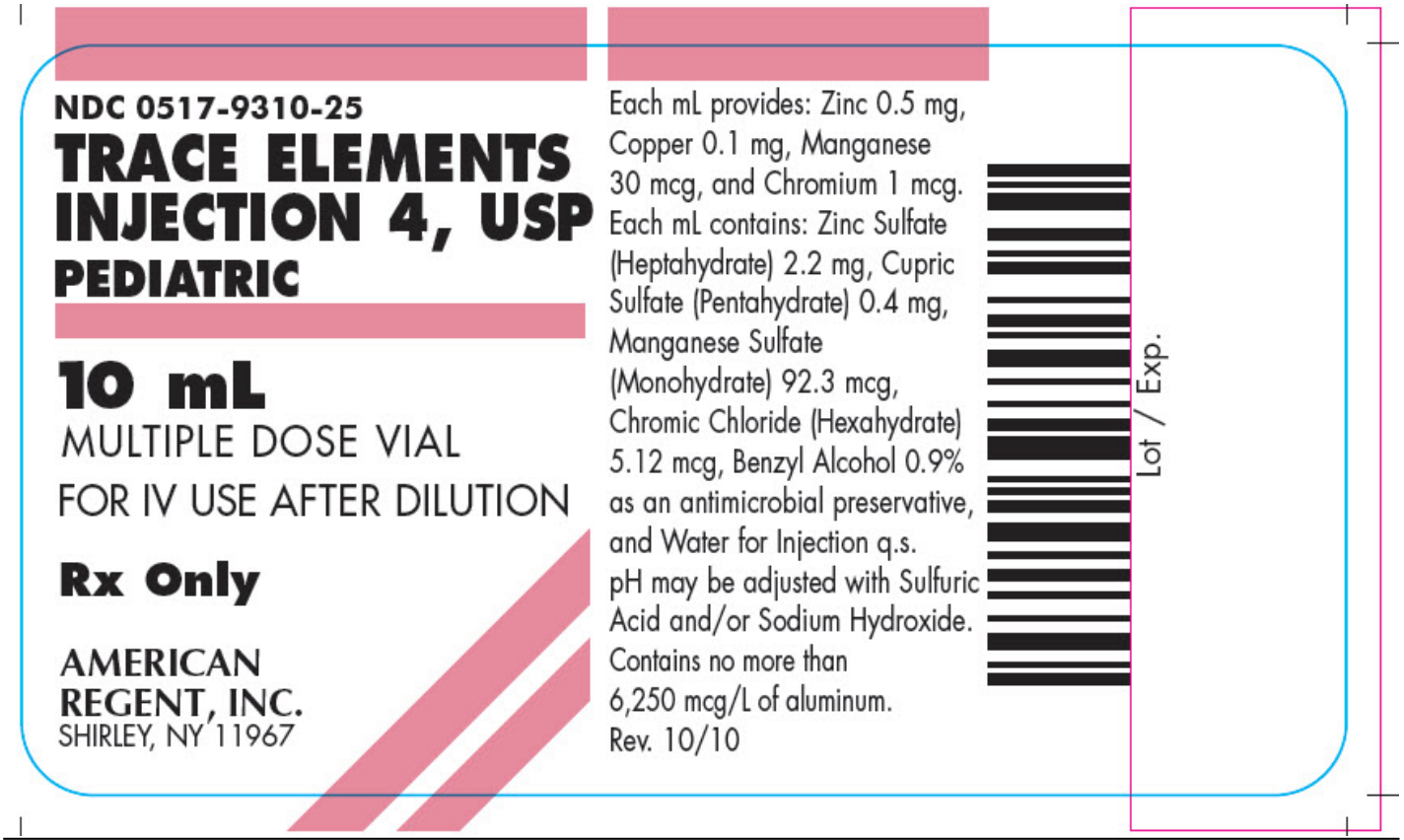
SHIRLEY, NY 11967



Carton

TRACE ELEMENTS INJECTION 4, USP
PEDIATRIC

NDC 0517-9310-25
25 x 10 mL
MULTIPLE DOSE VIALS

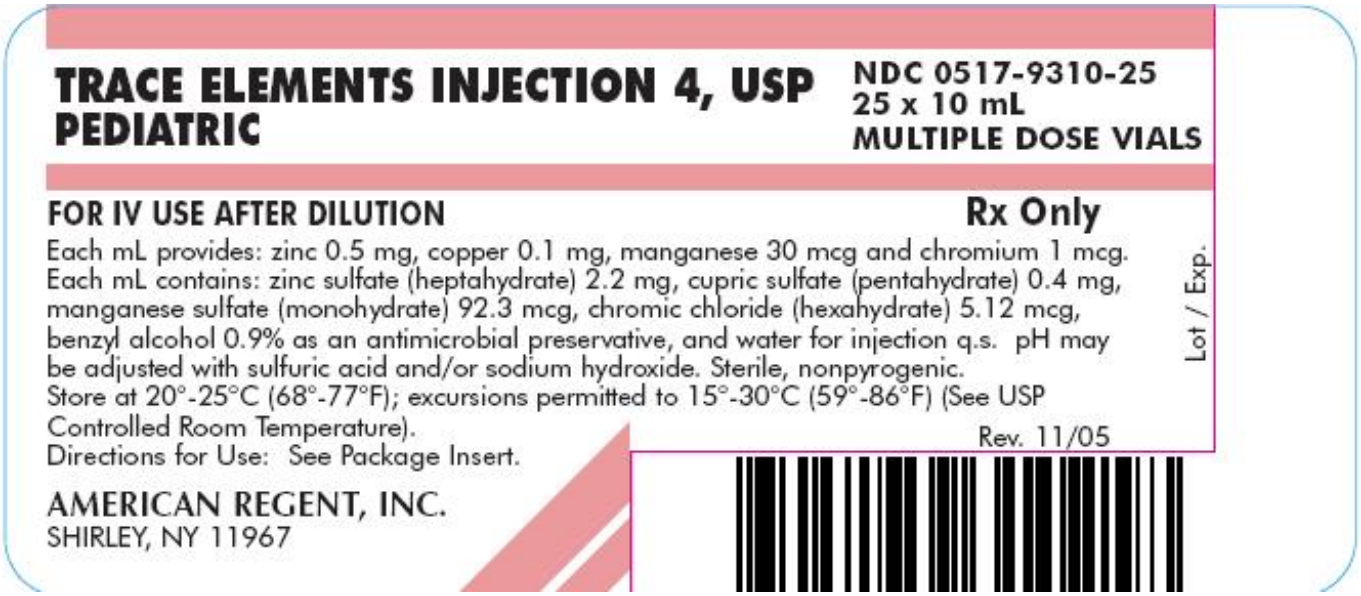
FOR IV USE AFTER DILUTION

Rx Only

Each mL provides: zinc 0.5 mg, copper 0.1 mg, manganese 30 mcg, and chromium 1 mcg. Each mL contains: zinc Sulfate (heptahydrate) 2.2 mg, cupric sulfate (pentahydrate) 0.4 mg, manganese sulfate (monohydrate) 92.3 mcg, chromic chloride (hexahydrate) 5.12 mcg, benzyl alcohol 0.9% as an antimicrobial preservative, and water for injection q.s. pH may be adjusted with sulfuric acid and/or sodium hydroxide. Sterile, nonpyrogenic.
Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F) (See USP Controlled room Temperature).
Directions for Use: See Package Insert.

AMERICAN REGENT, INC.
SHIRLEY, NY 11967

Rev 11/05



Serialization Label

TRACE ELEMENTS 4

trace elements 4 injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0517-9310
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ZINC SULFATE HEPTAHYDRATE (UNII: N57JI2K7WP) (ZINC CATION - UNII:13S1S8SF37)	ZINC CATION	2.2 mg in 1 mL

CUPRIC SULFATE (UNII: LRX7AJ16DT) (CUPRIC CATION - UNII:8CBV67279L)	CUPRIC CATION	0.4 mg in 1 mL
MANGANESE SULFATE (UNII: W00LYS4T26) (MANGANESE CATION (2+) - UNII:H6EP7W5457)	MANGANESE CATION (2+)	92.3 ug in 1 mL
CHROMIC CHLORIDE (UNII: KB1PCR9DMW) (CHROMIC CATION - UNII:X1N4508KF1)	CHROMIC CATION	5.12 ug in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BENZYL ALCOHOL (UNII: LKG8494WBH)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SULFURIC ACID (UNII: O40UQP6WCF)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0517-9310-25	25 in 1 TRAY	02/24/1994	
1		10 mL in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
UNAPPROVED DRUG OTHER		02/24/1994	

Labeler - American Regent, Inc. (002033710)

Establishment

Name	Address	ID/FEI	Business Operations
American Regent, Inc.		002033710	ANALYSIS(0517-9310) , MANUFACTURE(0517-9310)

Revised: 9/2019 American Regent, Inc.