

MULTITRACE® - 4 PEDIATRIC (TRACE ELEMENTS INJECTION 4, USP)

FOR IV USE AFTER DILUTION

Rx Only



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

Each mL provides: Zinc 1 mg, Copper 0.1 mg, Manganese 25 mcg and Chromium 1 mcg.

Each mL contains: Zinc Sulfate Heptahydrate 4.39 mg (equivalent to 1 mg Zinc); Cupric Sulfate Pentahydrate 0.4 mg (equivalent to 0.1 mg Copper); Manganese Sulfate Monohydrate 77 mcg (equivalent to 25 mcg Manganese); Chromic Chloride Hexahydrate 5.12 mcg (equivalent to 1 mcg Chromium); and Water for Injection, q.s. pH of the solution may have been adjusted with sulfuric acid and/or sodium hydroxide. Preservative Free.

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. Scorbatic 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 transferrin 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, and activator 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: MULTITRACE® - 4 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 MULTITRACE® - 4 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.

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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 **MULTITRACE® - 4 PEDIATRIC** 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 levels 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. 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: Each mL of the solution provides Zinc 1 mg, Copper 0.1 mg, Manganese 25 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 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 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 pediatric patients, a dosage level of 2 to 10 mcg manganese/kg/day is recommended.

CHROMIUM: 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 **MULTITRACE® - 4 PEDIATRIC** to parenteral nutrition solutions under a laminar flow hood is recommended. The trace elements present in **MULTITRACE® - 4 PEDIATRIC** 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°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F) (See USP Controlled Room Temperature).

HOW SUPPLIED: MULTITRACE® - 4 PEDIATRIC (TRACE ELEMENTS INJECTION 4, USP)

Each mL provides: Zinc 1 mg, Copper 0.1 mg, Manganese 25 mcg, and Chromium 1 mcg.

NDC 0517-9203-25

3 mL Single Dose Vial

Packaged in boxes of 25

IN9203
Rev. 8/18
MG #9791

**AMERICAN
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