Multrys[®]: A multiple trace elements injection for neonatal and pediatric patients weighing under 10 kg



Multrys (trace elements injection 4*, USP) is a combination of trace elements (zinc sulfate, cupric sulfate, manganese sulfate, and selenious acid) indicated for neonatal and pediatric patients weighing less than 10 kg.¹

The concentration of each element in Multrys has been formulated to meet the needs of neonatal and pediatric patients weighing less than 10 kg.¹

Multrys is used as a source of zinc, copper, manganese, and selenium for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated.¹

*Each mL of Multrys contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.

Aligns with current treatment guidelines

Multrys has been specifically developed to more closely align with the American Society for Parenteral and Enteral Nutrition Dosing Recommendations for trace elements supplementation than products previously marketed by American Regent^{®2}

Proven stability

Stability studies support that **Multrys** can be safely stored for up to 9 days when added to the parenteral nutrition admixture and refrigerated¹

Consistent supply

Multrys is proudly manufactured in the US with active pharmaceutical ingredients and components sourced in the US. Our supply chain is short so as a result, American Regent is positioned to provide you with supply consistency to help ensure critical medications reach patients quickly

Please see the table to the right for product information. For additional information on Multrys, please visit www.americanregent.com.

PRODUCT INFORMATION

Multrys [®] Neonatal and pediatric pa	ntients weighing less than 10 kg
Approval status	FDA-approved

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Availability	Available
Pack NDC	0517-9302-25
Trace elements per mL	 Zinc 1,000 mcg Copper 60 mcg Manganese 3 mcg Selenium 6 mcg
Vial type	Single-dose vial
Fill volume	1 mL
Preservative	Preservative-free
Specific gravity	1.004 (g/mL)
Cap color	Aqua
Aluminum content	No more than 1,500 mcg/L of aluminum
Pack size	25
Storage	Store at 20°C-25°C (68°F-77°F)
Trace element stability in TPN	Up to 9 days when added to the PN admixture and refrigerated

NDC=National Drug Code; PN=parenteral nutrition; TPN=total parenteral nutrition.

Multrys® (trace elements injection 4*, USP) more closely aligns with the daily recommendations for parenteral trace elements set forth by the American Society for Parenteral and Enteral Nutrition (ASPEN).²

*Each mL of Multrys contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.





DAILY PARENTERAL NUTRITION (PN) RECOMMENDATIONS COMPARISON— NEONATAL AND PEDIATRIC PATIENTS WEIGHING LESS THAN 10 KG

Trace element	ASPEN: PN trace elements daily dosing ²		Multrys label: Daily requirement of trace element supplementation for pediatric patients ¹		
	Preterm neonates	Term neonates 3 kg-10 kg	Less than 3 kg	3 kg-5 kg	5 kg-10 kg
Zinc	400 mcg/kg	250 mcg/kg	400 mcg/kg	250 mcg/kg	100 mcg/kg
Copper	20 mcg/kg	20 mcg/kg	20 mcg/kg	20 mcg/kg	20 mcg/kg
Manganese	1 mcg/kg	1 mcg/kg	1 mcg/kg	1 mcg/kg	1 mcg/kg
Selenium	2 mcg/kg	2 mcg/kg	2 mcg/kg	2 mcg/kg	2 mcg/kg
Chromium	0.05-0.3 mcg/kg	0.2 mcg/kg	0 mcg/kg	0 mcg/kg	0 mcg/kg

Multrys dosing: Added to parenteral nutrition¹

Pediatric patients weighing 0.4 kg to 0.59 kg: The total recommended dosage of Multrys is 0.2 mL every other day. Daily supplementation of zinc, copper, and selenium will be needed to meet daily requirements. Pediatric patients weighing 0.6 kg to less than 10 kg: The recommended dosage of Multrys is 0.3 mL/kg/day rounded to the nearest 0.1 mL for up to a maximum of 1 mL per day. Additional trace elements supplementation with Multrys: Multrys is recommended only for pediatric patients who require supplementation with all four of the individual trace elements (ie, zinc, copper, manganese, and selenium). To determine the additional amount of supplementation needed, compare the calculated daily recommended dosage based on the body weight of the patient to the amount of each trace element provided by Multrys and enteral nutrition sources. Multrys is not recommended for pediatric patients who may require a lower dosage of 1 or more of these individual trace elements. Avoid additional manganese supplementation with Multrys use. Accumulation of manganese in the brain can occur with long-term administration of higher than recommended dosage of 1 mcg/kg/day. For complete information, including dosage and administration, please see the Full Prescribing Information.



*Each mL of Multrys contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.

For intravenous use

INDICATIONS AND USAGE

Multrys is a combination of trace elements (zinc sulfate, cupric sulfate, manganese sulfate, and selenious acid) indicated in neonatal and pediatric patients weighing less than 10 kg as a source of zinc, copper, manganese, and selenium for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Contraindicated in patients with hypersensitivity to zinc or copper.

WARNINGS AND PRECAUTIONS

<u>Pulmonary Embolism due to Pulmonary Vascular Precipitates</u>: Pulmonary vascular precipitates causing pulmonary vascular emboli and pulmonary distress have been reported in patients receiving parenteral nutrition. If signs of pulmonary distress occur, stop the parenteral nutrition infusion and initiate a medical evaluation.

<u>Vein Damage and Thrombosis</u>: Multrys must be prepared and used as an admixture in parenteral nutrition solution. It is not for direct intravenous infusion. In addition, consider the osmolarity of the final parenteral nutrition solution in determining peripheral versus central administration. Solution with an osmolarity of 900 mOsmol/L or greater must be infused through a central catheter. The infusion of hypertonic nutrient solution into a peripheral vein may result in vein irritation, vein damage, and/or thrombosis.

<u>Neurologic Toxicity with Manganese</u>: Monitor for clinical signs and symptoms of neurotoxicity, whole blood manganese concentrations, and liver function tests. Discontinue Multrys and consider brain magnetic resonance imaging (MRI) if toxicity is suspected. Monitor patients for cholestasis or other biliary liver disease.

Hepatic Accumulation of Copper and Manganese: If a patient develops signs or symptoms of hepatobiliary disease during the use of Multrys, obtain serum concentrations of copper and ceruloplasmin as well as manganese whole blood concentrations; consider using individual trace element products in these patients.

<u>Aluminum Toxicity</u>: Multrys contains aluminum that may be toxic. Patients with renal impairment and preterm infants, including preterm neonates, are particularly at risk.

Monitoring and Laboratory Tests: Monitor blood zinc, copper, and selenium serum concentrations, whole blood manganese concentration, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count, and coagulation parameters.

<u>Hypersensitivity Reactions with Zinc and Copper</u>: If hypersensitivity reactions occur, discontinue and initiate appropriate medical treatment.

ADVERSE REACTIONS

The following adverse reactions were identified in clinical studies or post-marketing reports. Given that some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Adverse reactions with other components of parenteral nutrition solutions:

- Pulmonary embolism due to pulmonary vascular precipitates
- Vein damage and thrombosis
- Aluminum toxicity

Adverse reactions with the use of trace elements administered parenterally or by other routes of administration:

- Neurologic toxicity with manganese
- Hepatic accumulation of copper and manganese
- Hypersensitivity reactions with zinc and copper

USE IN SPECIFIC POPULATIONS

Hepatic Impairment - Hepatic accumulation of copper and manganese have been reported with long-term administration in parenteral nutrition. For patients with cholestasis, biliary

dysfunction, or cirrhosis, monitor hepatic and biliary function during long-term administration of Multrys.

OVERDOSAGE

There are reports on overdosage in the literature for the individual trace elements.

Management of overdosage is supportive care based on presenting signs and symptoms.

DOSAGE AND ADMINISTRATION Important Administration Information

Multrys is supplied as a single-dose vial. Prior to administration, Multrys *must be transferred to a separate parenteral nutrition container*, diluted, and used as an admixture in parenteral nutrition solution.

Overview of Dosing

Prior to administration of parenteral nutrition solution containing Multrys, correct severe fluid, electrolyte and acid-base disorders. It is recommended only for patients who require supplementation with all four of the individual trace elements (zinc, copper, manganese, and selenium). Multrys is not recommended for patients who may require a lower dosage of one or more of the individual trace elements. Avoid additional manganese supplementation with Multrys use.

For additional safety information, please see accompanying <u>Full Prescribing Information</u>.

REF-1825 6/2021

You are encouraged to report adverse drug events (ADEs) to American Regent®:

T 1.800.734.9236; E <u>pv@americanregent.com</u>; F 1.610.650.0170

ADEs may also be reported to the FDA:

1.800.FDA.1088 or www.fda.gov/medwatch

Medical information:

T 1.888.354.4855

(9:00 am–5:00 pm Eastern Time, Monday–Friday) <u>www.americanregent.com/medical-affairs</u>

For medical information outside of normal business hours that cannot wait until the next business day, please call 1.877.845.6371

REFERENCES:

- 1. Multrys (trace elements injection 4*, USP). Package insert. American Regent, Inc.®
- American Society for Parenteral and Enteral Nutrition. Appropriate dosing for parenteral nutrition: ASPEN Recommendations. November 17, 2020. Accessed August 2, 2023. https://www.nutritioncare.org/uploadedFiles/Documents/Guidelines and Clinical Resources/PN%20Dosing%201-Sheet-Nov%202020-FINAL.pdf



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