Trace Elements in Parenteral Nutrition

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AMERICAN REGENT®

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ASPEN=American Society for Parenteral and Enteral Nutrition

Tralement®
(trace elements injection 4*, USP)
*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.
For intravenous use

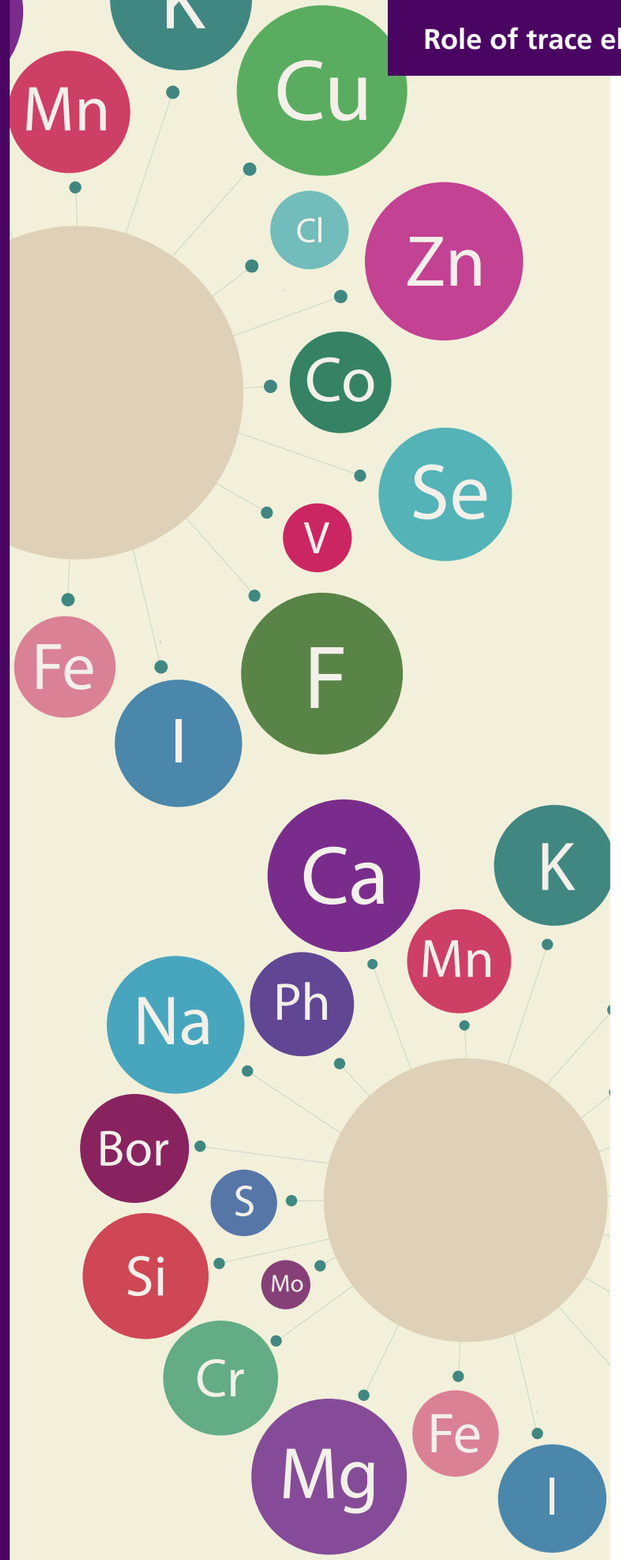
Multrys®
(trace elements injection 4*, USP)
*Each mL contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.
For intravenous use

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.
See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Role of trace elements (TEs) in parenteral nutrition (PN)

TEs are essential to a daily PN routine[1,2]

- While the importance of micronutrients has been known for decades, TE supplementation hasn't always been standard practice in PN
- This may have been due to a prior belief that macronutrients constituted complete nutrition in total PN
- Per current clinical recommendations, TEs are an essential part of the PN prescription, without which the nutrition provided to patients is incomplete



Individuals depicted throughout are not real patients or healthcare providers.

TRACE ELEMENTS (TEs) PLAY A SIGNIFICANT ROLE IN HEALTH AND WELL-BEING[3,4]

TEs are present in all living tissues and are essential to the function of metabolic and physiologic processes[5]

- Out of nearly 20 TEs deemed essential, only 4 are commonly added to parenteral nutrition (PN)[6,7]
- Copper, manganese, selenium, and zinc are commonly used TEs in the US[8]

CURRENT TRACE ELEMENT RECOMMENDATIONS[2,9]

2019 ASPEN Consensus for Adults recommended several overarching treatment principles for TEs in parenteral nutrition

- TEs are essential components of nutrition and PN
- TEs should be provided from Day 1 of PN until PN cessation
- The PN prescription should be individualized to the clinical requirement of the patient
- Micronutrient status should be monitored in long-term patients at baseline and at 6- to 12-month intervals
- At-risk patients should be monitored more frequently at the discretion of the treatment team

ASPEN=American Society for Parenteral and Enteral Nutrition

CURRENT TRACE ELEMENT (TE) RECOMMENDATIONS*

ASPEN

(American Society for Parenteral and Enteral Nutrition)

Routine and appropriate provision of certain vitamins and TEs in parenteral nutrition (PN) is essential in improving nutrition status for patients. This supplementation allows for improvement in underlying disease and in preventing complications of deficiency.[8]

ESPEN

(European Society for Clinical Nutrition and Metabolism)

All PN prescriptions should include a daily dose of multivitamins and TEs.[10]

AUSPEN

(Australasian Society for Parenteral and Enteral Nutrition)

TEs are essential and should be provided daily to patients receiving PN.[4]

*As with any management strategy, a nutrition strategy should be tailored to the individual patient, and the clinical judgment of the healthcare professional should always take precedence over recommendations in guidelines.[2,9]

INDICATIONS AND BENEFITS OF PARENTERAL NUTRITION (PN)

When is PN indicated?[11]

- PN is given to patients who are unable to meet nutrition needs through the gastrointestinal (GI) tract
- PN is often given to those with moderate to severe GI diseases and those individuals who cannot properly digest or absorb food, such as short bowel syndrome, GI fistulas, or bowel obstruction

What is the primary benefit of PN?

PN is a lifesaving or life-sustaining therapy. PN provides the nutrients required when a person cannot consume enough food or nutrients by mouth or through the GI tract. Additionally, when enteral nutrition is unable to provide patients with the required nutrients, PN is an optimal choice, especially during recovery from a disease, illness, or condition[11]

- Patients can become malnourished without proper nutrition and develop adverse conditions such as infections or even death[11]
- PN provides the nutrients needed for proper body functions and overall well-being. PN can also prevent the development of malnutrition[11]
- Malnutrition is associated with increased morbidity and mortality, and serious implications for recovery from disease, trauma, and surgery[12]

Patients of all ages (neonates, infants, children, adolescents, and adults) can receive PN.[11]

How long does a person require PN?

Patients can live well on PN for as long as needed. PN is often used briefly and then decreased or discontinued when the patient switches to enteral nutrition, nutritional needs are met via the GI tract, or eats enough by mouth. Some patients may need PN lifelong.[11]

TRACE ELEMENTS (TE) FOR CRITICALLY ILL PATIENTS

Inflammation, infection, and oxidative stress can increase metabolic requirements for certain TEs[1]

- TEs of concern in critically ill patients include zinc, iron, and selenium[2]
- Copper and manganese should be reduced in patients with cholestasis[1]
- Manganese and chromium are frequently found in elevated levels in long-term parenteral nutrition (PN) patients[1]
- Patients may require increased zinc and selenium if there are increased gastrointestinal losses[1]
- Preexisting malnutrition should be treated early for patients admitted to the hospital[2]
- To avoid deficiencies and excess, clinicians should have adequate knowledge of TE functions and requirements in patients receiving PN[2]

Critical illness may increase TE requirements due to[2]:

- Decreased intake
- Increased losses in some pathologies
- Increased usage to facilitate tissue repair

Insufficient or unbalanced TE therapy may put patients at greater risk of[2]:

- Poor wound healing
- Muscle weakness
- Inadequate immune response
- Organ dysfunction

PREVALENCE OF HOSPITAL MALNUTRITION

Parenteral nutrition (PN) therapy is often essential in diseases or conditions related to malnutrition including, but not limited to, gastrointestinal impairment, pancreatic cancer, organ failure, burns, and trauma[13]

- Malnutrition is not always treated with PN. Other treatment options may include oral or enteral nutrition
  - In the United States, hospital malnutrition has been a problem for decades and remains a problem today[14]
- Most hospital stays were 2x longer when malnutrition was involved[15]
  - Malnutrition affects more than 30% of hospitalized patients in the US and 2.2 million hospital stays[16,17]
  - Globally, hospital malnutrition affects approximately 30% to 50% of patients[14]

CLINICAL CONSEQUENCES OF TRACE ELEMENT (TE) DEFICIENCIES

Trace element	Clinical Consequences of Deficiency	
Copper (Cu)	Copper deficiency may cause[8]:	• Hypochromic microcytic anemia • Neutropenia • Osteopenia • Depigmentation of skin and hair • Skeletal abnormalities • Neurologic abnormalities
Manganese (Mn)	Manganese deficiency is rare, but reported symptoms/signs have included[8,18]:	• Dermatitis • Hypocholesterolemia • Weight loss • Decreased nail and hair growth
Selenium (Se)	Selenium deficiency may cause[8,19]:	• Cardiomyopathy • Skeletal muscle myopathy • Macrocytic anemia • Abnormalities in hair and nails
Zinc (Zn)	Zinc deficiency may cause[8,20]:	• Skin rash • Alopecia • Nonhealing ulcers • Delayed wound healing • Recurrent infections • Growth retardation • Delayed sexual development • Impaired cognitive function

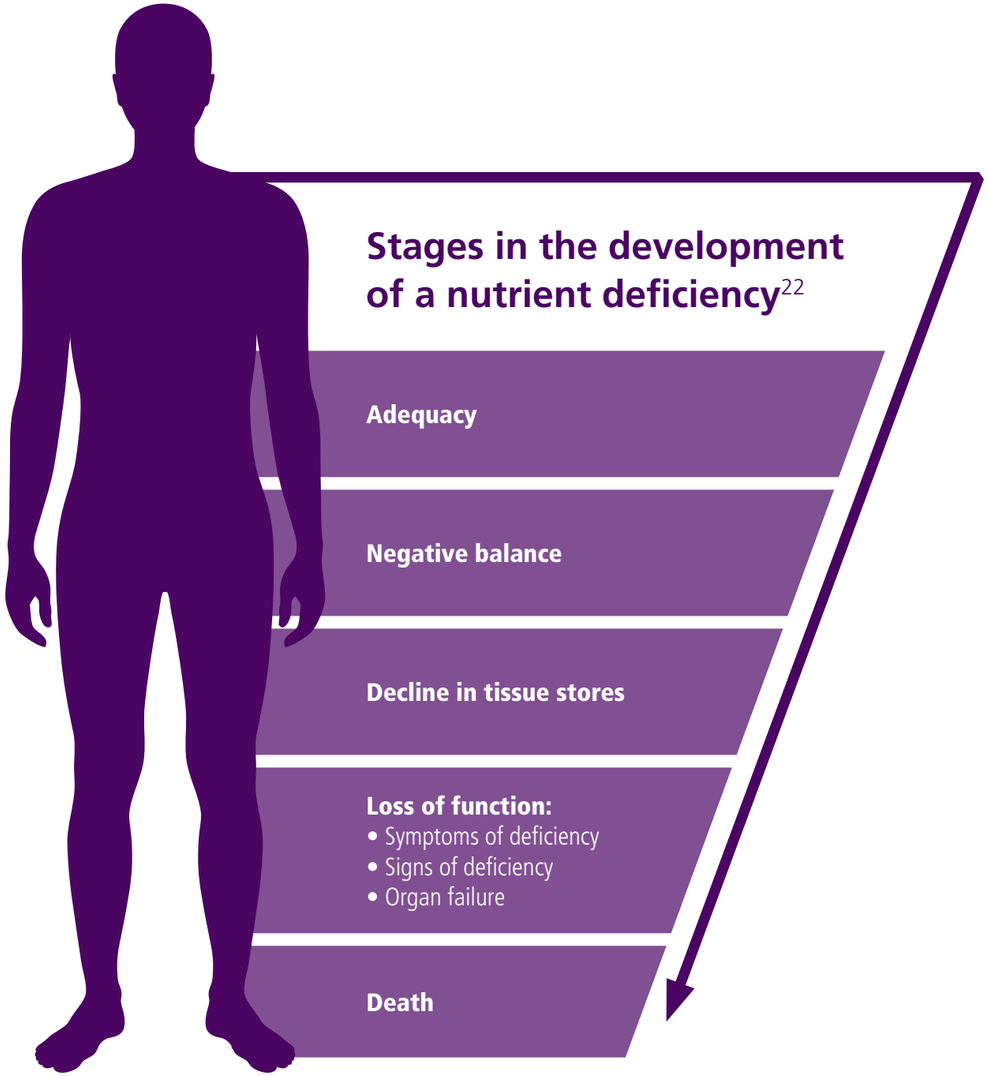
Role of trace elements in parenteral nutrition

CLINICAL CONSEQUENCES OF TRACE ELEMENT TOXICITIES

Trace element	Clinical Consequences of Toxicity	
Copper (Cu)	Chronic copper toxicity may cause[8]:	• Hepatic necrosis and cirrhosis • Renal failure • Neurologic disorders
Manganese (Mn)	Chronic oversupply of manganese can cause neurotoxicity and symptoms/signs, including[8,18]:	• Parkinson-like symptoms (tremor, hypotonia, bradykinesia, gait disturbance) • Headache • Visual disturbance • Seizures • Brain damage
Selenium (Se)	Selenium toxicity may cause[19]:	• Garlic smell to breath • Abdominal pain • GI symptoms (nausea and vomiting, diarrhea) • Loss of hair and nails • Peripheral neuropathy • Irritability and altered mental status
Zinc (Zn)	Chronic zinc toxicity may cause[8,20]:	• Decreased serum copper levels • Microcytosis and neutropenia • Reduced high-density lipoprotein (HDL) cholesterol • Impaired immune function

STAGES LEADING TO TRACE ELEMENT (TE) DEFICIENCY[21]

- Nutritional status can be profoundly affected by most disease states due to a combination of increasing demand and reduced intake
- As the concentration of micronutrients falls, certain tissues will begin to become affected



ATTRIBUTES OF MULTI-TRACE ELEMENT (MTE) FORMULATIONS

The World Health Organization advocates a systematic approach to prescribing parenteral nutrition (PN) to improve quality and minimize errors.[23]

PN is a complex prescription therapy with many potential safety concerns and a high risk for errors in the compounding process.[23,24]

MTE formulation attributes[25]

- Increases compounding workflow efficiency
- Potential for fewer errors
- Fewer steps than using individual trace element vials
- Fewer sterile transfers taking place

Trace element (TE) dosing and the American Society for Parenteral and Enteral Nutrition (ASPEN)

ASPEN daily dosing requirements for parenteral trace elements are continuously evolving.[8]

Current ASPEN Daily Dosing Recommendations[9]

Trace Element	Preterm Neonates	Term Neonates 3-10 kg	Children 10-40 kg	Adolescents >40 kg	ASPEN Adult Standard Daily Requirement
Zinc	400 mcg/kg	250 mcg/kg	50 mcg/kg (max 5,000 mcg/day)	2-5 mg	3-5 mg
Copper	20 mcg/kg	20 mcg/kg	20 mcg/kg (max 500 mcg/day)	200-500 mcg	0.3-0.5 mg
Selenium	2 mcg/kg	2 mcg/kg	2 mcg/kg (max 100 mcg/day)	40-60 mcg	60-100 mcg
Manganese	1 mcg/kg	1 mcg/kg	1 mcg/kg (max 55 mcg/day)	40-100 mcg	55 mcg
Chromium	0.05-0.3 mcg/kg	0.2 mcg/kg	0.2 mcg/kg (max 5 mcg/day)	5-15 mcg	≤10 mcg

Note: These requirements are different from the multi-trace element (MTE) products currently available in the US.

SPECIFIC TRACE ELEMENT (TE) BENEFITS

30 Zn

Zinc (Zn)

Zinc plays catalytic, structural, and regulatory roles, including:

- Cofactor of various enzymes (eg, DNA and RNA polymerases)[20,26]
- Coordinator of protein structural folding that interacts with a variety of proteins, lipids, and nucleic acids[20]
- Catalyst of essential biochemical reactions[20]
- Component of proteins, cell membranes, nucleic acids, and ribosomes[26]
- Patients with severe burns and some shorter-term gastrointestinal issues may require or benefit from higher doses[27]

Current ASPEN Daily Dosing Recommendations[9]

Trace Element	Preterm Neonates	Term Neonates 3-10 kg	Children 10-40 kg	Adolescents >40 kg	ASPEN Adult Standard Daily Requirement
Zinc	400 mcg/kg	250 mcg/kg	50 mcg/kg (max 5,000 mcg/day)	2-5 mg	3-5 mg

ASPEN=American Society for Parenteral and Enteral Nutrition

SPECIFIC TRACE ELEMENT (TE) BENEFITS

29
Cu

Copper (Cu)

- Copper is a cofactor for many metalloenzymes, acting as an oxidase to achieve reduction of molecular oxygen[26]
- Physiologic processes in which copper acts as a cofactor include connective tissue formation, iron metabolism and hematopoiesis, and CNS function[1]
- Evidence supporting dose levels came from a copper balance study[8,28]

Current ASPEN Daily Dosing Recommendations[9]

Trace Element	Preterm Neonates	Term Neonates 3-10 kg	Children 10-40 kg	Adolescents >40 kg	ASPEN Adult Standard Daily Requirement
Copper	20 mcg/kg	20 mcg/kg	20 mcg/kg (max 500 mcg/day)	200-500 mcg	0.3-0.5 mg

ASPEN=American Society for Parenteral and Enteral Nutrition

TE dosing, benefits, and ASPEN

SPECIFIC TRACE ELEMENT (TE) BENEFITS

34
Se

Selenium (Se)

- Selenium plays a role in antioxidant, anti-inflammatory, and immunological activities[1]
- Selenious acid is converted in vivo to hydrogen selenide, and hydrogen selenide acts as a selenium pool to form selenoproteins, such as glutathione peroxidases[26]
- Glutathione peroxidases assist in defense against oxidative stress[1]
- Critically ill patients or those with severe burns may benefit from higher doses[19]

Current ASPEN Daily Dosing Recommendations[9]

Trace Element	Preterm Neonates	Term Neonates 3-10 kg	Children 10-40 kg	Adolescents >40 kg	ASPEN Adult Standard Daily Requirement
Selenium	2 mcg/kg	2 mcg/kg	2 mcg/kg (max 100 mcg/day)	40-60 mcg	60-100 mcg

ASPEN=American Society for Parenteral and Enteral Nutrition

SPECIFIC TRACE ELEMENT (TE) BENEFITS

25 Mn

Manganese (Mn)[26]

- Manganese is essential for the catalytic activity of several metalloenzymes including manganese superoxide dismutase, arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase, and pyruvate carboxylase
- This TE contributes to the function of several other enzyme families, including oxidioreductases, transferases, hydrolases, lyases, isomerases, and ligases

Current ASPEN Daily Dosing Recommendations[9]

Trace Element	Preterm Neonates	Term Neonates 3-10 kg	Children 10-40 kg	Adolescents >40 kg	ASPEN Adult Standard Daily Requirement
Manganese	1 mcg/kg	1 mcg/kg	1 mcg/kg (max 55 mcg/day)	40-100 mcg	55 mcg

ASPEN=American Society for Parenteral and Enteral Nutrition

SPECIFIC TRACE ELEMENT (TE) BENEFITS

24 Cr

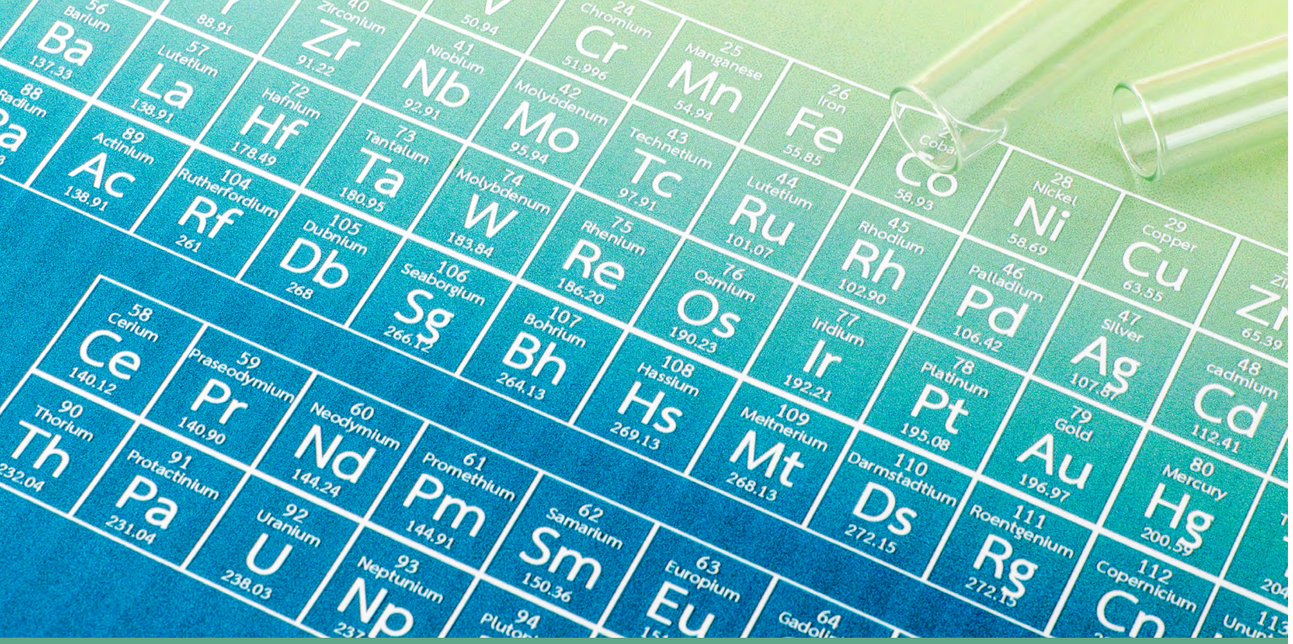
Chromium (Cr)

- In its biologically active trivalent state, chromium is a component of metalloenzymes and functions as a coenzyme in metabolic reactions[1,29]
- Chromium is important in promoting insulin activity in peripheral tissues by[29]:
  - Enhancing insulin stimulation of glucose oxidation and lipogenesis in adipose tissue
  - Increasing insulin-induced glycogenesis in muscle
- Consequently, insulin requirement is reduced[29]
- From 1979 to 2020, chromium dosing recommendations have evolved[8]

Current ASPEN Daily Dosing Recommendations[9]

Trace Element	Preterm Neonates	Term Neonates 3-10 kg	Children 10-40 kg	Adolescents >40 kg	ASPEN Adult Standard Daily Requirement
Chromium	0.05-0.3 mcg/kg	0.2 mcg/kg	0.2 mcg/kg (max 5 mcg/day)	5-15 mcg	≤10 mcg

ASPEN=American Society for Parenteral and Enteral Nutrition



Evolution of multi-trace elements (MTEs) and parenteral nutrition (PN) updates[8]

American Society for Parenteral and Enteral Nutrition (ASPEN) recommendations for trace elements have evolved over time.

Yet, many MTE formulations did not stay current with the changing recommendations.

MULTI-TRACE ELEMENTS (MTEs) AND PARENTERAL NUTRITION (PN)

1979	Four trace elements (TEs) are recommended for adult PN formulations by the Nutrition Advisory Group (NAG) of the American Medical Association.[8]
1984	New recommendations include the addition of selenium. Copper, manganese, and chromium doses are modified.[8]
1994	Recommended dose for selenium is increased, while manganese and chromium are decreased.[8]
2012	ASPEN recommends dose changes in MTE products and requests products be made without chromium.[8]
2019	ASPEN guidelines are updated with special recommendations regarding product shortages and warnings against rationing.[9]
2020	FDA approves Tralement® (trace elements injection 4*, USP), the first MTE injection formulation for PN for adult and pediatric patients weighing at least 10 kg.[30] ASPEN recommendations are updated for chromium.[9]
2021	FDA approves Multrys® (trace elements injection 4*, USP) for neonatal and pediatric patients weighing less than 10 kg.[31]

ASPEN=American Society for Parenteral and Enteral Nutrition

Tralement®
(trace elements injection 4*, USP)
*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.
For intravenous use

Multrys®
(trace elements injection 4*, USP)
*Each mL contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.
For intravenous use

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.
See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Tralement®

(trace elements injection 4*, USP)

*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

For intravenous use

Tralement® is indicated in adult and pediatric patients weighing at least 10 kg[26]

- First FDA-approved multi-trace element (MTE) injection[30]
- Aligns with American Society for Parenteral and Enteral Nutrition (ASPEN) dosing recommendations for adults[9,26]
- Convenient 1 mL vial[26]
- Confidence in supply from American Regent®
- Frees you to focus on patients, with the potential for less error, greater efficiency, and decreased costs

INDICATIONS AND USAGE

Tralement is indicated in adult and pediatric patients weighing at least 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.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Tralement is contraindicated in patients with hypersensitivity to zinc or copper.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

*Each mL of Tralement® contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

TRALEMENT® DOSING, ADULT

For adults and pediatric patients weighing at least 50 kg[26]

The recommended dosage of Tralement is 1 mL per day added to parenteral nutrition (PN).

- Tralement is not recommended for patients who may require a lower dosage of 1 or more of the individual trace elements (TEs)
- Tralement is recommended only for patients who require supplementation with all 4 of the individual TEs (ie, zinc, copper, manganese, and selenium)
- The dosage of the final PN solution containing Tralement must be based on the concentrations of all components in the solution, the patient's clinical condition, nutritional requirements, and the contribution of oral or enteral intake

Comparison of ASPEN Daily Adult TE Recommendations with Tralement[9,26]

Trace Element	ASPEN Adult Standard Daily Requirement	Tralement per 1 mL
Manganese	55 mcg	55 mcg
Copper	0.3-0.5 mg	0.3 mg
Zinc	3-5 mg	3 mg
Selenium	60-100 mcg	60 mcg
Chromium	≤10 mcg	0 mcg

ASPEN=American Society for Parenteral and Enteral Nutrition

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Pulmonary Embolism due to Pulmonary Vascular Precipitates: 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 infusion and initiate a medical evaluation.

Vein Damage and Thrombosis: Tralement 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. Solutions with osmolarity of 900 mOsmol/L or more must be infused through a central catheter. The primary complication of peripheral access is venous thrombophlebitis.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

*Each mL of Tralement® contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

TRALEMENT® DOSING, PEDIATRIC

For pediatric patients weighing 10 kg to 49 kg[26]

The recommended dosage of Tralement based on body weight is 0.2 mL to 0.8 mL per day added to parenteral nutrition (PN).

- Tralement does not provide the recommended daily dosage of zinc (in heavier patients in some weight bands), copper, or selenium
- Additional supplementation using single trace element (TE) products may be needed for these patients

For Pediatric Patients Weighing 10 kg to 49 kg[26]

Patient Population	Body Weight	Tralement Dosage	Manganese	Copper	Zinc	Selenium
Pediatric	10 kg to 19 kg	0.2 mL	11 mcg	60 mcg	600 mcg	12 mcg
Pediatric	20 kg to 29 kg	0.4 mL	22 mcg	120 mcg	1,200 mcg	24 mcg
Pediatric	30 kg to 39 kg	0.6 mL	33 mcg	180 mcg	1,800 mcg	36 mcg
Pediatric	40 kg to 49 kg	0.8 mL	44 mcg	240 mcg	2,400 mcg	48 mcg
Adult and Pediatric	More than 49 kg	1 mL	55 mcg	0.3 mg	3 mg	60 mcg

For complete dosing information, always refer to the Full Prescribing Information.

Important Administration Information

Tralement is supplied as a single-dose vial for *admixture use* only. It is *not for direct intravenous infusion*. Prior to administration, Tralement *must be transferred to a separate parenteral nutrition container*, diluted, and used as an admixture in parenteral nutrition solution.

Tralement is recommended only for patients who require supplementation with all four of the individual trace elements (ie, zinc, copper, manganese, and selenium).

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Neurologic Toxicity with Manganese: Monitor patients receiving long-term parenteral nutrition solutions containing Tralement for neurologic signs and symptoms, and routinely monitor whole blood manganese concentrations and liver function tests. Discontinue Tralement and consider brain magnetic resonance imaging (MRI) if toxicity suspected.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

Tralement® (trace elements injection 4*, USP)

*Each mL of Tralement® contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

TRALEMENT® DOSING, PEDIATRIC

Supplementation with individual trace elements (TEs) in pediatric patients weighing 10 kg to 49 kg[26]

For pediatric patients weighing 10 kg to 49 kg, additional zinc (in heavier patients in some weight bands), copper, and selenium may be needed to meet the recommended daily dosage of these trace elements, shown in the pediatric table on the previous page. 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 the recommended dose of Tralement and other oral or enteral nutrition sources.

Zinc: 50 mcg/kg/day (up to 3,000 mcg/day)

Copper: 20 mcg/kg/day (up to 300 mcg/day)

Selenium: 2 mcg/kg/day (up to 60 mcg/day)

Do not supplement Tralement with additional manganese. Accumulation of manganese in the brain can occur with long-term administration of higher than the recommended dose of 1 mcg/kg/day (up to 55 mcg/day).

Tralement is only recommended for patients who require supplementation with all 4 of the individual trace elements.

Up to 9-day stability[26]

Our American Regent® stability study demonstrated that Tralement can be safely stored (at 20°C to 25°C [68°F to 77°F]) for up to 9 days when added to the parenteral nutrition (PN) admixture and refrigerated, allowing for the preparation of PN admixtures in advance.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Hepatic Accumulation of Copper and Manganese: If a patient develops signs or symptoms of hepatic or biliary dysfunction during the use of Tralement, obtain serum concentrations of copper and ceruloplasmin as well as manganese whole blood concentrations. Consider using individual trace element products in patients with hepatic and/or biliary dysfunction.

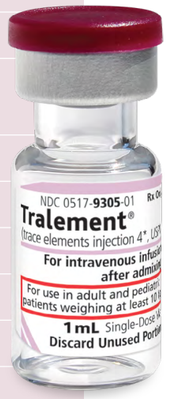
See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

*Each mL of Tralement® contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

TRALEMENT® PRODUCT SPECIFICATIONS

Tralement is indicated in adult and pediatric patients weighing at least 10 kg[26]

Product	Tralement
Approval Status[30]	FDA-approved
Availability	Available
Pack NDC	0517-9305-25
Strength	N/A
Trace Elements per mL[26]	• Zinc 3 mg • Copper 0.3 mg • Manganese 55 mcg • Selenium 60 mcg
Vial Type[26]	Single-dose vial
Fill Volume[26]	1 mL
Preservative[26]	Preservative-Free
Specific Gravity	1.009 (g/mL)
Cap Color	Garnet
Aluminum Content[26]	No more than 6,000 mcg/L of Aluminum
Pack Size	25 vials
Storage[26]	Store at 20°C-25°C (68°F-77°F)
Trace Element Stability in TPN[26]	Up to 9 days, when added to the PN admixture and refrigerated



PN: parenteral nutrition; TPN: total parenteral nutrition

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Aluminum Toxicity: Tralement contains aluminum that may be toxic. Increased risk in patients with renal impairment. Preterm infants, including preterm neonates, are particularly at risk.

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

Hypersensitivity Reactions with Zinc and Copper: If hypersensitivity reactions occur, discontinue Tralement and initiate appropriate medical treatment.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

Tralement® (trace elements injection 4*, USP)

*Each mL of Tralement® contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

SPECIAL PREPARATION AND ADMINISTRATION

Tralement® is indicated in adult and pediatric patients weighing at least 10 kg[26]

Special preparation and administration

- Tralement is *not for direct intravenous infusion*. Prior to administration, Tralement must be prepared and used as an admixture in a parenteral nutrition (PN) solution
- Add Tralement to the PN solution in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area)
- The key factor in the preparation is careful aseptic technique to avoid inadvertent touch contamination during mixing of solutions and addition of other nutrients
- Inspect the PN solution containing Tralement for particulate matter before admixing, after admixing, and prior to administration

Important Administration Information

- Tralement is supplied as a 1 mL single-dose vial to be added to parenteral nutrition admixtures and *is not for direct intravenous infusion*
- Tralement is not approved for pediatric patients weighing less than 10 kg
- Prior to administration of parenteral nutrition solution containing Tralement, correct severe fluid, electrolyte, and acid-base disorders
- Monitor trace element concentrations in blood during long-term administration of parenteral nutrition

Warnings and Precautions

Pulmonary Embolism due to Pulmonary Vascular Precipitates: 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 infusion and initiate a medical evaluation.

Vein Damage and Thrombosis: Tralement 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. Solutions with osmolarity of 900 mOsmol/L or more must be infused through a central catheter. The primary complication of peripheral access is venous thrombophlebitis.

Neurologic Toxicity with Manganese: Monitor patients receiving long-term parenteral nutrition solutions containing Tralement for neurologic signs and symptoms and routinely monitor whole blood manganese concentrations and liver function tests. Discontinue Tralement and consider brain magnetic resonance imaging (MRI) if toxicity suspected.

Hepatic Accumulation of Copper and Manganese: If a patient develops signs or symptoms of hepatic or biliary dysfunction during the use of Tralement, obtain serum concentrations of copper and ceruloplasmin as well as manganese whole blood concentrations. Consider using individual trace element products in patients with hepatic and/or biliary dysfunction.

Aluminum Toxicity: Tralement contains aluminum that may be toxic. Preterm infants, including preterm neonates, are particularly at risk.

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

Hypersensitivity Reactions with Zinc and Copper: If hypersensitivity reactions occur, discontinue Tralement and initiate appropriate medical treatment.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

Multrys®

(trace elements injection 4*, USP)

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

For intravenous use

†Multrys has been specifically formulated to more closely align with the ASPEN (American Society for Parenteral and Enteral Nutrition) Dosing Recommendations for trace element supplementation than previously marketed products.[9,32]

An FDA-approved multi-trace element formulation designed to address nutritional needs in neonatal and pediatric patients weighing less than 10 kg[31,32]

- Formulated to meet today's recommendations†
- Confidence in supply from American Regent®

Multrys (trace elements injection 4*, USP)
*Each mL of Multrys contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.

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.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Contraindicated in patients with hypersensitivity to zinc or copper.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

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

MULTRYS® DOSING[32]

- Prior to administration of parenteral nutrition (PN) solution containing Multrys, correct severe fluid, electrolyte, and acid-base disorders
- The dosage of the final PN solution containing Multrys must be based on the concentrations of all components in the solution, the patient's clinical condition, nutritional requirements, and the contribution of oral or enteral intake
- Monitor fluid and electrolyte status during treatment use of Multrys and adjust the PN solution as needed

RECOMMENDED DOSAGE[32]

For pediatric patients weighing 0.6 kg to <10 kg

Multrys is a fixed-combination product. Each mL of Multrys contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.

- 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**
- The recommended volume of Multrys to be added to PN ranges from 0.2 mL per day to 1 mL **per day** based on body weight. See Table 1 on the next page

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.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Pulmonary Embolism due to Pulmonary Vascular Precipitates: 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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

MULTRYS® RECOMMENDED DOSAGE

Table 1. Recommended Daily Volume of Multrys and Corresponding Amount of Each Trace Element (mcg)[32]

Body Weight	Recommended Weight-Based Dosage in Volume	Amount of Trace Element Provided by the Corresponding Multrys Volume			
		Manganese (mcg)	Copper (mcg)	Zinc (mcg)	Selenium (mcg)
0.6 kg to 0.8 kg	0.2 mL	0.6 mcg	12 mcg	200 mcg	1.2 mcg
0.9 kg to 1.1 kg	0.3 mL	0.9 mcg	18 mcg	300 mcg	1.8 mcg
1.2 kg to 1.4 kg	0.4 mL	1.2 mcg	24 mcg	400 mcg	2.4 mcg
1.5 kg to 1.7 kg	0.5 mL	1.5 mcg	30 mcg	500 mcg	3 mcg
1.8 kg to 2 kg	0.6 mL	1.8 mcg	36 mcg	600 mcg	3.6 mcg
2.1 kg to 2.3 kg	0.7 mL	2.1 mcg	42 mcg	700 mcg	4.2 mcg
2.4 kg to 2.6 kg	0.8 mL	2.4 mcg	48 mcg	800 mcg	4.8 mcg
2.7 kg to 2.9 kg	0.9 mL	2.7 mcg	54 mcg	900 mcg	5.4 mcg
3 kg to 9.9 kg	1 mL	3 mcg	60 mcg	1,000 mcg	6 mcg

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Vein Damage and Thrombosis: 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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Multrys® (trace elements injection 4*, USP)

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

MULTRYS® RECOMMENDED DOSAGE

For neonatal and pediatric patients weighing 0.4 kg to 0.59 kg[32]

Multrys is a fixed-combination product. Each mL of Multrys contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg.

Every other day recommended dosage

- The 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. See Table 2 on the next page

Additional trace element (TE) supplementation with Multrys

Multrys is recommended only for pediatric patients who require supplementation with all 4 of the individual TEs (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 TE provided by Multrys and enteral nutrition sources

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.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Neurologic Toxicity with Manganese: 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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

MULTRYS® DOSING AND DAILY REQUIREMENTS FOR SUPPLEMENTATION

Table 2. Daily Requirement for Element Supplementation for Pediatric Patients[32]

Trace Element	Patient Weight (kg)	Daily Requirement†
Zinc	Less than 3 kg	400 mcg/kg/day
	3 kg to 5 kg	250 mcg/kg/day
	5 kg to 10 kg	100 mcg/kg/day
Copper	—	20 mcg/kg/day
Selenium	—	2 mcg/kg/day
Manganese‡	—	1 mcg/kg/day

†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 with higher than the recommended dosage of 1 mcg/kg/day.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Multrys® (trace elements injection 4*, USP)

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

MULTRYS® DOSING

For pediatric patients weighing 0.4 kg to 0.59 kg and 4 kg to 9.9 kg, Multrys does not provide the recommended daily dosage of copper or selenium[32]

Copper: For patients weighing 0.4 to 0.59 kg or 4 kg to 9.9 kg, add cupric chloride to provide total daily recommended dose of 20 mcg/kg/day, using parenteral and/or enteral routes of administration

Selenium: For patients weighing 0.4 to 0.59 kg or 4 kg to 9.9 kg, add selenious acid to provide total daily recommended dose of 2 mcg/kg/day, using parenteral and/or enteral routes of administration

For pediatric patients weighing less than 3 kg, Multrys does not provide the recommended daily dosage of zinc[32]

Zinc: For patients weighing less than 3 kg, add zinc sulfate to provide total daily recommended dose of 400 mcg/kg/day, using parenteral and/or enteral routes of administration

Monitoring

Monitor zinc, copper, selenium serum concentrations, and manganese whole blood concentrations during long-term administration of parenteral nutrition.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Aluminum Toxicity: 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.

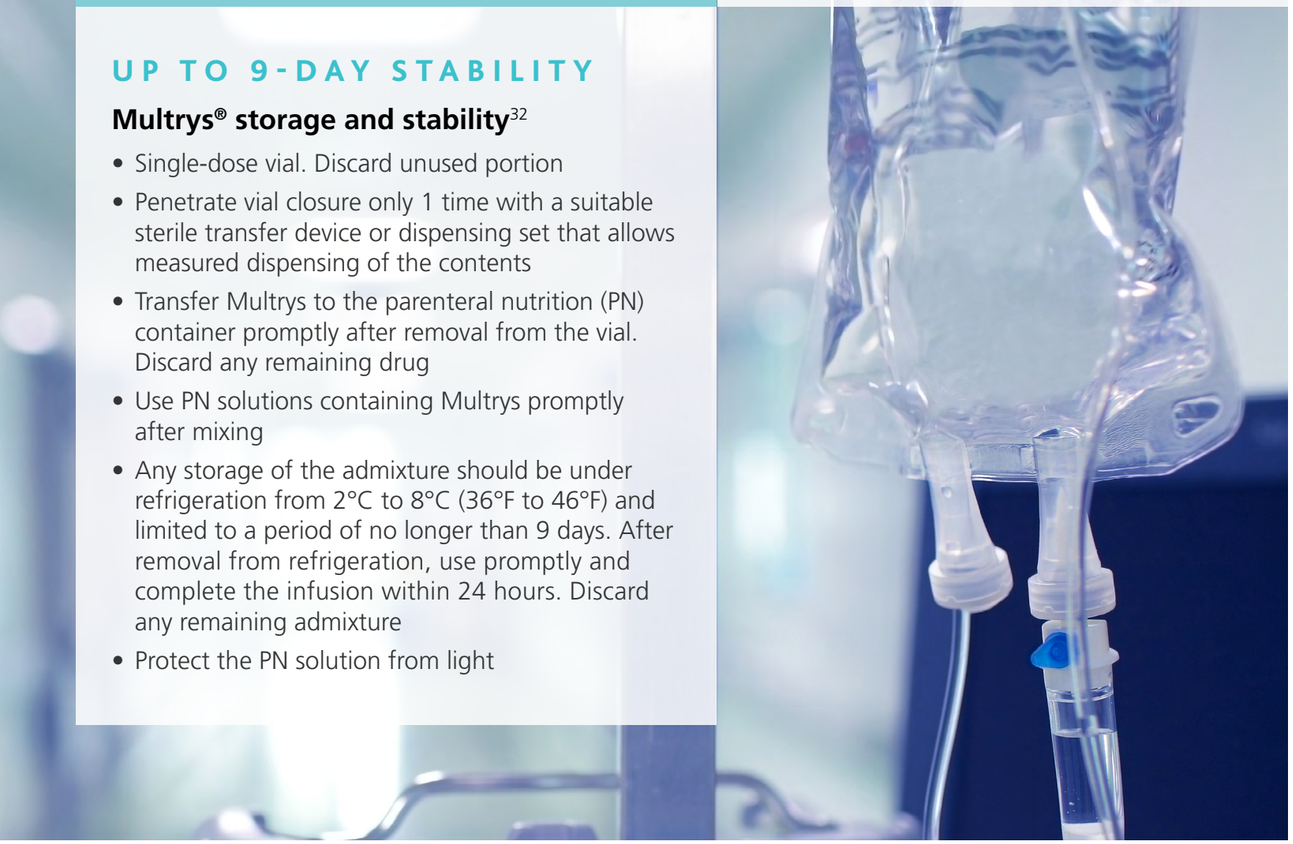
See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

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

UP TO 9-DAY STABILITY

Multrys® storage and stability[32]

- Single-dose vial. Discard unused portion
- Penetrate vial closure only 1 time with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents
- Transfer Multrys to the parenteral nutrition (PN) container promptly after removal from the vial. Discard any remaining drug
- Use PN solutions containing Multrys promptly after mixing
- Any storage of the admixture should be under refrigeration from 2°C to 8°C (36°F to 46°F) and limited to a period of no longer than 9 days. After removal from refrigeration, use promptly and complete the infusion within 24 hours. Discard any remaining admixture
- Protect the PN solution from light



SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Hypersensitivity Reactions with Zinc and Copper: 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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Multrys® (trace elements injection 4*, USP)

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

PRODUCT SPECIFICATIONS

Multrys® is indicated for pediatric patients weighing less than 10 kg[32]

Product	Multrys
Approval Status[31]	FDA-approved
Availability	Available
Pack NDC	0517-9302-25
Strength	N/A
Trace Elements per mL[32]	• Zinc 1,000 mcg • Copper 60 mcg • Manganese 3 mcg • Selenium 6 mcg
Vial Type[32]	Single-dose vial
Fill Volume[32]	1 mL
Preservative[32]	Preservative-Free
Specific Gravity	1.004 (g/mL)
Cap Color	Aqua
Aluminum Content[32]	No more than 1,500 mcg/L of Aluminum
Pack Size	25 vials
Storage[32]	Store at 20°C to 25°C (68°F to 77°F)
Trace Element Stability in TPN[32]	Up to 9 days when added to the PN mixture and refrigerated

PN=parenteral nutrition; TPN=total parenteral nutrition

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS (continued)

Adverse reactions with other components of parenteral nutrition solutions:

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

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Multrys® (trace elements injection 4*, USP)

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

MULTRYS® SPECIAL PREPARATION AND ADMINISTRATION

Multrys is indicated for pediatric patients weighing less than 10 kg[32]

Special preparation and administration

- Multrys is supplied as a single-dose vial. Prior to administration, Multrys *must be transferred to a separate parenteral nutrition (PN) container,* diluted, and used as an admixture in parenteral nutrition solution
- Add Multrys to the PN solution in a suitable work area, such as a laminar flow hood (or an equivalent clean air compounding area)
- The key factor in the preparation is careful aseptic technique to avoid inadvertent touch contamination during mixing of solutions and addition of other nutrients
- Inspect the PN solution containing Multrys for particulate matter before admixing, after admixing, and prior to administration

Additional dosage and administration details

- Multrys is for neonatal and pediatric patients weighing less than 10 kg
- Prior to administration of parenteral nutrition solution containing Multrys, correct severe fluid, electrolyte, and acid-base disorders
- Monitor trace element concentrations in blood during long-term administration of PN

Warnings and Precautions

Pulmonary Embolism due to Pulmonary Vascular Precipitates: 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.

Vein Damage and Thrombosis: 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.

Neurologic Toxicity with Manganese: 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.

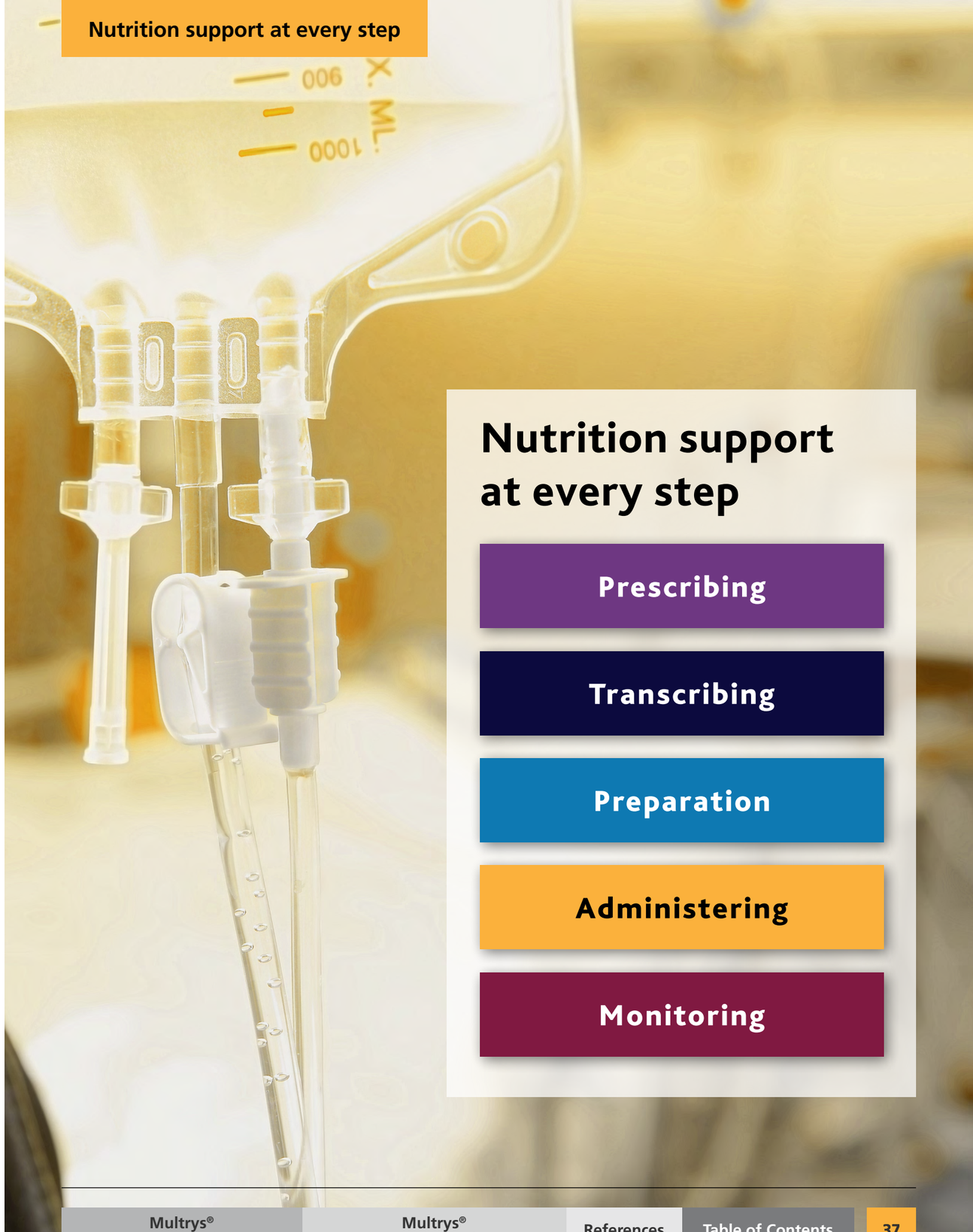
Hepatic Accumulation of Copper and Manganese: If a patient develops signs or symptoms of hepatobiliary disease during the use of Multrys, obtain serum concentrations of copper and ceruloplasmin as well as manganese whole blood concentrations; consider using individual trace element products in these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

Aluminum Toxicity: 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.

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

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.



Prescribing

- Determining optimal levels of trace elements (TEs) can be a challenge[8,33]
- Electronic or computerized parenteral nutrition (PN) orders can improve efficiency and safety and reduce errors[23]
- Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) deliver confidence that the PN you prescribe is aligned to ASPEN dosing recommendations and provide more complete nutrition by including recommended TEs as needed[9,26,32]

ASPEN=American Society for Parenteral and Enteral Nutrition

Transcribing

- A standardized order format helps support reduced errors when a patient is transitioned from hospital to home care[23]
- Tralement and Multrys multi-trace element (MTE) formulations help reduce the number of products needed in a PN order, thereby reducing the potential for transcribing errors

Tralement®

(trace elements injection 4*, USP)

*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Hypersensitivity Reactions with Zinc and Copper: If hypersensitivity reactions occur, discontinue Tralement 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.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

Nutrition support at every step

Preparation

- Parenteral nutrition (PN) preparation can be complex and require up to 15 separate components to be mixed with sterile technique and painstaking attention to detail[24]
- Multi-trace element (MTE) formulations decrease the need to compound separate components, helping mitigate potential errors and offering the possibility for greater efficiency and decreased costs[25]
- Stability studies demonstrate that Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) can be safely stored (at 20°C to 25°C [68°F to 77°F]) for up to 9 days when added to PN admixture and refrigerated, allowing for the preparation of PN admixtures in advance[26,32]

Multrys®

(trace elements injection 4*, USP)

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

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS (continued)

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

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Administering

- Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) are FDA-approved multi-trace element (MTE) formulations designed to closely align with ASPEN dosing recommendations[9,30,31]
- The concentration of each element in Tralement has been formulated to meet the needs of pediatric and adult patients weighing at least 10 kg[26]
- The concentration of each element in Multrys has been formulated to meet the needs of neonatal and pediatric patients weighing less than 10 kg[32]
- These MTE formulations from American Regent® give you confidence to treat a broad range of adult, pediatric, and neonatal patients as needed

ASPEN=American Society for Parenteral and Enteral Nutrition

Tralement®

(trace elements injection 4*, USP)

*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS (continued)

Adverse reactions with other components of parenteral nutrition solutions:

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

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

Nutrition support at every step

Monitoring

- Appropriate monitoring should be determined for the patient's condition to assess efficacy, detect and prevent complications, evaluate changes, and document outcomes[23]
- Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) may help ensure that patients receive complete nutrition[9,26,32]
  - Tralement is aligned with trace element (TE) dosage recommendations from ASPEN[9,26]
  - Multrys more closely aligns with ASPEN dosage recommendations for TE supplementation than products previously marketed by American Regent®[9,32]

Select Important Safety Information

- 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

ASPEN=American Society for Parenteral and Enteral Nutrition

Multrys®

(trace elements injection 4*, USP)

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

SELECT IMPORTANT SAFETY INFORMATION

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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Prescribing practices[23]

Prescribers should be educated on basic parenteral nutrition (PN) prescribing and monitoring.

PN education has been associated with improvement in safer prescribing practices.

TRANSITION OF CARE

Appropriate prescribing and ordering[23]

- Patients receive parenteral nutrition (PN) in a broad range of care settings—from the ICU to the home. This range of settings raises the potential for disparities in knowledge and skills in PN
- Lack of standardization can lead to errors in prescribing and transcription when a patient is transferred from 1 healthcare setting to another
- Adopting a standardized PN order format designed with ingredients listed in the same sequence may improve consistency, and clarifying orders decreases the risk of errors when patients transition care from 1 setting to another

Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) support simplicity and confidence in dosing, prescribing, transcribing, preparation, administration, and monitoring.

Tralement®

(trace elements injection 4*, USP)

*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS (continued)

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

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

Multrys®

(trace elements injection 4*, USP)

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

SELECT IMPORTANT SAFETY INFORMATION

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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Thousands of patients rely on PN each year, and TEs provide a critical component for complete nutrition therapy.[6]

SPECIFIC RISKS UPON INITIATION OF TRACE ELEMENTS (TEs)

Omitting TEs from the parenteral nutrition (PN) prescription can be a big risk

- TEs should be part of a complete PN regimen for most patients[2,9]
- ASPEN suggests a determination of nutrition risk be performed on all patients admitted to the ICU for whom intake is anticipated to be insufficient[34]

There are a few instances in long-term PN where the choice of TEs should be carefully considered[2]

- In certain conditions, such as manganese encephalopathy and hemochromatosis, individual TEs **may need to be omitted and not routinely administered**

ASPEN=American Society for Parenteral and Enteral Nutrition

UTILIZING A TEAM APPROACH TO SUPPORT NUTRITION

Many facilities incorporate a multidisciplinary team of professionals to provide and manage parenteral nutrition[35]

This team supports patient populations ranging from pediatrics to geriatrics, and may include a mix of dietitians, pharmacists, nurses, and physicians.

The team approach plays a critical role in providing care and in ensuring the administration of complete nutrition whether patients are in a hospital or other setting.

Clinical teams can work in a variety of settings besides hospitals, including home-care agencies, long-term care facilities, research facilities, and academia.

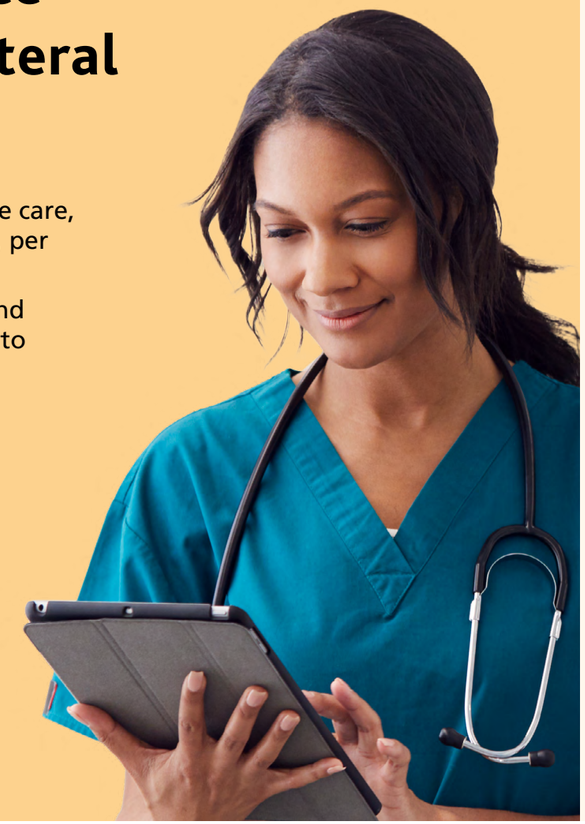
It is crucial that all members of the clinical team have knowledge of trace element (TE) functions, deficiencies, dosages, and stability factors.[2]

More on monitoring trace elements (TEs) in parenteral nutrition (PN) patients

Any PN order should include related orders for routine care, laboratory tests, and relevant monitoring parameters, per ASPEN recommendations.[23]

TE levels should be regularly monitored in patients, and individualized doses should be determined according to those levels[1]

Recommendations are not intended to supersede the judgment of the clinical team and should always be based on the circumstances of the individual patient.[23]



ASPEN=American Society for Parenteral and Enteral Nutrition

MONITORING TRACE ELEMENTS (TEs) IN PARENTERAL NUTRITION (PN) PATIENTS

ASPEN monitoring recommendations[23]

- Appropriate parameters and frequency of monitoring shall be determined for the patient's condition to assess efficacy, detect and prevent complications, evaluate changes, and document outcomes
- Appropriate monitoring includes fluid requirements, serum electrolyte concentrations, serum glucose concentrations, hepatic function, renal function, serum triglyceride concentrations, and signs or symptoms of vascular access device complications
- Patients new to PN should be monitored daily until stable
- Some patients may require more frequent monitoring such as those with preexisting electrolyte abnormalities or those at risk for refeeding syndrome or with unstable clinical status
- Monitor concentrations of copper and manganese in patients with cholestasis or cirrhosis

See Dosage and Administration information within the Full Prescribing Information for Tralement and Multrys.

ASPEN=American Society for Parenteral and Enteral Nutrition

Monitoring recommendations[26,32]

Tralement® (trace elements injection 4*, USP)

- Monitor blood zinc, copper, manganese, and selenium concentrations, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count, and coagulation parameters during use of parenteral nutrition containing Tralement
- Monitor for clinical signs and symptoms of zinc, copper, selenium, and manganese deficiency
- Zinc concentrations may vary, depending on the assay used and the laboratory reference range

Multrys® (trace elements injection 4*, USP)

- Monitor serum zinc, copper, and selenium concentrations and manganese fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count, and coagulation parameters during use of parenteral nutrition containing Multrys
- TE concentrations may vary, depending on the assay used and the laboratory reference range. The collection, processing, and storage of the blood samples should be performed according to the laboratory's sample requirements for analysis

Tralement®

(trace elements injection 4*, USP)

*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

SELECT IMPORTANT SAFETY INFORMATION

USE IN SPECIFIC POPULATIONS

Pregnancy - Risk Summary - Deficiency of trace elements may result in adverse pregnancy and fetal outcomes.

Lactation - Risk Summary - Zinc, copper, manganese, and selenium are present in human milk. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Tralement and any potential adverse effects on the breastfed infant from Tralement or from the underlying maternal condition.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

Multrys®

(trace elements injection 4*, USP)

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

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Contraindicated in patients with hypersensitivity to zinc or copper.

WARNINGS AND PRECAUTIONS

Pulmonary Embolism due to Pulmonary Vascular Precipitates: 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.

Vein Damage and Thrombosis: Multrys must be prepared and used as an admixture in parenteral nutrition solution. It is not for direct intravenous infusion. In addition, consider

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

MONITORING TRACE ELEMENTS (TEs) IN YOUR PATIENTS

Specific patient populations[2]

- Patients more likely to be depleted or who are at risk of depletion or toxicity should be monitored for vitamin and TE status

Certain considerations[2]

- In certain conditions, such as manganese (Mn) encephalopathy and hemochromatosis, individual TEs may need to be omitted and not routinely administered
- In certain weight ranges, Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) do not provide the recommended daily dosage of copper, selenium, or zinc. Refer to the Full Prescribing Information for complete dosing information

Monitoring Tralement[26]

- Monitor blood zinc, copper, manganese, and selenium concentrations, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count, and coagulation parameters during use of parenteral nutrition containing Tralement
- Monitor patients clinically for signs of zinc, copper, selenium, and manganese deficiency. Zinc concentrations may vary, depending on the assay used and the laboratory reference range
- Monitor patients receiving Tralement for cholestasis or other biliary liver disease. Consider individual TE products as an alternative to Tralement in patients with hepatic and/or biliary dysfunction

Do not supplement Tralement with additional manganese. Accumulation of manganese in the brain can occur with long-term administration with higher than the recommended dosage of 1 mcg/kg/day (up to 55 mcg/day). See Warnings and Precautions within the Full Prescribing Information.

Monitoring Multrys[32]

- Monitor zinc, copper, and selenium serum concentrations, manganese whole blood concentration, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count, and coagulation parameters during use of parenteral nutrition containing Multrys
- Monitor patients receiving Multrys for cholestasis or other biliary liver disease. Consider individual TE products as an alternative to Multrys in patients with hepatobiliary disease

Avoid additional manganese supplementation with Multrys use. Accumulation of manganese in the brain can occur with long-term administration with higher than the recommended dosage of 1 mcg/kg/day. See Warnings and Precautions within the Full Prescribing Information.

Tralement®

(trace elements injection 4*, USP)

*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

SELECT IMPORTANT SAFETY INFORMATION

USE IN SPECIFIC POPULATIONS (continued)

Pediatric Use - Refer to Full Prescribing Information for dosing. Do not supplement Tralement with additional manganese. Tralement is not approved for use in pediatric patients weighing less than 10 kg because the product does not provide an adequate dosage of zinc, copper, or selenium to meet the needs of this subpopulation and exceeds the recommended dosage of manganese.

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 Tralement.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.

More on monitoring trace elements in parenteral nutrition patients

SPECIFIC PATIENT POPULATIONS

Assessment may be recommended with lab values when a high degree of clinical suspicion exists for trace element (TE) deficiency due to the following clinical conditions.[2]

Conditions that may increase micronutrient losses or requirements	May be predisposed to retention of micronutrients or metabolites	Preexisting lifestyle factors
• Malnutrition • Altered GI anatomy • Clinical illness • Trauma or burns • Biliary disease	• Renal or liver failure • Cholestasis	• Self-neglect • Alcohol and substance abuse
Use of medication • Anticonvulsant and anti-retroviral therapies		
Baseline levels in long-term parenteral nutrition		

Monitor patients receiving Tralement® (trace elements injection 4*, USP) or Multrys® (trace elements injection 4*, USP) for cholestasis or other biliary liver disease. Consider individual TE products as an alternative in patients with hepatobiliary disease.[26,32]

Multrys®

(trace elements injection 4*, USP)

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

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

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.

Neurologic Toxicity with Manganese: 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.

See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

INDIVIDUAL TRACE ELEMENT (TE) SUPPLEMENTATION*

Patients may require increased or reduced individual TE supplementation in certain clinical situations.

Summary of TE in Parenteral Nutrition (PN) and Special Considerations[1]

Trace Element	Conditions to consider dose reduction	Conditions to consider increasing dose
Copper	Cholestasis	High gastrointestinal (GI) losses (diarrhea, ostomy outputs, nasogastric suctioning), burn patients
Chromium	Caution in renal insufficiency	Pregnant patients may have increased needs
Zinc	Not applicable	Patients with high GI losses, sepsis, hypercatabolic states, and burns
Selenium	Not applicable	Critical illness, burns, continuous renal replacement therapy, high urine output, diarrhea/fistula output, multiple drains, and medications such as corticosteroids and statins
Manganese	Cholestasis	Not applicable

*The dosage of the trace elements must be based on the patient's clinical condition, nutritional requirements, and the contribution of oral or enteral intake.

Tralement®

(trace elements injection 4*, USP)

*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

SELECT IMPORTANT SAFETY INFORMATION

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.

Tralement is recommended only for patients who require supplementation with all four of the individual trace elements (ie, zinc, copper, manganese, and selenium).

More on monitoring trace elements in parenteral nutrition patients

INDIVIDUAL TRACE ELEMENT (TE) SUPPLEMENTATION

Additional considerations for individual TE supplementation[2]

- Preexisting deficiencies—especially zinc, iron, and selenium—are often present in critically ill patients
- Deficiencies may occur due to:
  - inadequate nutrition therapy
  - decreased intake
  - increased bodily losses
  - increased requirements to facilitate tissue repair
- Deficiencies can lead to organ dysfunction, muscle weakness, poor wound healing, and altered immune status

Other individual TE products from American Regent®

Selenious Acid Injection, USP

600 mcg/10 mL of selenium

Supplied as 10 mL pharmacy bulk package

12 mcg/2 mL of selenium

Supplied as a 2 mL single-dose vial

FDA-approved

Zinc Sulfate Injection, USP

- 1 mg/mL of zinc
- 3 mg/mL of zinc
- 5 mg/mL of zinc

Supplied as pharmacy bulk package vials

FDA-approved

Selenious Acid Injection, USP

INDICATIONS AND USAGE

Selenious Acid Injection is indicated in adult and pediatric patients as a source of selenium for parenteral nutrition (PN) when oral or enteral nutrition is not possible, insufficient, or contraindicated.

CONTRAINDICATIONS

None.

Zinc Sulfate Injection, USP

INDICATIONS AND USAGE

Zinc Sulfate is a trace element indicated in adult and pediatric patients as a source of zinc for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated.

CONTRAINDICATIONS

Zinc Sulfate Injection is contraindicated in patients with known hypersensitivity to zinc.

See Full Prescribing Information for Selenious Acid and additional Important Safety Information on page 60.

See Full Prescribing Information for Zinc Sulfate and additional Important Safety Information on page 61.

AMERICAN REGENT®

OUR COMMITMENT TO THE PARENTERAL NUTRITION (PN) COMMUNITY

American Regent is focused on advancing the science and standard of care for trace elements and PN.

Supporting clinicians and their patients

- Proud to be a leading US injectable manufacturer
- 50+ years of history as an established leader in specialty injectables
- Ongoing commitment to supporting the clinical community through education and a focus on a reliable supply chain
- Committed to US-based manufacturing
  - 99% of our injectable drugs are formulated, filled, and finished in our US-based manufacturing facilities*

*In 2024, 99% of units shipped were formulated, filled, and finished in the U.S.

IMPORTANCE OF A RELIABLE PRODUCT SUPPLY CHAIN

Parenteral nutrition (PN) product shortages can be detrimental to patients and challenging for clinicians[2,36]

Product shortages can affect each step of the PN process, including procurement, management, prescribing, ordering, compounding, and administration—as well as monitoring and patient outcomes.[36]

Persistent shortages have led to a tendency of practitioners to provide less-than-adequate dosing, which may lead to nutrient deficiencies and impair growth and healing.[9]

- This could lead to increased length of hospital stay, increased morbidity, and mortality[36]

Almost **75%**

of active drug shortages are sterile injectables, which includes ingredients used in PN therapy.[36]

Ready access to multi-trace elements and individual trace elements must be a priority for the safe and appropriate provision of PN.[2]

American Regent is strategically positioned to address potential product shortages

We are committed to ensuring a reliable supply of our specialty injectable products to help clinicians provide optimal and timely patient care. Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) are proudly manufactured in the United States.

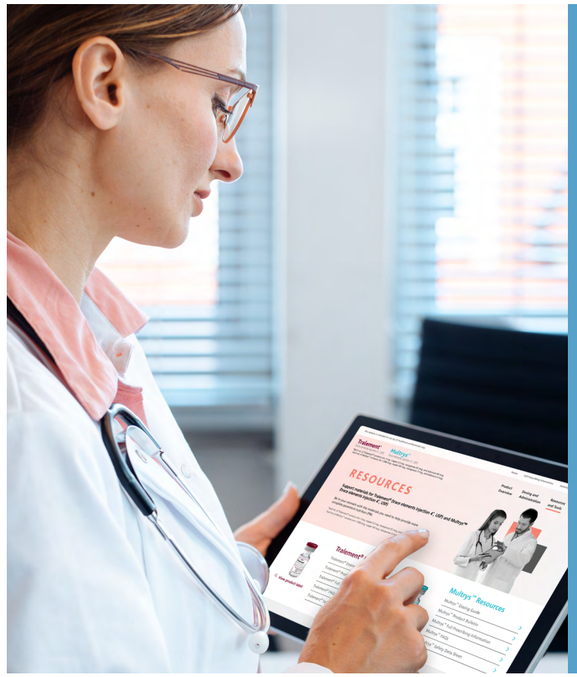
SUPPORTING ONGOING EDUCATION FOR PARENTERAL NUTRITION (PN)

Trace element (TE) recommendations have evolved over time, and so have we. Yet, our commitment to supporting the PN community with ongoing education has never changed.

ASPEN and American Regent share the commitment of elevating the visibility of TEs and supporting the essential role they play in the PN prescription.

Ongoing education makes a difference[37]

- In 4 observational studies, resources including a new order form and education were shown to lead to a substantial decrease in overall PN prescription errors, overutilization of PN, overfeeding, and/or associated costs



Support materials are available to you:

- Dosing guides
- Product bulletins
- FAQs
- Safety data sheets
- Ordering information
- American Regent contact information

Visit artraceelements.com

ASPEN=American Society for Parenteral and Enteral Nutrition

BE IN YOUR ELEMENT

American Regent empowers clinicians to do what they do best

Multi-trace element products from American Regent help deliver a level of simplicity, accuracy, and confidence to the parenteral nutrition (PN) treatment process.

This helps every member of the nutrition support team be their best while providing the most complete PN for their patients in need.

When you're in your element, it shows. Tralement® (trace elements injection 4*, USP) and Multrys® (trace elements injection 4*, USP) help you focus on what you do best.

See Full Prescribing Information for Tralement and additional Important Safety Information on page 56.
See Full Prescribing Information for Multrys and additional Important Safety Information on page 58.

Tralement® (trace elements injection 4*, USP)

*Each mL of Tralement contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

For intravenous use

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Tralement is contraindicated in patients with hypersensitivity to zinc or copper.

WARNINGS AND PRECAUTIONS

Pulmonary Embolism due to Pulmonary Vascular Precipitates: 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 infusion and initiate a medical evaluation.

Vein Damage and Thrombosis: Tralement 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. Solutions with osmolarity of 900 mOsmol/L or more must be infused through a central catheter. The primary complication of peripheral access is venous thrombophlebitis.

Neurologic Toxicity with Manganese: Monitor patients receiving long-term parenteral nutrition solutions containing Tralement for neurologic signs and symptoms, and routinely monitor whole blood manganese concentrations and liver function tests. Discontinue Tralement and consider brain magnetic resonance imaging (MRI) if toxicity suspected.

Hepatic Accumulation of Copper and Manganese: If a patient develops signs or symptoms of hepatic or biliary dysfunction during the use of Tralement, obtain serum concentrations of copper and ceruloplasmin as well as manganese whole blood concentrations. Consider using individual trace element products in patients with hepatic and/or biliary dysfunction.

Aluminum Toxicity: Tralement contains aluminum that may be toxic. Increased risk in patients with renal impairment. Preterm infants, including preterm neonates, are particularly at risk.

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

Hypersensitivity Reactions with Zinc and Copper: If hypersensitivity reactions occur, discontinue Tralement 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

Pregnancy - Risk Summary - Deficiency of trace elements may result in adverse pregnancy and fetal outcomes.

Lactation - Risk Summary - Zinc, copper, manganese, and selenium are present in human milk. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Tralement and any potential adverse effects on the breastfed infant from Tralement or from the underlying maternal condition.

Pediatric Use - Refer to Full Prescribing Information for dosing. Do not supplement Tralement with additional manganese. Tralement is not approved for use in pediatric patients weighing less than 10 kg because the product does not provide an adequate dosage of zinc, copper, or selenium to meet the needs of this subpopulation and exceeds the recommended dosage of manganese.

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 Tralement.

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.

Tralement is recommended only for patients who require supplementation with all four of the individual trace elements (ie, zinc, copper, manganese, and selenium).

INDICATIONS AND USAGE

Tralement is indicated in adult and pediatric patients weighing at least 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.

For additional safety information, please see Full Prescribing Information.

You are encouraged to report Adverse Drug Events to American Regent, Inc.® at 1-800-734-9236, or to the FDA by visiting www.fda.gov/medwatch, or by calling 1-800-FDA-1088.

REF-1535 7/2024

Tralement®
(trace elements injection 4*, USP)
*Each mL contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.
For intravenous use

Multrys® (trace elements injection 4*, USP)

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

For intravenous use

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Contraindicated in patients with hypersensitivity to zinc or copper.

WARNINGS AND PRECAUTIONS

Pulmonary Embolism due to Pulmonary Vascular Precipitates: 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.

Vein Damage and Thrombosis: 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.

Neurologic Toxicity with Manganese: 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.

Aluminum Toxicity: 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.

Hypersensitivity Reactions with Zinc and Copper: 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.

Multrys® Important Safety Information

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.

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.

For additional safety information, please see Full Prescribing Information.

You are encouraged to report adverse drug events to American Regent, Inc.® at 1-800-734-9236, or to the FDA by visiting www.fda.gov/medwatch or by calling 1-800-FDA-1088.

REF-1826 7/2024

Multrys®

(trace elements injection 4*, USP)

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

For intravenous use

Selenious Acid Injection, USP

Selenious Acid Injection, USP

For intravenous use

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Pulmonary Embolism due to Pulmonary Vascular Precipitates: If signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation.

Vein Damage and Thrombosis: Selenious Acid Injection has a low pH and must be prepared and used as an admixture in PN solutions. Solutions with osmolarity of 900 mOsm/L or more must be infused through a central venous catheter.

Aluminum Toxicity: Selenious Acid Injection contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Preterm infants are particularly at risk for aluminum toxicity because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which also contain aluminum.

Monitoring and Laboratory Tests: Monitor selenium concentrations, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count, and coagulation parameters throughout treatment.

ADVERSE REACTIONS

No selenium-related adverse reactions have been reported in clinical studies or postmarketing reports in patients receiving intravenously administered PN solutions containing selenious acid within the recommended dosage range.

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary: Administration of the recommended dose of Selenious Acid Injection in PN is not expected to cause major birth defects, miscarriage, or adverse maternal or fetal outcomes.

Lactation: Risk Summary: Selenium is present in human milk. There is no information on the effects of selenious acid on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Selenious Acid Injection and any potential adverse effects on the breastfed infant from Selenious Acid Injection or from the underlying maternal condition.

Pediatric Use: Safety and dosing recommendations in pediatric patients are based on clinical experience.

Geriatric Use: Dose selection should be individualized based on the patient's clinical condition, nutritional requirements, and additional nutritional intake provided orally or enterally to the patient.

INDICATIONS AND USAGE

Selenious Acid Injection is indicated in adult and pediatric patients as a source of selenium for parenteral nutrition (PN) when oral or enteral nutrition is not possible, insufficient, or contraindicated.

For additional safety information, please see Full Prescribing Information.

You are encouraged to report Adverse Drug Events to American Regent, Inc.® at 1-800-734-9236 or to the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

REF-1167 8/2021

Zinc Sulfate Injection, USP

Zinc Sulfate Injection, USP

For intravenous use after dilution and admixing.
***Pharmacy Bulk Package. Not for direct intravenous infusion*.**

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Zinc Sulfate Injection is contraindicated in patients with known hypersensitivity to zinc.

WARNINGS AND PRECAUTIONS

Pulmonary Embolism due to Pulmonary Vascular Precipitates: If signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation. The infusion set and catheter should be checked periodically for precipitates.

Vein Damage and Thrombosis: Zinc Sulfate Injection has a low pH and must be prepared and used as an admixture in PN solutions. Solutions with osmolarity of 900 mOsm/L or more must be infused through a central venous catheter. Aluminum Toxicity: Zinc Sulfate Injection contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Preterm infants are particularly at risk for aluminum toxicity because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which also contain aluminum.

Monitoring and Laboratory Tests: Monitor zinc concentrations, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count, and coagulation parameters throughout treatment.

Copper Deficiency: Several post-marketing cases have reported that high doses of supplemental zinc (approximately 10 times the recommended dosage of 3 mg/day Zinc Sulfate Injection in adults) taken over extended periods of time (ie, months to years) may result in decreased enteral copper absorption and copper deficiency.

Hypersensitivity Reactions: If hypersensitivity reactions occur, discontinue Zinc Sulfate Injection and initiate appropriate medical treatment.

ADVERSE REACTIONS

No zinc-related adverse reactions have been reported in clinical studies or postmarketing reports in patients receiving intravenously administered PN solutions containing zinc sulfate within the recommended dosage range.

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary: Administration of the recommended dose of Zinc Sulfate Injection in PN is not expected to cause major birth defects, miscarriage, or adverse maternal or fetal outcomes.

Lactation: Risk Summary: Zinc is present in human milk. There is no information on the effects of zinc sulfate on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Zinc Sulfate Injection and any potential adverse effects on the breastfed infant from Zinc Sulfate Injection or from the underlying maternal condition.

Pediatric Use: Safety and dosing recommendations in pediatric patients are based on published literature describing controlled studies of zinc-containing products in pediatric patients.

Geriatric Use: Dose selection should be individualized based on the patient's clinical condition, nutritional requirements, and additional nutritional intake provided orally or enterally to the patient.

OVERDOSAGE

There are reported cases of overdosage with intravenous zinc in parenteral nutrition.

INDICATIONS AND USAGE

Zinc Sulfate is a trace element indicated in adult and pediatric patients as a source of zinc for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated.

For additional safety information, please see Full Prescribing Information.

You are encouraged to report Adverse Drug Events to American Regent, Inc.® at 1-800-734-9236 or to the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

REF-1299 10/2020

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*Each mL of Tralement contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg.

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

"Parenteral nutrition (PN) represents one of the most notable achievements of modern medicine, serving as a therapeutic modality for all age groups across the healthcare continuum.

PN offers a life-sustaining option when intestinal failure prevents adequate oral or enteral nutrition."

— ASPEN 2017 Consensus Recommendation[13]

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