Tralement®

(trace elements injection 4*, USP)

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

PRODUCT INFORMATION BULLETIN

Tralement® is the first FDA-approved multi-trace element injection for parenteral nutrition.[1]

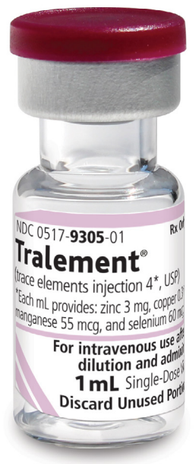
Tralement® (trace elements injection 4*, USP) is indicated in adult and pediatric patients weighing at least 10 kg as a source of zinc, copper, manganese and selenium for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated.[2]

- **Aligns with Current Treatment Guidelines**
  Tralement® has been specifically developed to align with the ASPEN recommendations for trace element supplementation. The concentration of each element in Tralement® has been formulated to meet the needs of a broad range of pediatric and adult patients.[2,3]

- **Dosing: Added to Parenteral Nutrition**
  A 1 mL dose of Tralement® per day for adults and pediatric patients weighing at least 50 kg simplifies treatment planning and preparation for healthcare workers, may save time, and may reduce the likelihood of errors.[2,4] Weight-dependent dosing is provided for pediatric patients between 10 kg to 49 kg.[2] Tralement® is not recommended for patients who may require a lower dosage of one or more of the individual trace elements.

- **Proven Stability**
  Stability studies support that Tralement® can be safely stored for up to 9 days when added to the parenteral nutrition admixture and refrigerated.[2]

- **Consistent Supply**
  Tralement® is proudly manufactured in America. American Regent is committed to providing a consistent supply to help ensure that your patient care needs are met.



Tralement® aligns with the daily recommendations for parenteral trace elements set forth by ASPEN.[2,3]

ADULT TRACE ELEMENT DOSING

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

Refer to the table below for specifications on Tralement® as it compares to the unapproved trace element products offered by American Regent. For additional information, visit www.americanregent.com.

AMERICAN REGENT TRACE ELEMENT PRODUCTS SPECIFICATIONS

Product	Tralement®	Multitrace®-4 Neonatal	Multitrace®-4 Pediatric
Approval Status	**FDA Approved**	**Marketed Unapproved**	**Marketed Unapproved**
Availability	Available	Available	Available
Pack NDC	0517-9305-25[2]	0517-6202-25[5]	0517-9203-25[6]
Strength	N/A	Neonatal	Pediatric
Trace Elements per mL	• zinc 3 mg • copper 0.3 mg • manganese 55 mcg • selenium 60 mcg	• zinc 1.5 mg • copper 0.1 mg • manganese 25 mcg • chromium 0.85 mcg	• zinc 1 mg • copper 0.1 mg • manganese 25 mcg • chromium 1 mg
Vial Type	Single Dose Vial	Single Dose Vial	Single Dose Vial
Fill Volume	1 mL	2 mL	3 mL
Preservative	Preservative Free	Preservative Free	Preservative Free
Specific Gravity	1.009 (g/mL)	1.004 (g/mL)	1.004 (g/mL)
Cap Color	Garnet	Salmon	Pink
Aluminum Content	No more than 6,000 mcg/L of Aluminum	No more than 6,250 mcg/L of Aluminum	No more than 6,250 mcg/L of Aluminum
Pack Size	25	25	25
Storage	Store at 20°C to 25°C (68°F to 77°F)	Store at 20°C to 25°C (68°F to 77°F)	Store at 20°C to 25°C (68°F to 77°F)
Trace Element Stability in TPN	Up to 9 days when added to the PN admixture and refrigerated	N/A	N/A

PEDIATRIC TRACE ELEMENT DOSING

Trace Element	ASPEN Dosing Recommendations[3]		Tralement® (trace elements injection 4*, USP)
	Children 10-40 kg	Adolescents Greater than 40 kg	Pediatric Weight-Based Dosage for Tralement® for Patients Weighing 10-49 kg[2]
Zinc	50 mcg/kg (max 5,000 mcg/day)	2-5 mg	50 mcg/kg/day (up to 3,000 mcg/day)
Copper	20 mcg/kg (max 500 mcg/day)	200-500 mcg	20 mcg/kg/day (up to 300 mcg/day)
Manganese	1 mcg/kg (max 55 mcg/day)	40-100 mcg	1 mcg/kg/day (up to 55 mcg/day)
Selenium	2 mcg/kg (max 100 mcg/day)	40-60 mcg	2 mcg/kg/day (up to 60 mcg/day)
Chromium	0.2 mcg/kg (max 5 mcg/day)	5-15 mcg	0 mcg

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

Tralement®

(trace elements injection 4*, USP)

For intravenous use

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.

IMPORTANT SAFETY 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.

Overview of Dosing

- Prior to administration of parenteral nutrition solution containing Tralement, correct severe fluid, electrolyte, and acid-base disorders.
- The dosage of the final parenteral nutrition 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.

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

See Full Prescribing Information on preparation, administration and dosing.

CONTRAINDICATIONS

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

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: 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: Assess for development of hepatic or biliary dysfunction. Monitor concentrations of copper and manganese in patients with cholestasis, biliary dysfunction or cirrhosis receiving Tralement long-term.
- Aluminum Toxicity: Tralement contains aluminum that may be toxic. Increased risk in patients with renal impairment, including preterm infants.
- 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 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 before dosing. Do not supplement Tralement with additional manganese. Tralement is not approved for use in pediatric patients weighing less than 10 kg.

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.

For additional safety information, please see Full Prescribing Information.

REF-1535 2/2021

References

1. Approved Drug Products with Therapeutic Equivalence Evaluations: https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=209376#121. Accessed April 12, 2021.
2. Tralement® (trace elements injection 4*) [package insert]. Shirley, NY: American Regent, Inc. 7/2020.
3. American Society for Parenteral and Enteral Nutrition (ASPEN) website: http://www.nutritioncare.org/uploadedFiles/Documents/Guidelines_and_Clinical_Resources/PN%20Dosing%201-Sheet-FINAL.pdf. Accessed April 12, 2021.
4. Vanek et al. A Call to Action to Bring Safer Parenteral Micronutrient Products to the U.S. Market. *Nutr Clin Pract.* August. 2015; 30 (4):559-569.
5. Multitrace®-4 Neonatal (trace elements injection 4, USP) [package insert]. Shirley, NY: American Regent, Inc. 7/2018.
6. Multitrace®-4 Pediatric (trace elements injection 4, USP) [package insert]. Shirley, NY: American Regent, Inc. 7/2018.

You are encouraged to report Adverse Drug Events (ADEs) to American Regent:
T 1.800.734.9236; E pv@americanregent.com; F 1.610.650.0170

ADEs may also be reported to the FDA:
1.800.FDA.1088 or www.fda.gov/medwatch

Medical Information:
1.888.354.4855
(9:00 am – 5:00 pm Eastern Time, Monday – Friday)

For medical inquiries outside of business hours that cannot wait until the next business day, please call 1.877.845.637.

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