Zinc Sulfate Injection 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.

### DOSAGE FORMS AND STRENGTHS

Zinc Sulfate Injection provides 3 mg/mL or 5 mg/mL of zinc.

### DOSAGE AND ADMINISTRATION

#### 2.1 Important Administration Information

- **Preparation Instructions for Administering a Parenteral Nutrition Container**
  - **Zinc Sulfate Injection** is supplied as a pharmacy bulk package for admixing use only. It is not for direct intravenous infusion.
  - Prior to administration, Zinc Sulfate Injection must be transferred to a separate parenteral nutrition container; diluted and used as an admixture in parenteral nutrition solutions.
  - The final parenteral nutrition solution is for intravenous infusion into a central or peripheral vein. The choice of a central or peripheral venous route should depend on the osmolarity of the final infusate. Solutions with osmolarity of 900 mOsm/L or greater must be infused through a 14- or 16-gauge catheter. (See Warnings and Precautions (5.2).)
  - **Preparation and Administration Instructions**
    - Zinc Sulfate Injection is not for direct intravenous infusion. Prior to administration, Zinc Sulfate Injection must be transferred to a separate parenteral nutrition container; diluted and used as an admixture in parenteral nutrition solutions.
    - Zinc Sulfate Injection should be transferred to the parenteral nutrition container following the admixture of amino acids, dextrose, lipid emulsion (if added), and electrolytes solutions.
  - Visually inspect the diluted parenteral nutrition solution containing Zinc Sulfate Injection for particulate matter before administering, after admixing, and prior to administration. The solution should be clear and there should be no precipitates. A slight yellow color does not alter the quality and efficacy of this product.
  - Because additives may be incompatible, evaluate all additions to the parenteral nutrition container for compatibility and stability of the resulting preparation. Consult with pharmacist, if available. Questions about compatibility may be directed to American Red Cross. (2.1, 2.4, 5.2)
  - Transfer Zinc Sulfate Injection to the parenteral nutrition container following the admixture of amino acids, dextrose, lipid emulsion (if added), and electrolytes solutions.
  - **Zinc Sulfate Injection Bulk Pharmacy Package for parenteral administration**
    - **Dosage and Administration**
      - **Recommended Dosage and Monitoring** in Adult and Pediatric Patients
        - Adults: 30 mg/kg to 50 mg/kg per day (up to 3 mg/day) of zinc.
        - 25 mg/kg (5 mg/mL) of zinc as a Pharmacy Bulk Package (3).
        - 10 mg/kg to 15 mg/kg (2 mg/mL) of zinc as a Pharmacy Bulk Package (3).
  - **Dosage Forms and Strengths**
    - Zinc Sulfate Injection, USP:
      - 30 mg/mL (3 mg/mL of zinc) as a Pharmacy Bulk Package (3).
      - 25 mg/mL (5 mg/mL of zinc) as a Pharmacy Bulk Package (3).

#### 2.2, 2.3, 2.4

- **Zinc Sulfate Injection** provides 3 mg/mL or 5 mg/mL of zinc.
- **Term neonates have higher requirements in the first 3 months of life.**
- Individualize the dosage based upon the patient’s clinical condition, nutritional requirements, and the contribution of oral or enteral zinc intake.

**INDICATIONS AND USAGE**

- **Initial U.S. Approval: 1957**

- **Use in Pediatric Vascular Perforation:** If signs of pulmonary distress occur, stop the infusion and initiate a mechanical ventilation. (5.1)
- **Von Willebrand Factor:** Solutions with osmolarity of 900 mOsm/L or more must be infused through a central venous catheter. (5.2)
- **Aluminum Toxicity:** Increase risk in patients with renal impairment, including preterm infants (5.3, 8.4).
- **Renal Function:** Monitor fluid and electrolyte status, serum sodium, blood glucose, liver and kidney function, blood count and coagulation parameters throughout treatment. (5.4, 5.2)
- **Copper Deficiency:** If signs and symptoms develop, interrupt treatment with Zinc Sulfate Injection and check zinc, copper, and ceruloplasmin levels. (5.5)
- **Hypersensitivity Reactions:** If reactions occur, discontinue Zinc Sulfate Injection and initiate appropriate medical treatment. (5.6)

#### WARNINGS AND PRECAUTIONS

- **No related adverse reactions in patients receiving intravenously administered parenteral nutrition solutions containing zinc within the recommended dosage range (6).**

- **ADVERSE REACTIONS**
  - No related adverse reactions in patients receiving intravenously administered parenteral nutrition solutions containing zinc within the recommended dosage range (6).

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*Sections or subsections omitted from the full prescribing information are not listed.
There are reported cases of overdosage with intravenous zinc in parenteral nutrition:

- One preterms infant born at 26 weeks gestation died of cardiac failure following a medication error in which the parenteral nutrition solution contained 330 mg/100 mL instead of 330 mcg/100 mL of zinc sulfate (overdose of 1000-fold).

Management

There is no known antidote for acute zinc toxicity. Management of zinc overdose is supportive care based on presenting signs and symptoms.

11 DESCRIPTION

Zinc Sulfate Injection, USP is a sterile, non-pyrogenic, clear, colorless, and odorless solution intended for use as a trace element and an additive to intravenous solutions for parenteral nutrition.

30 mg/10 mL Pharmacy Bulk Package vial:

- Each mL contains 3 mg of zinc sulfate and Water for Injection q.s.
- Each mL contains 5 mg of zinc present as 12.3 mg of zinc sulfate and Water for Injection q.s.
- Both presentations do not contain preservatives.
- The pH range is 2 to 4. ph may be adjusted with sulfuric acid.

Zinc Sulfate Injection contains no more than 2,500 mcg/ml of aluminum and has a calculated osmolality of 96.5 mOsm/L for 3 mg/mL and 157.2 mOsm/L for 5 mg/mL.

Zinc sulfate hepatophydrate has a molecular weight of 287.56 g/mol and a formula of ZnSO4·H2O.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Zinc is an essential trace element. Zinc functions as a cofactor of various enzymes including DNA polymerases, RNA polymerases, alcohol dehydrogenase, and alkaline phosphatases. Zinc is a coordinator of protein structural folding, such as folding of "Zinc finger" motif that interacts with a variety of proteins, lipids, and nucleic acids. In addition, zinc is a catalyst of essential biochemical reactions, including activation of substrates of carbonyl reductase in erythrocytes. Also, zinc is a signaling mediator modulating multiple signaling pathways.

12.2 Pharmacodynamics

Zinc sulfate exposure-response relationships and the time course of pharmacodynamic responses are unknown.

12.3 Pharmacokinetics:

- Distribution

Over 85% of total body zinc is found in skeletal muscle and bone. Other organs containing zinc are the liver, kidney, skin, brain, and heart. In blood, zinc is mainly localized within erythrocytes. Approximately 80% of serum zinc is bound to albumin and the remainder to alpha-2-macroglobulin and amino acids.

Elimination

In adults, zinc is primarily excreted via the gastrointestinal tract and eliminated in the feces. A smaller amount of zinc is excreted via the kidneys in the urine. Urinary excretion rates in very low birth weight preterm infants are relatively high in the neonatal period, and they decline to a level on a body weight basis that is similar to that of normal adults by two months of age. Additionally, endogenous zinc loss occurs from hair, skin desquamation and sweat.

16 HOW SUPPLIED/STORAGE AND HANDLING

Zinc Sulfate Injection, USP is a clear, colorless solution supplied as:

- 30 mg/10 mL (0.3 mg/mL) of zinc in a 10 mL Pharmacy Bulk Package vial. Cartons of 25 vials (NDC 0517-6103-25).
- 25 mg/5 mL (0.5 mg/mL) of zinc in a 5 mL Pharmacy Bulk Package vial. Cartons of 25 vials (NDC 0517-8005-25).

Vial closure is not made with natural rubber latex.

Store at 20° to 25°C (68° to 77°F), excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

For storage of admixed solution see Dosage and Administration (2.3).

17 PATIENT COUNSELING INFORMATION

Inform patients, caregivers or home healthcare providers of the following risks of Zinc Sulfate Injection:

- Pulmonary edema due to pulmonary vascular precipitates [see Warnings and Precautions (5.1)].
- Vein damage and thrombosis [see Warnings and Precautions (5.2)].
- Aluminum toxicity [see Warnings and Precautions (5.3)].
- Copper deficiency [see Warnings and Precautions (5.8)]
- Hypersensitivity reactions [see Warnings and Precautions (5.6)].

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

- Seven adult patients received overdosage of 40 mg to 75 mg elemental zinc per day in parenteral nutrition solution for 26 to 60 days; 6 of the 7 patients developed hyperamylasemia (peak amylase values of 557 to 1856 U/L, normal range: 13 to 150). Serum zinc concentrations ranged from 310 to 670 mcg/dL. None of the patients developed clinical signs of pancreatitis. Five of the 7 patients died of septic complications.

- One adult patient died of infectious complications after receiving an inadvertent overdosage of 7.4 grams of zinc sulfate (equivalent to 1.2 grams of elemental zinc per day for 2.5 days) in parenteral nutrition solution over 60 hours. The serum zinc concentration was 4184 mcg/dL. Symptoms of zinc overdose also included hyperamylasemia, thrombocytopenia, anemia, vomiting and diarrhea.

In adults, zinc is primarily excreted via the gastrointestinal tract and eliminated in the feces. A smaller amount of zinc is excreted via the kidneys in the urine. Urinary excretion rates in very low birth weight preterm infants are relatively high in the neonatal period, and they decline to a level on a body weight basis that is similar to that of normal adults by two months of age. Additionally, endogenous zinc loss occurs from hair, skin desquamation and sweat.