HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SELENIOUS ACID INJECTION safely and effectively. See full prescribing information for SELENIOUS ACID INJECTION.

SELENIOUS ACID INJECTION, for intravenous use
Initial U.S. Approval: 2019

----------RECENT MAJOR CHANGES----------

Dosage and Administration, Preparation Instructions for Admixing Using a Parenteral Nutrition Container (2.3) 10/2020

----------INDICATIONS AND USAGE----------

Selenious Acid Injection is a trace element indicated in adult and pediatric patients as a source of selenium for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated. (1)

----------DOSAGE AND ADMINISTRATION----------

- *Pharmacy Bulk Package. Not for direct intravenous infusion.* (2.1)
- See full prescribing information for information on preparation, administration, and general dosing considerations. (2.1, 2.2, 2.3, 2.4)

Recommended Dosage (2.5)

- Selenious Acid Injection provides 60 mcg/mL of selenium.
- Individualize the dosage based upon the patient's clinical condition, nutritional requirements, and the contribution of oral or enteral selenium intake. The following dosages are general recommendations intended for most patients. However, based upon clinical requirements, some patients may require a higher dosage:
  - *Adults*: 60 mcg/day
    Pediatric Patients 7 kg and above: 2 mcg/kg/day (up to 60 mcg/day)
  - *Pediatric Patients less than 7 kg:* 2 to 4 mcg/kg/day
- Monitor selenium concentrations during treatment.

----------DOSAGE FORMS AND STRENGTHS----------

Selenious Acid Injection, USP: 600 mcg/10 mL (60 mcg/mL) of selenium as a Pharmacy Bulk Package vial. (3)

----------CONTRAINDICATIONS----------

None. (4)

----------WARNINGS AND PRECAUTIONS----------

- Pulmonary Embolism due to Pulmonary Vascular Precipitates: If signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation. (5.1)
- Vein Damage and Thrombosis: Solutions with osmolarity of 900 mOsmol/L or more must be infused through a central venous catheter. (2.1, 5.2)
- Aluminum Toxicity: Increased risk in patients with renal impairment, including preterm infants. (5.3, 5.4)
- 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. (5.4, 2.4)

----------ADVERSE REACTIONS----------

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

To report SUSPECTED ADVERSE REACTIONS, contact American Regent Inc. at 1-800-734-9236 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Information

Selenious Acid Injection is supplied as a pharmacy bulk package for *admixing use* only. It is *not for direct intravenous infusion*. Prior to administration, Selenious Acid Injection *must be transferred to a separate parenteral nutrition container, prepared* 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 mOsmol/L or greater must be infused through a central venous catheter *[see Warnings and Precautions (5.2)]*.

2.2 Preparation and Administration Instructions

- Selenious Acid Injection is *not for direct intravenous infusion*. Prior to administration, Selenious Acid Injection *must be prepared and used as an admixture* in parenteral nutrition solutions.
- Selenious Acid Injection is to be prepared only 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.
- Visually inspect the prepared parenteral nutrition solution containing Selenious Acid Injection for particulate matter before admixing, after admixing, and prior to administration.

2.3 Preparation Instructions for Admixing Using a Parenteral Nutrition Container

- Inspect Selenious Acid Injection Bulk Pharmacy Package for particulate matter.
- Transfer Selenious Acid Injection to the parenteral nutrition solution following the admixture of amino acids, dextrose, lipid (if added), and electrolytes solutions.
- 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 Regent. If it is deemed advisable to introduce additives to the parenteral nutrition container, use aseptic technique.
- Inspect the final parenteral nutrition solution containing Selenious Acid Injection to ensure that:
    - Precipitates have not formed during mixing or addition of additives.
    - The emulsion has not separated, if lipids have been added. Separation of the emulsion can be visibly identified by a yellowish streaking or the accumulation of yellowish droplets in the admixed emulsion.
    - Discard if any precipitates are observed.

Stability and Storage

- Penetrate vial closure only one time with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents.
- Use Selenious Acid Injection for admixing promptly once the sterile transfer set has been inserted into the Pharmacy Bulk Package container or not more than 4 hours at room temperature (25ºC/77ºF) after the container closure has been penetrated. Discard any remaining drug.
- Use parenteral nutrition solution containing Selenious Acid Injection 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 time no longer than 9 days. After removal from refrigeration, use promptly and complete the infusion within 24 hours. Discard any remaining admixture.
- Protect the admixed parenteral nutrition solution from light.

2.4 Dosing Considerations

- The dosage of the final parenteral nutrition solution containing Selenious Acid Injection must be based on the concentrations of all components in the solution and the recommended daily nutritional requirements *[see Dosage and Administration (2.5)]*. Consult the prescribing information of all added components to determine the recommended nutritional requirements for dextrose, amino acids and lipid emulsion, as applicable.
- Prior to administration of parenteral nutrition solution containing Selenious Acid Injection, correct severe fluid, electrolyte and acid-base disorders.

2.5 Recommended Dosage in Adults and Pediatric Patients

- Selenious Acid Injection provides 60 mcg/mL of selenium.
- The dosage of Selenious Acid Injection should be individualized based on the patient's clinical condition, nutritional requirements, and the contribution of oral or enteral selenium intake. The dosages in the following table are general recommendations intended for most patients. However, based on clinical requirements, some patients may require a higher dosage.

Population	**Recommended Dosage**
Adults	60 mcg/day
Pediatric Patients 7 kg and above	2 mcg/kg/day (up to 60 mcg/day)
Pediatric Patients less than 7 kg	2 to 4 mcg/kg/day

- Monitor selenium concentrations during treatment. Selenium concentrations may vary depending on the assay used and the laboratory reference range. The lower end of the range reported in healthy adults is 7 to 10 mcg/dL.

3 DOSAGE FORMS AND STRENGTHS

Selenious Acid Injection, USP: 600 mcg/10mL (60 mcg/mL) of selenium as a clear, colorless solution in a 10 mL Pharmacy Bulk Package vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 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. The cause of precipitate formation has not been determined in all cases; however, in some fatal cases, pulmonary emboli occurred as a result of calcium phosphate precipitates. Precipitation has occurred following passage through an in-line filter; *in vivo* precipitate formation may also have occurred. If signs of pulmonary distress occur, stop the parenteral nutrition infusion and initiate a medical evaluation. In addition to inspection of the solution *[see Dosage and Administration (2.2, 2.3)]*, the infusion set and catheter should also periodically be checked for precipitates.

5.2 Vein Damage and Thrombosis

Selenious Acid Injection has a low pH and must be prepared and used as an admixture in parenteral nutrition solutions. 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 an osmolarity of 900 mOsmol/L or greater must be infused through a central catheter *[see Dosage and Administration (2.1)]*. The infusion of hypertonic nutrient injections into a peripheral vein may result in vein irritation, vein damage, and/or thrombosis. The primary complication of peripheral access is venous thrombophlebitis, which manifests as pain, erythema, tenderness or a palpable cord. Remove the catheter as soon as possible, if thrombophlebitis develops.

5.3 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.

Patients with impaired kidney function, including preterm neonates, who receive greater than 4 to 5 mcg/kg/day of parenteral aluminum can accumulate aluminum to levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

Exposure to aluminum from Selenious Acid Injection is not more than 0.6 mcg/kg/day. When prescribing Selenious Acid Injection for use in parenteral nutrition containing other small volume parenteral products, the total daily patient exposure to aluminum from the admixture should be considered and maintained at no more than 5 mcg/kg/day *[see Use in Specific Populations (8.4)]*.

5.4 Monitoring and Laboratory Tests

Monitor selenium concentrations, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count and coagulation parameters during treatment *[see Dosage and Administration (2.5)]*.

6 ADVERSE REACTIONS

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

The following adverse reactions associated with use of other components of parenteral nutrition solutions were identified in clinical studies or postmarketing reports. Because 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:

- Pulmonary embolism 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)]*

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Administration of the recommended dose of Selenious Acid Injection in parenteral nutrition is not expected to cause major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with intravenous selenious acid.

The estimated background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Disease-associated Maternal and/or Embryo-Fetal Risk

Deficiency of trace elements, including selenium, is associated with adverse pregnancy and fetal outcomes. Pregnant women have an increased metabolic demand for trace elements, including selenium. Parenteral nutrition with selenium should be considered if a pregnant woman's nutritional requirements cannot be fulfilled by oral or enteral intake.

8.2 Lactation

Risk Summary

Selenium is present in human milk. Administration of the approved recommended dose of Selenious Acid Injection in parenteral nutrition is not expected to cause harm to a breastfed infant. 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.

8.4 Pediatric Use
Selenious Acid Injection is approved for use in the pediatric population, including neonates, as a source of selenium for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated. Safety and dosing recommendations in pediatric patients are based on clinical experience *[see Dosage and Administration (2.5)]*.

Because of immature renal function, preterm infants receiving prolonged parenteral nutrition treatment with Selenious Acid Injection may be at higher risk of aluminum toxicity *[see Warnings and Precautions (5.3)]*.

8.5 Geriatric Use
Reported clinical experience with intravenous selenious acid has not identified a difference in selenium requirements between elderly and younger patients. In general, 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.

10 OVERDOSAGE
There are no known cases of overdosage with intravenous selenious acid in parenteral nutrition.

Overdosage has been reported with oral selenium. Available selenium concentrations in these subjects have been reported using various assays and laboratory-based reference ranges over a period of time. Interpret results in the context of current reported ranges.

For oral selenium, the Tolerable Upper Limit (UL) is 400 mcg/day and the No Observed Adverse Effect Level (NOAEL) is 800 mcg/day. The estimated oral bioavailability of selenium is approximately 70%.

Acute Oral Toxicity Effects
Serious adverse events and deaths have been reported with acute oral toxicity, however, there is no clear correlation between the amount ingested, signs and symptoms of toxicity, or selenium blood concentrations.

With severe toxicity, the most common presenting symptoms within a few hours post-ingestion of oral doses greater than 1 gram/day of selenium are gastrointestinal (nausea, vomiting, diarrhea, and abdominal pain), altered mental status, and "garlic" breath odor.

Death from circulatory collapse has been reported after oral ingestion of 5 to 10 grams of selenium. Selenium serum or blood concentrations in fatal cases have been reported in the range of 190 mcg/dL to 3,800 mcg/dL.

Mild to moderate intoxication (myalgia, muscle spasms, and irritability) has been reported in patients with selenium serum or blood concentrations in the range of 41 to 750 mcg/dL.

Chronic Selenosis
Chronic daily exposure to selenium from dietary sources (0.003 to 0.007 grams/day) or oral supplements (0.0016 to 0.25 grams/day) may result in alopecia and nail brittleness. Other signs include gastrointestinal disturbances, skin rash, garlic breath, fatigue, irritability, and nervous system abnormalities including paresthesia and ataxia.

Selenium serum or blood concentrations in patients in China exposed through oral (non-dietary) supplementation were in the range of 32 to 150 mcg/dL.

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

11 DESCRIPTION

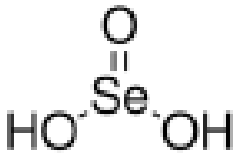
Selenious Acid Injection, USP is a sterile, non-pyrogenic, clear, colorless solution intended for use as a trace element and additive to intravenous solutions for parenteral nutrition.

Each mL contains 60 mcg selenium present as 98 mcg of selenious acid and Water for Injection q.s. The pH range is 1.8 to 2.4; pH may be adjusted with Nitric Acid.

Each Pharmacy Bulk Package vial contains 10 mL of selenious acid solution and does not contain preservatives.

Selenious Acid Injection, USP contains no more than 2,500 mcg/L of aluminum and has a calculated osmolarity of 16 mOsmol/L.

Selenious acid has a molecular weight of 128.97 g/mol and a formula of H_2SeO_3.



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Selenious acid is converted *in vivo* to hydrogen selenide via glutathione-involved electron reductions. Hydrogen selenide acts as a selenium pool to form selenoproteins which include, but are not limited to, glutathione peroxidase, iodothyronine deiodinase, peroxidase and thioredoxins.

12.2 Pharmacodynamics

Selenious acid exposure-response relationships and the time course of pharmacodynamic responses is unknown.

12.3 Pharmacokinetics

Distribution
In humans 85% of intravenous administered ^{75}Se-sodium selenite was protein-bound within 4 to 6 hours and 95% by 24 hours.

Elimination
Selenium is primarily eliminated in urine.

16 HOW SUPPLIED/STORAGE AND HANDLING

Selenious Acid Injection, USP is a clear, colorless solution available as 600 mcg/10mL (60 mcg/mL) of selenium in a 10 mL Pharmacy Bulk Package vial.

Carton of 5 vials (NDC 0517-6560-05)

Store at 20°C to 25°C (68°F to 77°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 Selenious Acid Injection:

- Pulmonary embolism 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)]*

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