CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203923Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use the Sodium Thiosulfate Injection safely and effectively. See full prescribing information for Sodium Thiosulfate Injection.

Sodium Thiosulfate Injection, USP
Initial U.S. Approval: 1992

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

Sodium thiosulfate is indicated for sequential use with sodium nitrite for treatment of acute cyanide poisoning that is judged to be life-threatening. (1)

- Use with caution if the diagnosis of cyanide poisoning is uncertain. (1)

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

Age	Intravenous Dose of Sodium Nitrite and Sodium Thiosulfate
Adults	**1.) Sodium Nitrite** -10 mL of sodium nitrite at the rate of 2.5 to 5 mL/minute **2.) Sodium Thiosulfate** - 50 mL of sodium thiosulfate immediately following administration of sodium nitrite.
Children	**1.) Sodium Nitrite** - 0.2 mL/kg (6 mg/kg or 6-8 mL/m^2 BSA) of sodium nitrite at the rate of 2.5 to 5 mL/minute not to exceed 10 mL **2.) Sodium Thiosulfate** - 1 mL/kg of body weight (250 mg/kg or approximately 30-40 mL/m^2 of BSA) not to exceed 50 mL total dose immediately following administration of sodium nitrite.

Redosing: If signs of cyanide poisoning reappear, repeat treatment using one-half the original dose of both sodium nitrite and sodium thiosulfate.
Monitoring: Blood pressure must be monitored during treatment. (2.2)

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

- Injection, 12.5 grams/50 mL (250 mg/mL). (3)

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

- None. (4)

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

- Sulfites: Sodium thiosulfate may contain trace impurities of sodium sulfite (5.1)

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

Most common adverse reactions are:

- Hypotension, headache, disorientation (6)

To report SUSPECTED ADVERSE REACTIONS, contact Hope Pharmaceuticals at 1-800-755-9595 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------USE IN SPECIFIC POPULATIONS----------

- Renal impairment: Sodium thiosulfate is substantially excreted by the kidney. The risk of toxic reactions to this drug may be greater in patients with impaired renal function. (8.6).

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 02/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Indication

Sodium Thiosulfate Injection is indicated for sequential use with sodium nitrite for the treatment of acute cyanide poisoning that is judged to be life-threatening. When the diagnosis of cyanide poisoning is uncertain, the potential risks associated with Sodium Thiosulfate Injection should be carefully weighed against the potential benefits, especially if the patient is not in extremis.

1.2 Identifying Patients with Cyanide Poisoning

Cyanide poisoning may result from inhalation, ingestion, or dermal exposure to various cyanide-containing compounds, including smoke from closed-space fires. Sources of cyanide poisoning include hydrogen cyanide and its salts, cyanogenic plants, aliphatic nitriles, and prolonged exposure to sodium nitroprusside.

The presence and extent of cyanide poisoning are often initially unknown. There is no widely available, rapid, confirmatory cyanide blood test. Treatment decisions must be made on the basis of clinical history and signs and symptoms of cyanide intoxication. If clinical suspicion of cyanide poisoning is high, Sodium Thiosulfate Injection and Sodium Nitrite Injection should be administered without delay.

Table 1. Common Signs and Symptoms of Cyanide Poisoning

Symptoms	Signs
• Headache • Confusion • Dyspnea • Chest Tightness • Nausea	• Altered Mental Status (e.g., confusion, disorientation) • Seizures or Coma • Mydriasis • Tachypnea/Hyperpnea (early) • Bradypnea/Apnea (late) • Hypertension (early)/ Hypotension (late) • Cardiovascular Collapse • Vomiting • Plasma Lactate Concentration ≥ 8 mmol/L

In some settings, panic symptoms including tachypnea and vomiting may mimic early cyanide poisoning signs. The presence of altered mental status (e.g., confusion and disorientation) and/or mydriasis is suggestive of true cyanide poisoning although these signs can occur with other toxic exposures as well.

The expert advice of a regional poison control center may be obtained by calling 1-800-222-1222.

Smoke Inhalation

Not all smoke inhalation victims will have cyanide poisoning and may present with burns, trauma, and exposure to other toxic substances making a diagnosis of cyanide poisoning particularly difficult. Prior to administration of Sodium Thiosulfate Injection smoke-inhalation victims should be assessed for the following:

- Exposure to fire or smoke in an enclosed area
- Presence of soot around the mouth, nose, or oropharynx
- Altered mental status

Although hypotension is highly suggestive of cyanide poisoning, it is only present in a small percentage of cyanide-poisoned smoke inhalation victims. Also indicative of cyanide poisoning is a plasma lactate concentration greater than or equal to 10 mmol/L (a value higher than that typically listed in the table of signs and symptoms of isolated cyanide poisoning because carbon monoxide associated with smoke inhalation also contributes to lactic acidemia). If cyanide poisoning is suspected, treatment should not be delayed to obtain a plasma lactate concentration.

1.3 Use with Other Cyanide Antidotes

Caution should be exercised when administering cyanide antidotes, other than sodium nitrite, simultaneously with Sodium Thiosulfate Injection, as the safety of co-administration has not been established. If a decision is made to administer another cyanide antidote, other than sodium nitrite, with Sodium Thiosulfate Injection, these drugs should not be administered concurrently in the same IV line. [see *Dosage and Administration (2.2)*]

2 DOSAGE AND ADMINISTRATION

2.1 Administration Recommendation

Comprehensive treatment of acute cyanide intoxication requires support of vital functions. Administration of sodium nitrite and sodium thiosulfate should be considered adjunctive to appropriate supportive therapies. Airway, ventilatory and circulatory support, and oxygen administration should not be delayed to administer sodium nitrite and sodium thiosulfate.

Sodium nitrite injection and sodium thiosulfate injection are administered by slow intravenous injection. They should be given as early as possible after a diagnosis of acute life-threatening cyanide poisoning has been established. Sodium nitrite should be administered first, followed immediately by sodium thiosulfate. Blood pressure must be monitored during infusion in both adults and children. The rate of infusion should be decreased if significant hypotension is noted.

Age	Intravenous Dose of Sodium Nitrite and Sodium Thiosulfate
Adults	**1.) Sodium Nitrite** -10 mL of sodium nitrite at the rate of 2.5 to 5 mL/minute **2.) Sodium Thiosulfate** - 50 mL of sodium thiosulfate immediately following administration of sodium nitrite.
Children	**1.) Sodium Nitrite** -0.2 mL/kg (6 mg/kg or 6-8 mL/m^2 BSA) of sodium nitrite at the rate of 2.5 to 5 mL/minute not to exceed 10 mL **2.) Sodium Thiosulfate** - 1 mL/kg of body weight (250 mg/kg or approximately 30-40 mL/m^2 of BSA) not to exceed 50 mL total dose immediately following administration of sodium nitrite.

NOTE: If signs of poisoning reappear, repeat treatment using one-half the original dose of both sodium nitrite and sodium thiosulfate.

In adult and pediatric patients with known anemia, it is recommended that the dosage of sodium nitrite should be reduced proportionately to the hemoglobin concentration.

All parenteral drug products should be inspected *visually* for particulate matter and discoloration prior to administration, whenever solution and container permit.

2.2 Recommended Monitoring

Patients should be monitored for at least 24-48 hours after Sodium Thiosulfate Injection administration for adequacy of oxygenation and perfusion and for recurrent signs and symptoms of cyanide toxicity. When possible, hemoglobin/hematocrit should be obtained when treatment is initiated. Measurements of oxygen saturation using standard pulse oximetry and calculated oxygen saturation values based on measured PO_2 are unreliable in the presence of methemoglobinemia.

2.3 Incompatibility Information

Chemical incompatibility has been reported between Sodium Thiosulfate Injection and hydroxocobalamin and these drugs should not be administered simultaneously through the same IV line. No chemical incompatibility has been reported between sodium thiosulfate and sodium nitrite, when administered sequentially through the same IV line as described in Dosage and Administration.

3 DOSAGE FORMS AND STRENGTHS

Sodium Thiosulfate Injection consists of:

- One vial of sodium thiosulfate injection USP 12.5 grams/50 mL (250 mg/mL)

Administration of the contents of one vial constitutes a single dose.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Sulfites

Sodium thiosulfate drug product may contain trace impurities of sodium sulfite. The presence of a trace amount of sulfites in this product should not deter administration of the drug for treatment of emergency situations, even if the patient is sulfite-sensitive.

6 ADVERSE REACTIONS

There have been no controlled clinical trials conducted to systematically assess the adverse events profile of sodium thiosulfate.

The medical literature has reported the following adverse events in association with sodium thiosulfate administration. These adverse events were not reported in the context of controlled trials or with consistent monitoring and reporting methodologies for adverse events. Therefore, frequency of occurrence of these adverse events cannot be assessed.

Cardiovascular system: hypotension
Central nervous system: headache, disorientation

Gastrointestinal system: nausea, vomiting
Hematological: prolonged bleeding time
Body as a Whole: salty taste in mouth, warm sensation over body

In humans, rapid administration of concentrated solutions or solutions not freshly prepared, and administration of large doses of sodium thiosulfate have been associated with a higher incidence of nausea and vomiting. However, administration of 0.1 g sodium thiosulfate per pound up to a maximum of 15 g in a 10-15% solution over 10-15 minutes was associated with nausea and vomiting in 7 of 26 patients without concomitant cyanide intoxication.

In a series of 11 human subjects, a single intravenous infusion of 50 mL of 50% sodium thiosulfate was associated with increases in clotting time 1-3 days after administration. However, no significant changes were observed in other hematological parameters.

7 DRUG INTERACTIONS

Formal drug interaction studies have not been conducted with Sodium Thiosulfate Injection.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects. Pregnancy Category C.
There are no adequate and well-controlled studies in pregnant women. Sodium Thiosulfate Injection should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

There are no reported epidemiological studies of congenital anomalies in infants born to women treated with sodium thiosulfate during pregnancy. In animal studies, there are no teratogenic effects in offspring of hamsters treated during pregnancy with sodium thiosulfate in doses similar to those given intravenously to treat cyanide poisoning in humans. Other studies suggest that treatment with sodium thiosulfate ameliorates the teratogenic effects of maternal cyanide poisoning in hamsters. In other studies, sodium thiosulfate was not embryotoxic or teratogenic in mice, rats, hamsters, or rabbits at maternal doses of up to 550, 400, 400 and 580 mg/kg/day, respectively.

8.3 Nursing Mothers

It is not known whether sodium thiosulfate is excreted in human milk. Because Sodium Thiosulfate Injection may be administered in life-threatening situations, breast-feeding is not a contraindication to its use. Because many drugs are excreted in human milk, caution should be exercised following Sodium Thiosulfate Injection administration to a nursing woman. There are no data to determine when breastfeeding may be safely restarted following administration of sodium thiosulfate.

8.4 Pediatric Use

There are case reports in the medical literature of sodium nitrite in conjunction with sodium thiosulfate being administered to pediatric patients with cyanide poisoning; however, there have been no clinical studies to evaluate the safety or efficacy of sodium thiosulfate in the pediatric population. As for adult patients, dosing recommendations for pediatric patients have been based on theoretical calculations of antidote detoxifying potential, extrapolation from animal experiments, and a small number of human case reports.

8.5 Geriatric Use

Sodium thiosulfate is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

8.6 Renal Disease

Sodium thiosulfate is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

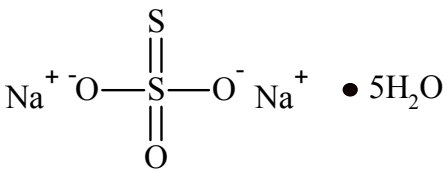
10 OVERDOSAGE

There is limited information about the effects of large doses of sodium thiosulfate in humans. Oral administration of 3 g sodium thiosulfate per day for 1-2 weeks in humans resulted in reductions in room air arterial oxygen saturation to as low as 75%, which was due to a rightward shift in the oxygen hemoglobin dissociation curve. The subjects returned to baseline oxygen saturations 1 week after discontinuation of sodium thiosulfate. A single intravenous administration of 20 mL of 10% sodium thiosulfate reportedly did not change oxygen saturations.

11 DESCRIPTION

Sodium thiosulfate has the chemical name thiosulfuric acid, disodium salt, pentahydrate. The chemical formula is $Na_2S_2O_3 \cdot 5H_2O$ and the molecular weight is 248.17. The structural formula is:

Structure of Sodium Thiosulfate Pentahydrate



Sodium Thiosulfate Injection is a cyanide antidote which contains one 50 mL glass vial containing a 25% solution of sodium thiosulfate

injection.

Sodium thiosulfate injection is a sterile aqueous solution and is intended for intravenous injection. Each vial contains 12.5 grams of sodium thiosulfate in 50 mL solution (250 mg/mL). Each mL also contains 2.8 mg boric acid and 4.4 mg of potassium chloride. The pH of the solution is adjusted with boric acid and/or sodium hydroxide. Sodium thiosulfate injection is a clear solution with a pH between 7.5 and 9.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Exposure to a high dose of cyanide can result in death within minutes due to the inhibition of cytochrome oxidase resulting in arrest of cellular respiration. Specifically, cyanide binds rapidly with cytochrome a3, a component of the cytochrome c oxidase complex in mitochondria. Inhibition of cytochrome a3 prevents the cell from using oxygen and forces anaerobic metabolism, resulting in lactate production, cellular hypoxia and metabolic acidosis. In massive acute cyanide poisoning, the mechanism of toxicity may involve other enzyme systems as well.

The synergy resulting from treatment of cyanide poisoning with the combination of sodium nitrite and sodium thiosulfate is the result of differences in their primary mechanisms of action as antidotes for cyanide poisoning.

Sodium Nitrite

Sodium nitrite is thought to exert its therapeutic effect by reacting with hemoglobin to form methemoglobin, an oxidized form of hemoglobin incapable of oxygen transport but with high affinity for cyanide. Cyanide preferentially binds to methemoglobin over cytochrome a_3, forming the nontoxic cyanomethemoglobin. Methemoglobin displaces cyanide from cytochrome oxidase, allowing resumption of aerobic metabolism. The chemical reaction is as follows:

$NaNO_2$ + Hemoglobin → Methemoglobin
HCN + Methemoglobin → Cyanomethemoglobin

Vasodilation has also been cited to account for at least part of the therapeutic effect of sodium nitrite. It has been suggested that sodium nitrite-induced methemoglobinemia may be more efficacious against cyanide poisoning than comparable levels of methemoglobinemia induced by other oxidants. Also, sodium nitrite appears to retain some efficacy even when the formation of methemoglobin is inhibited by methylene blue.

Sodium Thiosulfate

The primary route of endogenous cyanide detoxification is by enzymatic transulfuration to thiocyanate (SCN^-), which is relatively nontoxic and readily excreted in the urine. Sodium thiosulfate is thought to serve as a sulfur donor in the reaction catalyzed by the enzyme rhodanese, thus enhancing the endogenous detoxification of cyanide in the following chemical reaction:

$$Na_2S_2O_3 + CN^- \xrightarrow{\text{Rhodanese}} SCN^- + Na_2SO_3.$$

12. 2 Pharmacodynamics

In dogs, pretreatment with sodium thiosulfate to achieve a steady state level of 2 µmol/mL increased the rate of conversion of cyanide to thiocyanate over 30-fold.

12.3 Pharmacokinetics

Sodium Thiosulfate

Thiosulfate taken orally is not systemically absorbed. Most of the thiosulfate is oxidized to sulfate or is incorporated into endogenous sulphur compounds; a small proportion is excreted through the kidneys. Approximately 20-50% of exogenously administered thiosulfate is eliminated unchanged via the kidneys. After an intravenous injection of 1 g sodium thiosulfate in patients, the reported serum thiosulfate half-life was approximately 20 minutes. However, after an intravenous injection of a substantially higher dose of sodium thiosulfate (150 mg/kg, that is, 9 g for 60 kg body weight) in normal healthy men, the reported elimination half-life was 182 minutes.

Cyanide

The apparent terminal elimination half life and volume of distribution of cyanide, in a patient treated for an acute cyanide poisoning with sodium nitrite and sodium thiosulfate administration, have been reported to be 19 hours and 0.41 L/kg, respectively. Additionally, an initial elimination half life of cyanide has been reported to be approximately 1-3 hours.

Thiocyanate

After detoxification, in healthy subjects, thiocyanate is excreted mainly in the urine at a rate inversely proportional to creatinine clearance. In healthy subjects, the elimination half-life and volume of distribution of thiocyanate have been reported to be 2.7 days and 0.25 L/kg, respectively. However, in subjects with renal insufficiency the reported elimination half life is approximately 9 days.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the potential carcinogenicity of sodium thiosulfate.

Mutagenesis:

The mutagenic potential of sodium thiosulfate has been examined in the *in vitro* Bacterial Reverse Mutation Assay (Ames Assay). Sodium thiosulfate was not mutagenic in the absence of metabolic activation in *S. typhimurium* strains TA98, TA100, TA1535, TA537, or TA1538. Sodium thiosulfate was not mutagenic in the presence of metabolic activation in strains TA 98, TA1535, TA1537, TA1538 or *E. coli* strain WP2.

Fertility:

Clinical studies to evaluate the potential effects of sodium thiosulfate intake on fertility of either males or females have not been reported.

There are no preclinical studies examining the effects of sodium thiosulfate on fertility.

13.2 Animal Pharmacology

Due to the extreme toxicity of cyanide, experimental evaluation of treatment efficacy has predominantly been completed in animal models. The efficacy of sodium thiosulfate treatment alone to counteract the toxicity of cyanide was initially reported in 1895 by Lang. The efficacy of amyl nitrite treatment in cyanide poisoning of the dog model was first reported in 1888 by Pedigo. Further studies in the dog model, which demonstrated the utility of sodium nitrite as a therapeutic intervention, were reported in 1929 by Mladoveanu and Gheorghiu. However, Hugs and Chen et al. independently reported upon the superior efficacy of the combination of sodium nitrite and sodium thiosulfate in 1932-1933. Treatment consisted of intravenously administered 22.5 mg/kg (half the lethal dose) sodium nitrite or 1 g/kg sodium thiosulfate alone or in sequence immediately after subcutaneous injection of sodium cyanide into dogs over a range of doses. Subsequent doses of 10 mg/kg sodium nitrite and/or 0.5 g/kg sodium thiosulfate were administered when clinical signs or symptoms of poisoning persisted or reappeared. Either therapy administered alone increased the dose of sodium cyanide required to cause death, and when administered together, sodium nitrite and sodium thiosulfate resulted in a synergistic effect in raising the lethal dose of sodium cyanide. The combined therapy appeared to have reduced efficacy when therapy was delayed until signs of poisoning (e.g. convulsions) appeared; however, other investigators have reported survival in dogs that were administered antidotal treatment after respiratory arrest had occurred.

Animal studies conducted in other species (e.g., rat, guinea pig, sheep, pigeon and cat) have also supported a synergistic effect of intravenous sodium nitrite and sodium thiosulfate in the treatment of cyanide poisoning.

While intravenous injection of sodium nitrite and sodium thiosulfate was effective in reversing the effects of lethal doses of cyanide in dogs, intramuscular injection of sodium nitrite, with or without sodium thiosulfate, was found not to be effective in the same setting.

14 CLINICAL STUDIES

The human data supporting the use of sodium nitrite for cyanide poisoning consists primarily of published case reports. There are no randomized controlled clinical trials. Nearly all the human data describing the use of sodium thiosulfate report its use in conjunction with sodium nitrite. Dosing recommendations for humans have been based on theoretical calculations of antidote detoxifying potential, extrapolation from animal experiments, and a small number of human case reports.

There have been no human studies to prospectively and systematically evaluate the safety of sodium thiosulfate or sodium nitrite in humans. Available human safety information is based largely on anecdotal case reports and case series of limited scope.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each Sodium Thiosulfate carton (NDC 60267-705-50) consists of the following:

- One 50 mL glass vial of sodium thiosulfate injection 250 mg/mL (containing 12.5 grams of sodium thiosulfate);

Storage

Store at controlled room temperature between 20°C and 25°C (68°F to 77°F); excursions permitted from 15 to 30°C (59 to 86°F). Protect from direct light. Do not freeze.

(Note: Sodium Nitrite must be obtained separately.)

17 PATIENT COUNSELING INFORMATION

Sodium Thiosulfate Injection is indicated for cyanide poisoning and in this setting, patients will likely be unresponsive or may have difficulty in comprehending counseling information.

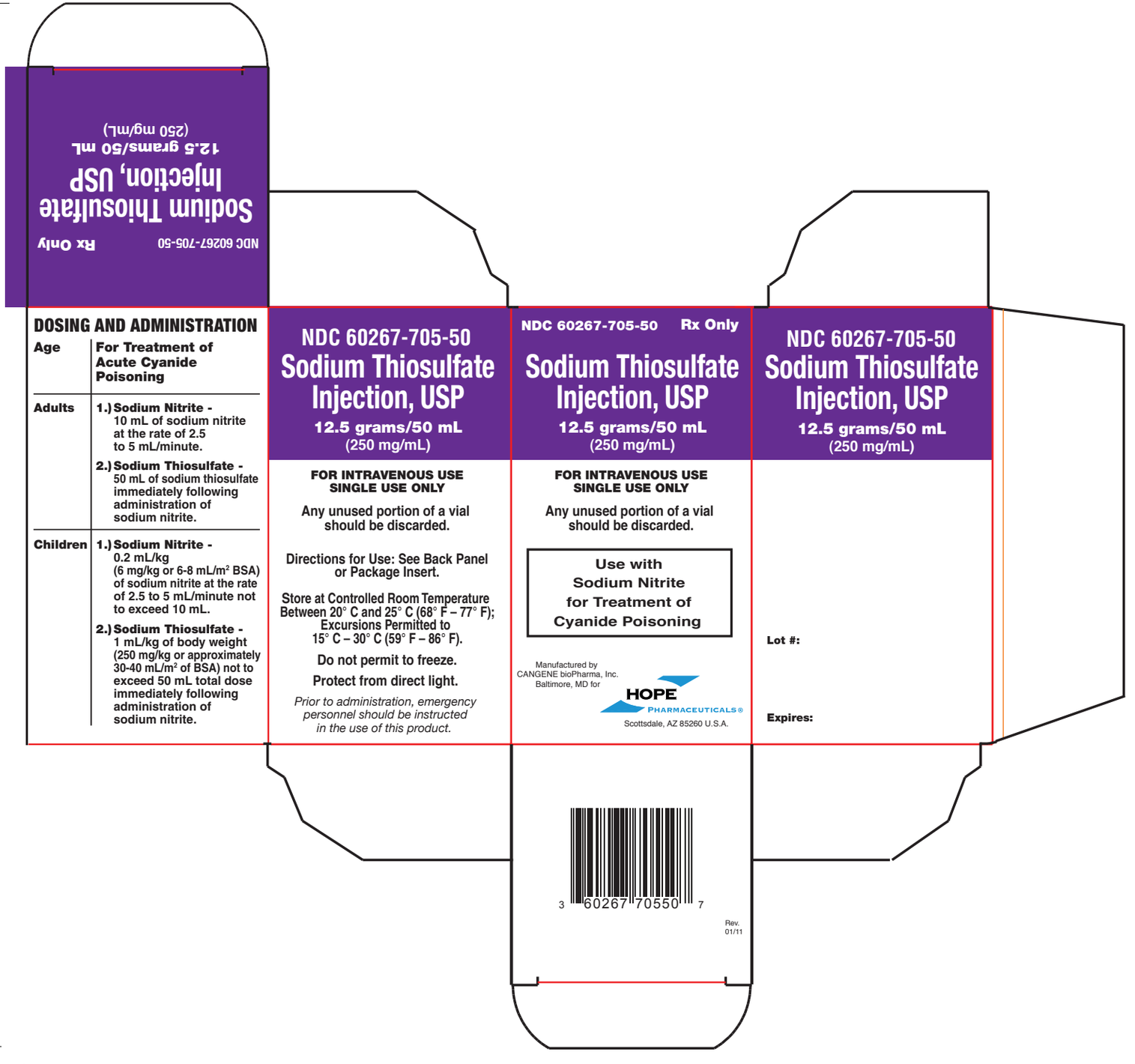
17.1 Hypotension

When feasible, patients should be informed of the possibility of hypotension.

17.2 Monitoring

Where feasible, patients should be informed of the need for close monitoring of blood pressure and oxygenation.

Manufactured by Cangene BioPharma, Inc., Baltimore, Maryland 21230 for
Hope Pharmaceuticals, Scottsdale, Arizona 85260


Sodium Thiosulfate Injection, USP
12.5 grams/50 mL
(250 mg/mL)
NDC 60267-705-50 Rx Only
DOSING AND ADMINISTRATION
Age
For Treatment of Acute Cyanide Poisoning
Adults
1.) Sodium Nitrite - 10 mL of sodium nitrite at the rate of 2.5 to 5 mL/minute.
2.) Sodium Thiosulfate - 50 mL of sodium thiosulfate immediately following administration of sodium nitrite.
Children
1.) Sodium Nitrite - 0.2 mL/kg (6 mg/kg or 6-8 mL/m² BSA) of sodium nitrite at the rate of 2.5 to 5 mL/minute not to exceed 10 mL.
2.) Sodium Thiosulfate - 1 mL/kg of body weight (250 mg/kg or approximately 30-40 mL/m² of BSA) not to exceed 50 mL total dose immediately following administration of sodium nitrite.
NDC 60267-705-50
Sodium Thiosulfate Injection, USP
12.5 grams/50 mL
(250 mg/mL)
FOR INTRAVENOUS USE
SINGLE USE ONLY
Any unused portion of a vial should be discarded.
Directions for Use: See Back Panel or Package Insert.
Store at Controlled Room Temperature Between 20° C and 25° C (68° F – 77° F); Excursions Permitted to 15° C – 30° C (59° F – 86° F).
Do not permit to freeze.
Protect from direct light.
Prior to administration, emergency personnel should be instructed in the use of this product.
NDC 60267-705-50 Rx Only
Sodium Thiosulfate Injection, USP
12.5 grams/50 mL
(250 mg/mL)
FOR INTRAVENOUS USE
SINGLE USE ONLY
Any unused portion of a vial should be discarded.
Use with Sodium Nitrite for Treatment of Cyanide Poisoning
Manufactured by CANGENE bioPharma, Inc. Baltimore, MD for
HOPE PHARMACEUTICALS®
Scottsdale, AZ 85260 U.S.A.
3 60267 70550 7
Rev. 01/11
NDC 60267-705-50
Sodium Thiosulfate Injection, USP
12.5 grams/50 mL
(250 mg/mL)
Lot #:
Expires:
Rx Only
NDC 60267-705-50
Sodium Thiosulfate Injection, USP
12.5 grams/50 mL
(250 mg/mL)

NDC 60267-705-50 **Rx Only**
50 mL Vial

Sodium Thiosulfate Injection, USP

FOR INTRAVENOUS USE
12.5 grams/50 mL
(250 mg/mL)

HOPE
PHARMACEUTICALS®
Scottsdale, Arizona 85260 U.S.A.

3 60267 70550 7

Single Use Only.
Discard Unused Portion.

Directions: See package insert.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever the solution and container permit.

Do not permit to freeze.

Protect from direct light.

Store At Controlled Room Temperature Between 20° C and 25° C (68° F – 77° F); Excursions Permitted to 15° C – 30° C (59° F – 86° F)

Manufactured by
CANGENE bioPharma, Inc.
Baltimore, MD 21230 for

Hope Pharmaceuticals
Scottsdale, Arizona 85260 U.S.A.

Rev. 01/11

LOT 2107-104 EXP: 03/13

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/s/

RIGOBERTO A ROCA
02/14/2012