

DBL™ SODIUM THIOSULFATE INJECTION

Name of medicine

Sodium thiosulfate

Presentation

DBL™ Sodium Thiosulfate Injection is a clear, colourless, sterile solution. Each 10 mL vial and 50 mL vial contains 2.5 g and 12.5 g of sodium thiosulfate (25% w/v solution) respectively. Each vial also contains 10.5 mg/mL sodium phosphate - dibasic dodecahydrate and 1.0 mg/mL sodium metabisulfite in water for injections. Sodium hydroxide and sulphuric acid are added as necessary to adjust the pH. The pH of the solution is between 7.0 and 9.0.

Uses

Actions

Sodium thiosulfate is an antidote for cyanide poisoning. Cyanide poisoning can be rapidly fatal. When hydrogen cyanide gas is inhaled or large doses of cyanide are taken, toxicity occurs within a few seconds, and death occurs within minutes. The potentially lethal dose of potassium or sodium cyanide is 200 to 300 mg and of hydrocyanic acid is 50 mg. With smaller doses, toxicity occurs within minutes, and may include the following symptoms: constriction of the throat, nausea, vomiting, giddiness, headache, palpitations, hyperpnoea, then dyspnoea, bradycardia (which may be preceded by tachycardia), unconsciousness, violent convulsions followed by death.

Sodium thiosulfate is generally used in conjunction with sodium nitrite in the treatment of cyanide poisoning. Cyanide has a high affinity for ferric ions, and reacts readily with the ferric ion of mitochondrial cytochrome oxidase. Sodium nitrite reacts with haemoglobin to form methaemoglobin, and cyanide preferentially binds to methaemoglobin, restoring cytochrome oxidase activity. As cyanide dissociates from methaemoglobin, it is converted to the relatively non-toxic thiocyanate by the enzyme rhodanese. Sodium thiosulfate acts as a sulfur donor for rhodanese. The lack of a suitable sulfur donor is the rate limiting step for this reaction, and thus provision of sulfur by sodium thiosulfate administration enhances the endogenous cyanide detoxification capacity of the body.

Pharmacokinetics

Sodium thiosulfate is poorly absorbed orally, but is rapidly distributed throughout extracellular fluid after IV administration. The volume of distribution of sodium thiosulfate is 150 mL/kg. Sodium thiosulfate is excreted in the urine, with a clearance half life of 0.25 to 3 hours being reported when a single bolus dose of 1 g of sodium thiosulfate is given.

Indications

DBL™ Sodium Thiosulfate Injection is indicated as an antidote in the treatment of cyanide poisoning. It is frequently used in conjunction with sodium nitrite.

Sodium thiosulfate is also indicated to prevent sodium nitroprusside induced cyanide poisoning.

Dosage and administration

DBL™ Sodium Thiosulfate Injection is for single use in one patient only. Discard any residue.

DBL™ Sodium Thiosulfate Injection is administered by slow intravenous injection. If sodium nitrite is administered in the treatment of cyanide poisoning, sodium thiosulfate should be administered immediately following the sodium nitrite infusion.

Therapy should be administered immediately based upon reasonable suspicion of cyanide toxicity. The characteristic smell of bitter almonds may not be obvious, and is not detectable by all individuals.

Cyanide poisoning

Adult dose: The usual adult dose is 12.5 g (50 mL of a 25% solution) administered intravenously at a rate of 1.25 g/min (5 mL/min). If signs of cyanide toxicity are still present 30 mins to 2 hours after administration, both sodium nitrite and sodium thiosulfate may be repeated at half the original dose.

Paediatric dose: The usual paediatric dose is 412.5 mg/kg (1.65 mL/kg of a 25% solution) or 7 g/m² (28 mL/m²) administered at a rate of 0.625 to 1.25 g/min (2.5 to 5 mL/min). A maximum dose of 12.5 g (50 mL of a 25% solution) is recommended.

Alternatively, a paediatric dose based on haemoglobin concentration has been recommended.

Haemoglobin concentration	Dose of sodium thiosulfate
80 g/L (8 g/dL)	1.10 mL/kg of 25% solution
100 g/L (10 g/dL)	1.35 mL/kg of 25% solution
120 g/L (12 g/dL)	1.65 mL/kg of 25% solution
140 g/L (14 g/dL)	1.95 mL/kg of 25% solution

Prevention of sodium nitroprusside induced cyanide toxicity

Adult dose: Administer intravenously concurrently with sodium nitroprusside at 5 to 10 times the dose rate of sodium nitroprusside.

Contraindications

There are no specific contraindications to sodium thiosulfate administration.

Warnings and precautions

Sodium thiosulfate should be administered with caution in patients sensitive to sodium thiosulfate.

Sodium thiosulfate should also be administered with caution in patients with hypertension, since sodium thiosulfate may exacerbate the condition.

Sodium thiosulfate should be administered with caution in patients with oedematous sodium retaining conditions, such as cirrhosis of the liver, congestive heart failure, renal function impairment, and toxemia of pregnancy, since sodium thiosulfate may also exacerbate these conditions.

Use in pregnancy

Little is known about the effects of sodium thiosulfate on pregnancy and the foetus, however, problems in pregnancy have not been documented. Concerns about adverse effects on the foetus may have little relevance in the context of life threatening cyanide poisoning in the pregnant woman.

Use in lactation

It is not known whether sodium thiosulfate is distributed into breast milk. Concerns about adverse effects on the breastfed infant may have little relevance in the context of life threatening cyanide poisoning in the mother.

Adverse effects

Sodium thiosulfate has low toxicity, and adverse reactions at the recommended doses are usually mild.

Cardiovascular system: hypotension.

Central nervous system: headache, disorientation, psychotic behaviour, including agitation, delusions and hallucinations may result from excess thiocyanate production.

Gastrointestinal system: diarrhoea (usually from oral doses), osmotic disturbances. Nausea and vomiting may result from excess thiocyanate production.

Genitourinary system: diuretic effects are possible.

Musculoskeletal system: arthralgia, hyperreflexia and muscle cramps may result from excess thiocyanate production.

Ocular system: blurred vision may result from excess thiocyanate production.

Ototoxicity: tinnitus may occur from excess thiocyanate production.

Overdosage

Clinical features

Overdose of sodium thiosulfate during treatment of cyanide poisoning results in thiocyanate toxicity. Symptoms of thiocyanate toxicity may be seen at serum thiocyanate concentrations above 10 mg/100 mL (1.72 mmol/L). Thiocyanate toxicity becomes life threatening at serum concentrations of 20 mg/100 mL (3.44 mmol/L). The symptoms of thiocyanate toxicity include arthralgias, blurred vision, hyperreflexia, muscle cramps, nausea and vomiting, psychotic behaviour and tinnitus.

Treatment

Treatment of overdose involves the following measures:

- enhancing thiocyanate elimination using haemodialysis
- supportive treatment as required.

In case of overdose, immediately contact the Poisons Information Centre on 0800 764 766 for advice.

Pharmaceutical precautions

Store below 25°C. Protect from light. For shelf life, refer to label for expiry date.

Medicine classification

General sale medicine.

Package quantities

10 mL vial: boxes of 5 vials

50 mL vial: boxes of 1 vial

Name and address

Hospira NZ Limited
23 Haining Street
Te Aro
Wellington
New Zealand

Date of preparation

7 December 2011