

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DBL™ Sodium Thiosulfate Injection 25% w/v solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium thiosulfate pentahydrate 2.5 g in 10 mL (25%w/v solution).

Excipient(s) with known effect

- Sodium metabisulfite

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

DBL™ Sodium Thiosulfate Injection is a clear, colourless, sterile solution. The pH of the solution is between 7.0 and 9.0.

4. CLINICAL PARTICULARS

4.1 Therapeutic 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.

4.2 Dose and method of administration

Dose

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.

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.

Special populations

Cyanide poisoning

Paediatric population

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

Method of 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.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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 toxaemia of pregnancy, since sodium thiosulfate may also exacerbate these conditions.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

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.

Breast-feeding

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.

Fertility

No data available.

4.7 Effects on ability to drive and use machinery

No data available.

4.8 Undesirable effects

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

Psychiatric disorders: Psychotic behaviour, including agitation, delusions and hallucinations may result from excess thiocyanate production.

Nervous system disorders: Headache, disorientation.

Eye disorders: Blurred vision may result from excess thiocyanate production.

Ear and labyrinth disorders: Tinnitus may occur from excess thiocyanate production.

Vascular disorders: Hypotension.

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

Musculoskeletal and connective tissue disorders: Arthralgia, hyperreflexia and muscle cramps may result from excess thiocyanate production.

Renal and urinary disorders: Diuretic effects are possible.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

4.9 Overdose

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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antidotes, ATC code: V03AB06

Mechanism of action

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.

5.2 Pharmacokinetic properties

Absorption and Distribution

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.

Elimination

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.

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dibasic sodium phosphate dodecahydrate

Sodium metabisulfite

Water for injection

Sodium hydroxide (for pH-adjustment)

Sulfuric acid (for pH-adjustment)

6.2 Incompatibilities

No data available.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25°C. Protect from light.

6.5 Nature and contents of container

10 mL glass vial: boxes of 5 vials

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

General sale medicine

8. SPONSOR

Pfizer New Zealand Limited

PO Box 3998

Auckland, New Zealand, 1140

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

26 January 1984

10. DATE OF REVISION OF THE TEXT

13 February 2019

Summary table of changes

Section changed	Summary of new information
All	Reformatting according to MedSafe Data Sheet guidance
4.3	Added hypersensitivity as contraindication
4.8	Amended MedDRA System Organ Classes
5.1	Added Pharmacotherapeutic group and ATC code
6.1	Added excipients used in pH-adjustment.

6.4	Amended storage conditions.
6.5	Added container closure material.