AUSTRALIAN PRODUCT INFORMATION – DBL™ Sodium Thiosulfate Injection (Sodium thiosulfate pentahydrate)

1. NAME OF THE MEDICINE

Sodium thiosulfate pentahydrate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 mL vial of DBL™ Sodium Thiosulfate Injection contains Sodium thiosulfate pentahydrate 2.5 g.

Each vial also contains 10.5 mg/mL dibasic sodium phosphate dodecahydrate and 1.0 mg/mL sodium metabisulfite in water for injections. Sodium hydroxide and sulfuric acid are added as necessary to adjust the pH.

Excipients with known effect:

- Sodium metabisulfite

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

Dosage

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/m^2 (28 mL/m^2) 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.

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

There are no specific contraindications to sodium thiosulfate administration.

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.

Use in the elderly

No data available.

Paediatric use

No data available.

Effects on laboratory tests

No data available.

4.5 Interactions with other medicines and other forms of interactions

No data available.

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

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.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (undesirable 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.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

Signs and Symptoms

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 information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

Clinical trials

No data available.

5.2 Pharmacokinetic properties

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.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Refer to section 2 Qualitative and Quantitative Composition

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

DBL™ Sodium Thiosulfate Injection available in clear glass Type I vial containing the equivalent of 2.5 g of sodium thiosulfate in 10 mL solution, as packs of 5.

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physicochemical properties

Chemical Structure

Molecular formula: $Na_2S_2O_3.5H_2O$

Molecular weight: 248.2

CAS number

10102-17-7

7. MEDICINE SCHEDULE (POISONS STANDARD)

Not scheduled.

8. SPONSOR

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9. DATE OF FIRST APPROVAL

30 August 2007

10. DATE OF REVISION

21 October 2020

Summary Table of Changes

Section changed	Summary of new information
8	Update to Australian sponsor details