

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DBL™ Sodium Nitrite Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Nitrite injection is made up of sodium nitrite in water for injections.

Each 10 mL ampoule contains 300 mg of sodium nitrite.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sodium Nitrite Injection is a clear, colourless, sterile solution for injection.

The pH of the solution is between 7.0 and 9.0.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Sodium Nitrite Injection is indicated as an antidote in the treatment of cyanide poisoning, in conjunction with sodium thiosulfate.

4.2 Dose and method of administration

Dose

Therapy should be instituted 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. Sodium nitrite should only be administered in severe cases.

Sodium Nitrite Injection is administered by intravenous injection. Sodium thiosulfate should be administered immediately following the sodium nitrite dosage. Methaemoglobin concentration should be monitored and must not exceed 40%.

Adult dose: The usual adult dose is 300 mg (10 mL of a 3% solution) administered intravenously at a rate of 75 to 150 mg/min (2.5 to 5 mL/min).

Paediatric population

The usual paediatric dose is 4 mg/kg body weight (0.13 mL of a 3% solution/kg body weight) [range 4.0 to 10 mg/kg body weight, 0.13 to 0.33 mL/kg body weight] or 180 to 240 mg/m² (6 to 8 mL of a 3% solution/m²) administered at a rate of 75 to 150 mg/min (2.5 to 5 mL of a 3% solution/min). It is advisable to begin with doses at the lower end of the recommended

range and increase to the desired effect. A maximum dose of 300 mg (10 mL of a 3% solution) is recommended.

For children under 25 kg, where anaemia is suspected, it is recommended that the dose of sodium nitrite be reduced relative to the haemoglobin measurement. The table below outlines a dosage regimen as a function of haemoglobin concentration.

Children under 25 kg: Maximum initial dose of sodium nitrite according to haemoglobin level.			
Haemoglobin (g/L)	Maximum Dose Sodium Nitrite (mg/kg)	Initial Sodium Nitrite	Maximum Dose 3% Sodium Nitrite Solution (mL/kg)
70	5.8		0.19
80	6.6		0.22
90	7.5		0.25
100	8.8		0.27
110	9.1		0.30
120	10.0		0.33
130	10.8		0.36
140	11.6		0.39

In both adults and children, if symptoms of cyanide toxicity recur, treatment with half the original dose of sodium nitrite and sodium thiosulfate treatment may be repeated 30 minutes after the initial dose.

4.3 Contraindications

Sodium Nitrite Injection should not be administered to asymptomatic patients who have been exposed to cyanide. Use should be reserved for patients with definite indications of severe poisoning, such as loss of consciousness and deteriorating vital functions.

Sodium Nitrite Injection should not be administered to patients with smoke inhalation and combined carbon monoxide and cyanide poisoning unless hyperbaric oxygen therapy is available and such therapy has been initiated, since such patients may develop further hypoxia from methaemoglobin induction.

4.4 Special warnings and precautions for use

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

Sodium nitrite should also be administered with caution in patients with acquired or congenital methaemoglobinaemia, since sodium nitrite will exacerbate this condition.

Hypotension may occur following rapid administration of sodium nitrite. Blood pressure should be monitored carefully during sodium nitrite administration, and the infusion rate slowed if hypotension occurs.

Patients with glucose-6-phosphate dehydrogenase deficiency are theoretically at great risk from sodium nitrite therapy because of the likelihood of haemolysis, although no such cases have been reported.

Patient monitoring

Methaemoglobin levels should be monitored during sodium nitrite treatment to avoid excessive methaemoglobin induction and should not exceed 40%.

Blood pressure should be monitored carefully during sodium nitrite administration, since hypotension may result if the rate of administration is too fast.

4.5 Interaction with other medicines and other forms of interaction

No data available.

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy

Little is known about the effects of sodium nitrite 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. Animal experiments indicate that some sodium nitrite crosses the placenta and that foetal methaemoglobinaemia may be induced. The risk to the foetus from severe maternal cyanide poisoning *should be evaluated against* the risk of foetal methaemoglobinaemia.

Lactation

It is not known whether sodium nitrite is distributed into breastmilk. Concerns about adverse effects on the breastfed infant may have little relevance in the context of life threatening cyanide poisoning in the mother. No animal studies have addressed the question of sodium nitrite excretion in breastmilk or its possible effects on the nursing infant.

4.7 Effects on ability to drive and use machinery

No data available.

4.8 Undesirable effects

Cardiovascular system: vasodilation resulting in syncope, hypotension and tachycardia, methaemoglobinaemia

Central nervous system: headache, dizziness

Gastrointestinal system: nausea, vomiting, abdominal pain

Respiratory system: tachypnoea, dyspnoea, cyanosis

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 nitrite results in methaemoglobinaemia. Symptoms of methaemoglobinaemia may be seen at blood methaemoglobin concentrations of 15%, but symptoms do not usually appear until the blood methaemoglobin concentration reaches 30 to 40%. The symptoms of methaemoglobinaemia include cyanosis, headache, unusual tiredness or weakness, tachycardia, shortness of breath, extreme dizziness or fainting, and coma. Cardiovascular collapse, convulsions and death may occur after sodium nitrite overdose. The mean lethal oral dose of sodium nitrite in adults is approximately 1 g if no treatment is received, although survival after this dose has been reported.

Treatment

Treatment of overdose involves the following measures:

- supportive and symptomatic treatment.
- intravenous administration of methylene blue (1 to 2 mg/kg body weight) over 5 to 10 minutes. The dose may be repeated after 1 hour if necessary, but the total dose should not exceed 7 mg/kg. extreme caution should be exercised when administering methylene blue to patients likely to have substantial amounts of cyanide bound to methaemoglobin because methylene blue will increase the cyanide release.
- oxygen and exchange transfusion should be considered when methaemoglobinaemia is severe.

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

Mechanism of action

Sodium nitrite is an antidote for cyanide poisoning. Cyanide poisoning can be rapidly fatal. When hydrogen cyanide gas or large doses are taken, toxicity occurs within a few seconds, and death occurs within minutes. 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 nitrite is generally used in conjunction with sodium thiosulfate, and often amyl 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 (EC 2.8.1.1). Sodium thiosulfate acts as a sulfur donor for rhodanese.

Sodium nitrite also produces vasodilation by relaxing vascular smooth muscle.

5.2 Pharmacokinetic properties

Sodium nitrite is rapidly absorbed following oral administration. After intravenous administration the time to peak effect of sodium nitrite is 30 to 70 minutes. An injection of 1 mg/kg sodium nitrite produces a peak methaemoglobin concentration of approximately 6%.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

Reproductive and developmental toxicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Water for injection

6.2 Incompatibilities

Sodium nitrite is reported to be incompatible with the following: acetanilide, antipyrine, caffeine, citrate, chlorates, hypophosphites, iodides, mercury salts, morphine, oxidizing agents, permanganate, phenazone, sulfites, tannic acid, and vegetable astringent decoctions, infusions or tinctures.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

Strength	Pack size
300 mg in 10 mL	5 x 10 mL ampoule

6.6 Special precautions for disposal

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

7. MEDICINE SCHEDULE

Pharmacy Only Medicine

8. SPONSOR

Pfizer New Zealand Limited

P O Box 3998

Auckland, New Zealand, 1140

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

26 Jan 1984

10. DATE OF REVISION OF THE TEXT

30 January 2019

Summary table of changes

Section changed	Summary of new information
All	Reformat to MedSafe Data Sheet guidance