DBL™ SODIUM NITRITE INJECTION

Name of medicine
Sodium Nitrite

Presentation
The molecular formula of sodium nitrite is NaNO₂. It has a molecular weight of 69.0. The CAS Registry number of sodium nitrite is 7632-00-0.

Sodium Nitrite Injection is a clear, colourless, sterile solution of sodium nitrite in water for injections. Each 10 mL ampoule contains 300 mg of sodium nitrite. The pH of the solution is between 7.0 and 9.0.

Uses

Actions
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.

Pharmacokinetics
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%.

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

Dosage and administration
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 dose: 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.

<table>
<thead>
<tr>
<th>Haemoglobin (g/L)</th>
<th>Maximum Initial Dose Sodium Nitrite (mg/kg)</th>
<th>Maximum Initial Dose 3% Sodium Nitrite Solution (mL/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>5.8</td>
<td>0.19</td>
</tr>
<tr>
<td>80</td>
<td>6.6</td>
<td>0.22</td>
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<tr>
<td>90</td>
<td>7.5</td>
<td>0.25</td>
</tr>
<tr>
<td>100</td>
<td>8.8</td>
<td>0.27</td>
</tr>
<tr>
<td>110</td>
<td>9.1</td>
<td>0.30</td>
</tr>
<tr>
<td>120</td>
<td>10.0</td>
<td>0.33</td>
</tr>
<tr>
<td>130</td>
<td>10.8</td>
<td>0.36</td>
</tr>
<tr>
<td>140</td>
<td>11.6</td>
<td>0.39</td>
</tr>
</tbody>
</table>

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.

**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.

**Warnings and precautions**
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.
Pregnancy and Lactation

Use in 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.

Use in 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.

Adverse 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

Overdosage

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.

Pharmaceutical precautions

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

Special Precautions for Storage
Store below 25°C. Protect from light.

Medicine classification
Pharmacy Only Medicine
### Package quantities

<table>
<thead>
<tr>
<th>Strength</th>
<th>Pack size</th>
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<tbody>
<tr>
<td>300 mg in 10 mL</td>
<td>5 x 10 mL ampoule</td>
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### Name and address

Pfizer New Zealand Limited,  
PO Box 3998  
Auckland, New Zealand, 1140  
  
Toll Free Number: 0800 736 363

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