SODIUM NITROPRUSSIDE

SCOPE (Area): FOR USE IN: Critical Care Unit, ED and Theatre
EXCLUSIONS: Paediatrics (seek Paediatrician advice) and General Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

BRAND NAMES
DBL Sodium Nitroprusside®.
Nitropress®.

PHARMACOLOGY AND PHARMACOKINETICS
Sodium nitroprusside relaxes vascular smooth muscle resulting in venous and arterial vasodilatation reducing both preload and afterload. The venous vasodilatation is greater than the arterial vasodilatation, but this difference is less marked than that produced by glyceryl trinitrate. Sodium nitroprusside has a rapid onset of action of 2 minutes, as well as a rapid loss of effect once an infusion is ceased due to a half life of 2 minutes. Sodium nitroprusside is metabolised by combining with haemoglobin to form cyanmethaemoglobin and cyanide ions – this metabolic route is extremely important in the toxicity associated with sodium nitroprusside. Cyanide is naturally present in the serum in small amounts and endogenous thiosulfate combines with cyanide (in a reaction mediated by the liver enzyme rhodanase) to produce thiocyanate. A lack of rhodanase (e.g. in severe liver failure) or depletion of thiosulfate (from combining with high levels of cyanide produced from high dose or prolonged sodium nitroprusside infusions) will lead to cyanide accumulation and possible severe toxicity (including death). Thiocyanate is excreted renally and has a half life of 3-7 days. Accumulation of thiocyanate may occur with prolonged sodium nitroprusside infusions (especially in renal failure) also leading to serious toxicity.

See Adverse Reactions ‘Cyanide toxicity’ box.

INDICATIONS
- Hypertensive emergency.
- Control of hypertension in aortic dissection.
- (Short term treatment of acute cardiac failure).

CONTRAINDICATIONS
- Compensatory hypertension (e.g. arteriovenous shunt or coarctation of the aorta).
- Cerebral or coronary artery disease.
- Vitamin B12 deficiency.
- Hypovolaemia.
- Uncorrected anaemia.
- Congenital (Leber’s) optic atrophy or tobacco amblyopia - these patients have unusually high pre-existing cyanide to thiocyanate ratios, probably due to defective or absent rhodanase.
- Acute congestive heart failure associated with reduced peripheral vascular resistance (such as high output heart failure that may be seen in endotoxic sepsis).

PRECAUTIONS
- **Cyanide or thiocyanate toxicity** – may occur with prolonged or high doses of sodium nitroprusside – see Adverse Reactions ‘Cyanide toxicity’ box.
- **Severe hepatic impairment** – avoid use of sodium nitroprusside as likely to have lower levels of the liver enzyme rhodanase leading to increased cyanide levels.
- **Renal impairment** - excretion of thiocyanate is reduced increasing the risk of toxicity; monitor thiocyanate concentrations during prolonged treatment.
- **Aortic dissection** – sodium nitroprusside may cause a reflex tachycardia, use with extreme caution.
- **Increased intracranial pressure, encephalopathy and hypothermia** - risk of aggravating condition further with sodium nitroprusside use.
- **Pulmonary impairment** – sodium nitroprusside may worsen hypoxaemia.
- **Extravasation** – irritation, rash, flushing, reddening of the skin at injection site and streaking have been reported.
- **Hypothyroidism** - thiocyanate (degradation product of sodium nitroprusside) inhibits both uptake and binding of iodine.
- **Elderly** – may require lower doses of sodium nitroprusside.

PREGNANCY AND BREASTFEEDING
Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS
- **Phosphodiesterase 5 inhibitors** (sildenafil, tadalafil and vardenafil) - exaggerated hypotension may occur if sodium nitroprusside is given in the 24 hours post-dose sildenafil or vardenafil, or 48 hours post-dose tadalafil. Avoid concomitant use where possible.
- **Drugs that lower blood pressure** – additive hypotensive effects when used with sodium nitroprusside.

DOSAGE AND ADMINISTRATION
Requires continuous ECG monitoring and invasive blood pressure monitoring. For administration only
- in Critical Care Unit, ED or Theatre
- by MET or Code Blue

Administer via CVC, midline or large peripheral vein (avoid extravasation). If using peripherally, a second peripheral line is required to ensure continuity of the infusion. Avoid administration on lines where other infusions may be bolused.

Cyanide begins to accumulate at doses >2 microgram/kg/minute. Doses above this level or prolonged dosing (longer than 48 hours) increases the risk of cyanide toxicity. Sodium nitroprusside infusions should not continue for longer than 72 hours. See Adverse Reactions ‘Cyanide toxicity’ box for more information.

Infusion bag or syringe must be protected from light and covered with opaque material (such as black plastic bag supplied with Nitropress® or aluminium foil). It is not necessary to cover the drip chamber or tubing.
Sodium nitroprusside must be diluted prior to use and is only compatible with glucose 5% infusion fluid.

**IV infusion (via CVC, midline or large peripheral vein):**
Withdraw 2 mL from a 100 mL glucose 5% minibag.
**DBL sodium nitroprusside® 50 mg (dry powder vial):** add 2 mL glucose 5% withdrawn from minibag to reconstitute powder. This gives 50 mg/2 mL.
**Nitropress® 50 mg/2 mL vial:** already in solution, discard 2 mL glucose 5% withdrawn from minibag.

For either brand: Sodium nitroprusside 50 mg (2 mL from ONE reconstituted vial) added to remaining 98 mL glucose 5% in the minibag.

**Total Volume:** 100 mL.
**Final concentration:** 500 microgram/mL.
**Starting rate:** 0.5 microgram/kg/min.
**Rate increase:** Increase by 0.5 microgram/kg/min every few minutes until the desired response or maximum dose is reached.

**Usual rate range:** 0.5-8 microgram/kg/min. Titrate according to blood pressure required.
**Maximum rate:** 10 microgram/kg/min (for a maximum of 10 minutes to avoid cyanide toxicity – see Adverse Reactions ‘Cyanide toxicity’ box). Reduce dose to 5 microgram/kg/min after running at maximum rate for 10 minutes to decrease risk of cyanide toxicity. If hypertension still not controlled, pursue other pharmacological methods of lowering blood pressure.

**Ceasing infusion:** Wean over at least 10-30 minutes to avoid rebound hypertension EXCEPT in suspected cyanide toxicity – stop immediately.

**Syringe Pump IV infusion (via CVC, midline or large peripheral vein):**
**For use in ED only**
**DBL sodium nitroprusside® 50 mg (dry powder vial):** add 2 mL glucose 5% (withdrawn from a glucose 5% minibag) to reconstitute powder. This gives 50 mg/2 mL.
**Nitropress® 50 mg/2 mL vial:** already in solution.

For either brand: Sodium nitroprusside 25 mg (1 mL of reconstituted solution) diluted to 50 mL with glucose 5% in a luer lock syringe.

**Total Volume:** 50 mL.
**Final concentration:** 500 microgram/mL.
**Rate:** as for IV infusion above.

**Contact pharmacy or on-call pharmacist when infusion commenced to ensure ongoing supply and access to cyanide antidote if required.**

**Rate table for sodium nitroprusside 500 mcg/mL IV infusion usual range:**

<table>
<thead>
<tr>
<th>Weight</th>
<th>0.5 mcg/kg/min</th>
<th>1 mcg/kg/min</th>
<th>2 mcg/kg/min</th>
<th>3 mcg/kg/min</th>
<th>5 mcg/kg/min</th>
<th>10 mcg/kg/min</th>
<th>Maximum 10 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 kg</td>
<td>3 mL/hr</td>
<td>6 mL/hr</td>
<td>12 mL/hr</td>
<td>18 mL/hr</td>
<td>30 mL/hr</td>
<td>60 mL/hr</td>
<td></td>
</tr>
<tr>
<td>60 kg</td>
<td>3.6 mL/hr</td>
<td>7.2 mL/hr</td>
<td>14.4 mL/hr</td>
<td>21.6 mL/hr</td>
<td>36 mL/hr</td>
<td>72 mL/hr</td>
<td></td>
</tr>
<tr>
<td>70 kg</td>
<td>4.2 mL/hr</td>
<td>8.4 mL/hr</td>
<td>16.8 mL/hr</td>
<td>25.2 mL/hr</td>
<td>42 mL/hr</td>
<td>84 mL/hr</td>
<td></td>
</tr>
<tr>
<td>80 kg</td>
<td>4.8 mL/hr</td>
<td>9.6 mL/hr</td>
<td>19.2 mL/hr</td>
<td>28.8 mL/hr</td>
<td>48 mL/hr</td>
<td>96 mL/hr</td>
<td></td>
</tr>
<tr>
<td>90 kg</td>
<td>5.4 mL/hr</td>
<td>10.8 mL/hr</td>
<td>21.6 mL/hr</td>
<td>32.4 mL/hr</td>
<td>54 mL/hr</td>
<td>108 mL/hr</td>
<td></td>
</tr>
<tr>
<td>100 kg</td>
<td>6 mL/hr</td>
<td>12 mL/hr</td>
<td>24 mL/hr</td>
<td>36 mL/hr</td>
<td>60 mL/hr</td>
<td>120 mL/hr</td>
<td></td>
</tr>
</tbody>
</table>

DRG0033: Sodium Nitroprusside
Ratification Date: February 2014
Review Date: February 2019 Version 3
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General Administration Information

- **Infusion preparation:**
  Mix infusion thoroughly after adding sodium nitroprusside to avoid inadvertently giving a more concentrated dose.
  Sodium nitroprusside solutions have a very faint brownish tinge. Any other colour (e.g. blue, green or dark red) solutions, or those with particulate matter should not be used.
  Infusion stable for 24 hours.
  Infusion must be protected from light and covered with opaque material (such as black plastic bag supplied with Nitropress® or aluminium foil). It is not necessary to cover the drip chamber or tubing. Leave vials in their box until preparing infusion.

- **Infusion pump:** Volumetric pump.

- **Routes of administration:**
  - IV injection: No
  - IV intermittent infusion (15-60 minutes): Yes
  - IV continuous infusion: Yes
  - IM injection: No
  - Subcut injection: No

- **Compatible/incompatible IV drugs/fluids:**
  Consult the Australian Injectable Drugs Handbook (‘Yellow book’) in your ward area. **Assume all unlisted drugs and IV fluids are incompatible** – contact Pharmacy for further advice.

### MONITORING (INCLUDING BLOOD TESTS)

- Hypotension from excessive dosing with sodium nitroprusside is self limiting and will abate quickly once the infusion is ceased, if appropriate the patient can be put in a head down position to maximise venous return. If hypotension does not resolve within ten minutes of cessation of infusion, sodium nitroprusside is not the cause.
- Some references recommend taking thiocyanate levels for infusions going longer than 48 hours, however these bloods are analysed in NSW with a turnaround time of 2 weeks so are not practical.
- Dose range and clinical goals should be documented by the Medical Officer.

### NURSING PRACTICE POINTS

- Requires continuous ECG monitoring.
- Continuous blood pressure monitoring via arterial line. Small changes in infusion rate may result in dramatic changes to blood pressure.
- Monitor for signs of cyanide or thiocyanate toxicity – see Adverse Reaction ‘Cyanide toxicity’ box.
- Monitor central venous pressure (if CVC in situ).
- Monitor cardiac output and systemic vascular resistance by Vigileo monitor (arterial waveform analysis).
- Monitor for extravasation if administering peripherally.

### ADVERSE EFFECTS:

Most often due to avoidable excessive hypotension or excessive cyanide accumulation; thiocyanate toxicity may also occur, especially with renal impairment – see ‘Cyanide toxicity’ box below.

- **Common (with too rapid a reduction in blood pressure)** – hypotension, nausea, vomiting, sweating, apprehension, headache, restlessness, muscle twitching, retrosternal discomfort, palpitations, dizziness and abdominal pain.

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- **Infrequent** – postural hypotension, hypothyroidism, tachycardia, bradycardia, ECG changes, paraesthesia, feeling of warmth, rash, flushing, worsen hypoxaemia and increased intracranial pressure.
- **Rare** – thrombocytopenia, methaemoglobinaemia (with total doses >10 mg/kg) and phlebitis.

**Cyanide toxicity**

Toxicity may occur, particularly with prolonged infusion (>48 hours) or higher than recommended maximum dose, due to accumulation of cyanide or thiocyanate. In normal renal function cyanide accumulates with infusion rate of >2 microgram/kg/minute. Risk of toxicity is greater in renal impairment because of reduced excretion of thiocyanate. Cyanide is much more toxic than thiocyanate.

If cyanide toxicity is suspected the sodium nitroprusside infusion must be stopped IMMEDIATELY. Acidosis may not manifest until cyanide has been at dangerous levels for over an hour, and cannot be relied upon as a diagnostic tool. Seek Specialist advice regarding management. One of cyanide’s antidotes (sodium thiosulfate) is stocked in the Pharmacy (1 box of 5 vials), and will be supplied to the ward involved if a sodium nitroprusside infusion is commenced. Sodium thiosulfate contains 2.5 g/10 mL in each vial, dose is 150-200 mg/kg (e.g. 10.5-14 g (42-56 mL) for a 70 kg patient). Administer undiluted at a rate of 2.5-5 mL/minute. This may be repeated, at half the original dose, after 2 hours. Contact Pharmacy or on-call Pharmacist immediately if sodium thiosulfate is used as further supply will need to be obtained. Dialysis does not remove cyanide, but does however remove thiocyanate.

**Cyanide** toxicity causes tachycardia, sweating, hyperventilation, headache, arrhythmias, metabolic acidosis, areflexia, coma, hypotension, pink colour of skin and mucous membranes, shallow breathing, dilated pupils and death.

**Thiocyanate** toxicity causes confusion, psychosis, tinnitus, blurred vision, nausea, dyspnoea, hypothyroidism and ataxia.

**DRUG PRESENTATIONS, LOCATION AND STORAGE**

Sodium nitroprusside 50 mg (powder) vials and 50 mg/2 mL vials.
Imprest locations (at the time of guideline development): Theatre.
Store below 30°C. Protect ampoules and infusion from light.