Ballarat Health Services

DRUG GUIDELINE

SODIUM NITROPRUSSIDE

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

BRAND NAMES
DBL Sodium Nitroprusside®.

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 2-10 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 acute aortic dissection with 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; ideally monitor thiocyanate concentrations during prolonged treatment.
- **Aortic dissection –** sodium nitroprusside may cause reflex tachycardia, use with extreme caution.
- **Increased intracranial pressure, encephalopathy or 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.
- **Riociguat** – contraindicated. Nitrates potentiate the hypotensive effect of riociguat.
- **Drugs that lower blood pressure** – additive hypotensive effects with sodium nitroprusside.
- **Nitric oxide (inhaled), dapsone (topical) -** increases the risk of methaemoglobinaemia with sodium nitroprusside.

DOSAGE AND ADMINISTRATION

Requires continuous ECG monitoring and invasive blood pressure monitoring.
For administration only

- **in Intensive Care Unit, ED, CVS or Theatre**
- **by MET or Code Blue**

Administer via CVC, midline or large peripheral vein (avoid extravasation). If administering peripherally use a dedicated line (a second peripheral line is required for other infusions/access). Avoid administration on lines where other infusions may be bolused or flushed.

Cyanide begins to accumulate at doses greater than 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 and cyanide antidotes' box for more information.

Patients should remain lying down, as sitting or standing may cause severe postural hypotension.

Infusion bag or syringe must be protected from light and covered with opaque material (such as a black plastic bag or aluminium foil). It is not necessary to cover tubing.

Sodium nitroprusside must be diluted prior to use preferably with glucose 5% infusion fluid.

IV infusion (via CVC, midline or large peripheral vein):

Withdraw 2 mL from a 100 mL glucose 5% minibag.
Sodium nitroprusside 50 mg (2 mL from ONE vial) added to remaining 98mL glucose 5% in the minibag. Cover minibag with black bag from vial box or aluminium foil. Tubing does not require cover.
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. Note: blood pressure can drop precipitously with small dose changes.
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 or methaemoglobinaemia – stop immediately and see Adverse Reactions and box below regarding monitoring for 'cyanide toxicity and cyanide antidotes'.** Blood pressure effect wears off within 1-10 minutes when dose is reduced/ceased.

Syringe Unit/Pump IV infusion (via CVC, midline or large peripheral vein):

Sodium nitroprusside 25 mg (1 mL from PART of ONE vial) diluted to 50 mL with glucose 5% in a luer lock syringe. Cover syringe with black bag from vial box or aluminium foil – ensure does not effect reading of syringe by unit/pump. Tubing does not require cover.
Total Volume: 50 mL.
Final concentration: 500 microgram/mL.
Rate: as for IV infusion above.

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

Weight*	0.5 microg/kg/min	1 microg/kg/min	2 microg/kg/min	3 microg/kg/min	5 microg/kg/min	10 microg/kg/min **Maximum 10 minutes**
50 kg	3 mL/hr	6 mL/hr	12 mL/hr	18 mL/hr	30 mL/hr	60 mL/hr
60 kg	3.6 mL/hr	7.2 mL/hr	14.4 mL/hr	21.6 mL/hr	36 mL/hr	72 mL/hr
70 kg	4.2 mL/hr	8.4 mL/hr	16.8 mL/hr	25.2 mL/hr	42 mL/hr	84 mL/hr
80 kg	4.8 mL/hr	9.6 mL/hr	19.2 mL/hr	28.8 mL/hr	48 mL/hr	96 mL/hr
90 kg	5.4 mL/hr	10.8 mL/hr	21.6 mL/hr	32.4 mL/hr	54 mL/hr	108 mL/hr
100 kg Max*	6 mL/hr	12 mL/hr	24 mL/hr	36 mL/hr	60 mL/hr	120 mL/hr **Absolute max rate***

***Weight capped at 100 kg. Note that the pump will allow doses up to 250 kg, ensure no weight greater than 100 kg is entered. Maximum rate 10 microg/kg/min for 10 minutes only.**

General Administration Information

- **Infusion preparation:**
  Mix infusion thoroughly after adding sodium nitroprusside to avoid inadvertently giving a more concentrated dose. May be diluted with other compatible fluids, but glucose 5% is preferred.

Sodium nitroprusside solutions have a faint brownish tinge. Any other colour (e.g. blue, green or 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 the vial or aluminium foil). It is not necessary to cover tubing. To protect from light, leave vials in their box until preparing infusion.

- **Infusion pump:** Alaris® LVP or syringe unit with Guardrails® or syringe pump in ED.
- **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.
- Monitor renal and hepatic function.
- If methaemoglobinaemia (see adverse effects) is suspected, undertake arterial blood gas.
- 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 and may cause headache, dizziness, retrosternal discomfort, palpitations and nausea.
- Monitor for signs of cyanide or thiocyanate toxicity – see Adverse Reaction 'Cyanide toxicity' box.
- Monitor acid-base balance and oxygen saturation.
- Monitor central venous pressure (if CVC in situ).
- Monitor cardiac output and systemic vascular resistance by arterial waveform analysis.
- Ensure patency of IV access prior to commencement of infusion, and monitor for extravasation if administering peripherally.
- All injections, infusions and lines are to be labelled as per CPP0022 Labelling of Injectable Medicines and Lines.

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 and cyanide antidotes' box below.

- **Common –** hypotension, nausea, vomiting, sweating, apprehension, headache, restlessness, muscle twitching, retrosternal discomfort, palpitations, dizziness and abdominal pain.
- **Infrequent –** postural hypotension, hypothyroidism, tachycardia, bradycardia, ECG changes, paraesthesia, feeling of warmth, rash, flushing, worsen hypoxaemia and increased intracranial pressure, ischaemia due to reduced perfusion pressure .
- **Rare –** thrombocytopenia, methaemoglobinaemia (headache, fatigue, cyanosis, tachypnoea, dyspnoea, tachycardia, altered levels of consciousness, chocolate brown blood, myocardial infarction and diffuse hypoxic brain injury) and phlebitis.

Cyanide toxicity:

Toxicity may occur, particularly with prolonged infusion (greater than 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 greater than 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 from Austin Poisons Information Centre 131126 regarding management. Further information can be obtained from the Austin Clinical Guidelines website http://www.austin.org.au/page?ID=1791 (under cyanide). See bottom of box for more information regarding cyanide antidotes.

Contact Pharmacy or on-call Pharmacist immediately if cyanide antidotes are used as further supply will need to be obtained. Dialysis does not remove cyanide, but does remove thiocyanate.

Cyanide toxicity causes venous hyperoxaemia with bright red venous blood, tachycardia, sweating, hyperventilation, headache, arrhythmias, metabolic (lactic) 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.

Cyanide Antidotes:

Two cyanide antidotes (hydroxocobalamin and sodium thiosulfate) are both stocked in ED in a box labelled ‘Cyanokit’. As per the Poisons Information Centre at the time of this guideline release hydroxocobalamin is first line treatment both from efficacy and low toxicity. Second line is sodium thiosulfate.

First line cyanide antidote:

Hydroxocobalamin (Cyanokit) 5 g. Reconstitute in vial with 200 mL of sodium chloride 0.9%, inverting repeatedly for one minute – DO NOT SHAKE. Infuse intravenously over 15 minutes. May be given as a push if critically unwell. Pharmacy do not keep more stock, however a second dose is kept at the Ballarat Gold Mine 53272555.

Second line cyanide antidote (if hydroxocobalamin already given or unavailable):

Sodium thiosulfate 12.5 g (50 mL). Administer IV undiluted over 10 minutes. This dose may be repeated after 30-60 minutes if no clinical improvement. Contact Pharmacy for more stock.

DRUG PRESENTATIONS AND STORAGE

Sodium nitroprusside 50 mg/2 mL vials.

Store below 25°C. Protect ampoules and infusion from light.
