

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

Sodium Nitroprusside Injection IP

NIPRESSTM

(Lyophilized)

COMPOSITION

Each vial contains:

Sodium Nitroprusside Dihydrate IP 50 mg

CLINICAL PHARMACOLOGY

The principal pharmacological action of sodium nitroprusside is relaxation of vascular smooth muscle and consequent dilation of peripheral arteries and veins. Sodium nitroprusside is more active on veins than on arteries. Dilation of the veins promotes peripheral pooling of blood and decreases venous return to the heart, thereby reducing left ventricular end-diastolic pressure and pulmonary capillary wedge pressure (preload). Arteriolar relaxation reduces systemic vascular resistance, systolic arterial pressure, and mean arterial pressure (afterload). Dilation of the coronary arteries also occurs.

In association with the decrease in blood pressure, sodium nitroprusside administered intravenously to hypertensive and normotensive patients produces slight increases in heart rate and a variable effect on cardiac output.

Pharmacokinetics

Infused sodium nitroprusside is rapidly distributed to a volume that is approximately coextensive with the extracellular space. The drug is cleared from this volume by intraerythrocytic reaction with hemoglobin (Hgb), and sodium nitroprusside's resulting circulatory half-life is about 2 minutes.

The products of the nitroprusside/hemoglobin reaction are cyanmethemoglobin (cyanmet Hgb) and cyanide ion (CN⁻). Safe use of sodium nitroprusside injection must be guided by knowledge of the further metabolism of these products. The essential features of nitroprusside metabolism are:

- one molecule of sodium nitroprusside is metabolised by combination with hemoglobin to produce one molecule of cyanmethemoglobin and four CN⁻ ions;
 - methemoglobin, obtained from hemoglobin, can sequester cyanide as cyanmethemoglobin;
 - thiosulfate reacts with cyanide to produce thiocyanate;
 - thiocyanate is eliminated in the urine;
 - cyanide not otherwise removed binds to cytochromes; and
 - cyanide is much more toxic than methemoglobin or thiocyanate.
- Cyanide binds avidly (but reversibly) to ferric ion (Fe⁺⁺⁺), most body stores of which are found in erythrocyte methemoglobin (metHgb) and in mitochondrial cytochromes. When CN⁻ is infused or generated within the bloodstream, essentially all of it is bound to methemoglobin until intraerythrocytic methemoglobin has been saturated.

THERAPEUTIC INDICATIONS

Sodium nitroprusside is indicated for:

1. Immediate reduction of blood pressure in patients with hypertensive crises.
2. Producing controlled hypotension during anaesthesia in order to reduce bleeding in surgical procedures where surgeon and anaesthetist deem it appropriate.
3. Short term therapy of cardiac failure, to enhance cardiac output and lower myocardial oxygen requirements.

DOSAGE & ADMINISTRATION

SODIUM NITROPRUSSIDE IS ONLY TO BE USED AS AN INFUSION WITH STERILE 5% GLUCOSE IN WATER. NOT FOR DIRECT INJECTION.

Reconstitution: The contents of a vial of 50mg Sodium Nitroprusside for Injection USP should be dissolved in 2mL to 3mL of Glucose I.V. Infusion 5%. No other diluent should be used. Depending on the desired concentration, all of the prepared stock solution should be diluted in 500mL to 1000mL of Glucose I.V. Infusion B.P. 5%.

Amount of Sodium Nitroprusside	50 mg	50 mg
Volume of Glucose I.V. Infusion 5%	500 mL	1000 mL
Final Concentration	100 micrograms/mL	50 micrograms/mL

THE INFUSION FLUID FOR SODIUM NITROPRUSSIDE SHOULD NOT BE EMPLOYED AS A VEHICLE FOR THE SIMULTANEOUS ADMINISTRATION OF ANY OTHER DRUG.

Dosage

Adult: Initially 5 mcg/kg/min (0.005 mg/kg) of a solution containing 50 mg of NIPRESS, dissolved in 500 to 1000 ml of 5% Dextrose Injection, has to be administered intravenously by slow infusion. The dose has to be adjusted in the increments of 0.5 mcg/min as needed up to limit of 10 mcg/kg/min or a total dose of 3.5 mg/kg in brief infusions.

Children: 1.4 mcg/kg/min, adjusted slowly, if necessary. A fresh solution should be prepared immediately before use.

CONTRAINDICATIONS

Sodium nitroprusside should not be used in the treatment of compensatory hypertension, e.g. arteriovenous shunt or coarctation of the aorta.

It is also contraindicated in physically poor-risk patients (A.S.A. Risk 5), in patients with uncorrected anemia or hypovolemia or in those with known inadequate cerebral circulation, severe renal disease or disease states associated with vitamin B₁₂ deficiency.

Patients with congenital (Leber's) optic atrophy or with tobacco amblyopia have unusually high cyanide/thiocyanate ratios. These rare conditions are probably associated with defective or absent rhodanase, and sodium nitroprusside should be avoided in these patients.

WARNINGS AND PRECAUTIONS

The principal hazards of Sodium Nitroprusside administration are excessive hypotension and excessive accumulation of cyanide.

Excessive Hypotension : Sodium Nitroprusside can cause precipitous decreases in blood pressure. In patients not properly monitored, these decreases can lead to irreversible ischemic injuries or death. Sodium nitroprusside should be used only when available equipment and personnel allow blood pressure to be continuously monitored.

Cyanide Poisoning : Except when used briefly or at low (less than 2micrograms/kg/min) infusion rates, sodium nitroprusside gives rise to important quantities of cyanide ion, which can reach toxic, potentially lethal levels.

General: Like other vasodilators, sodium nitroprusside can cause increases in intracranial pressure.

Hepatic: Use caution when administering nitroprusside to patients with hepatic insufficiency.

Use in Anaesthesia: When sodium nitroprusside (or any other vasodilator) is used for controlled hypotension during anaesthesia, the patient's capacity to compensate for anemia and hypovolemia may be diminished. If possible, pre-existing anemia and hypovolemia should be corrected prior to administration of sodium nitroprusside.

Monitoring of Blood Pressure: Direct monitoring of blood pressure is mandatory.

Postural Hypotension: Patients should remain recumbent during the infusion to avoid severe postural hypotensive effects.

Hypothyroidism: Since thiocyanate inhibits both the uptake and binding of iodine, caution should be exercised in using sodium nitroprusside in patients with hypothyroidism and severe renal dysfunction.

Hypothermia: The drug should be used with extreme caution if the patient is hypothermic.

Stress: If in the clinical situation, stress, induced by pain or manipulation is reduced or eliminated during sodium nitroprusside infusion, the patient could experience a greater than expected reduction in blood pressure unless the rate of infusion is adjusted downward as required.

Pregnancy and Lactation

Use in Pregnancy

Category C

There are no adequate or well-controlled studies of sodium nitroprusside in pregnant women. It is not known whether sodium nitroprusside can cause foetal harm when administered to a pregnant woman or can affect reproductive capacity. Sodium nitroprusside should be given to a pregnant woman only if clearly needed. There have been no reports on its use in the hypertension of preclampsia.

It crosses the placenta. Short term use for control of hypertensive crises may be safe provided the maternal pH and cyanide levels are monitored.

Use in Lactation

It is not known whether sodium nitroprusside or its metabolites are excreted into breast milk, nor whether they have a harmful effect on the newborn. Therefore, the drug is not recommended for nursing mothers, unless the expected benefits outweigh any potential risk.

ADVERSE EFFECTS

Overvigorous treatment may cause an excessive drop in LV end-diastolic pressure, severe hypotension, and myocardial ischemia. Fatigue, nausea, vomiting, and disorientation tend to arise specially when treatment continues for more than 48 hours. In patients with renal failure, thiocyanate accumulates with high dose infusions and may produce hypothyroidism after prolonged therapy. Hypoxia may result from increased ventilation perfusion mismatch with pulmonary vasodilation.

OVERDOSE

Overdosage of nitroprusside can be manifested as excessive hypotension or cyanide toxicity or as thiocyanate toxicity.

Treatment of cyanide toxicity: Cyanide levels can be measured by many laboratories, and blood-gas studies that can detect venous hyperoxemia or acidosis are widely available. Acidosis may not appear until more than an hour after the appearance of dangerous cyanide levels, and laboratory tests should not be awaited. Reasonable suspicion of cyanide toxicity is adequate grounds for initiation of treatment.

Treatment of cyanide toxicity consists of:

- discontinuing the administration of sodium nitroprusside;
- providing a buffer for cyanide by using sodium nitrite to convert as much hemoglobin into methemoglobin as the patient can safely tolerate; and then
- infusing sodium thiosulfate in sufficient quantity to convert the cyanide into thiocyanate.

Hemodialysis is ineffective in removal of cyanide, but it will eliminate most thiocyanate.

DRUG INTERACTIONS

Ganglion blocking agents and other antihypertensive agents, volatile liquid anaesthetics, inhaled anaesthetics, negative inotropes and most other circulatory depressants potentiate the hypotensive action of sodium nitroprusside.

The transition from sodium nitroprusside to oral antihypertensive therapy may predispose to severe, sudden hypertension.

STORAGE

Store at a temperature not exceeding 25°C. Protect from light.

PRESENTATION

One vial of 50 mg in a box.

Manufactured by:



UNIT II: Plot No.2, Industrial Area, Lodhimajra, Baddi, H.P. -173 205, India.

H.O.: Ram Mandir Road, Goregaon (W), Mumbai - 400 104, India.

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