For adjunctive treatment of hypertension:

a) 1/4 inch applied to pinna q6–8h (Norsworthy 2007)

- **FERRETS:**

For adjunctive therapy for heart failure:

a) 1/8th inch strip applied to inside of pinna q12h for the first 24 hours of therapy (Hoeffer 2000)

b) For dilative cardiomyopathy: 1/8th of an inch applied to shaved skin once to twice daily. Apply to ear pinna or skin of thigh. May cause hypotension. (Williams 2000)

Monitoring

- Clinical efficacy
- Sites of application for signs of rash
- Blood pressure, particularly if hypotensive effects are seen

Client Information

- Dosage is measured in inches of ointment; use papers supplied with product to measure appropriate dose. Wear gloves (non-permeable) when applying.
- Do not pet animal where ointment has been applied
- Rotate application sites. Recommended application sites include: groin, inside the ears, and thorax. Rub ointment into skin well. If rash develops, do not use that site again until cleared.
- Contact veterinarian if rash persists or animal's condition deteriorates
- There is no danger of explosion or fire with the use of this product

Chemistry/Synonyms

Famous as an explosive, nitroglycerin (NTG) occurs undiluted as a thick, volatile, white-pale yellow flammable, explosive liquid with a sweet, burning taste. The undiluted drug is soluble in alcohol and slightly soluble in water. Because of obvious safety reasons, nitroglycerin is diluted with lactose, dextrose, propylene glycol, alcohol, etc. when used for pharmaceutical purposes.

Nitroglycerin may also be known as: glyceryl trinitrate, glonoine, GTN; nitroglycerol, NTG, trinitrin, or trinitroglycerin, *Minitran*®, *Nitro-bid*®, *Nitrek*® and *Nitro-Dur*®.

Storage/Stability

The topical ointment should be stored at room temperature and the cap firmly attached. For storage/stability and compatibility for dosage forms other than the topical ointment, see specialized references or the package inserts for each product.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 3 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Note: Many dosage forms of nitroglycerin are available for human use, including sublingual tablets, buccal tablets, lingual spray, extended-release oral capsules and tablets, and parenteral solutions for IV infusion. Because the use of nitroglycerin in small animal medicine is practically limited to the use of topical ointment or transdermal patches, those other dosage forms are not listed here.

Nitroglycerin Topical Ointment: 2% in a lanolin-white petrolatum base in 30 g and 60 g tubes and UD 1 g; *Nitro-bid*® (Fougera); generic; (Rx)

Nitroglycerin Transdermal Systems (patches): 0.1 mg/hr 0.2 mg/hr, 0.3 mg/hr, 0.4 mg/hr, 0.6 mg/hr & 0.8 mg/hr; *Minitran*® (3M); *Nitro-Dur*® (Key); *Nitrek*® (Bertek); generic; (Rx) **Note:** Various products contain differing quantities of nitroglycerin and patch surface area size, but release rates of drug are identical for a given mg/hr.

NITROPRUSSIDE SODIUM

(nye-troe-***pruss***-ide) Nitropress®, Sodium Nitroprusside

VASODILATOR

Prescriber Highlights

- Vascular, smooth muscle relaxant used for acute/severe hypertension; acute heart failure secondary to mitral regurgitation & in combination with dopamine for refractory CHF
- Contraindications: Compensatory hypertension, inadequate cerebral circulation, or during emergency surgery in patients near death. Caution: Geriatric patients, hepatic insufficiency, severe renal impairment, hyponatremia, or hypothyroidism.
- Adverse effects: Hypotensive effects; potentially: nausea, retching, restlessness, apprehension, muscle twitching, dizziness
- May be irritating at the infusion site; avoid extravasation.
- Continued use may lead to potential thiocyanate & cyanide toxicity
- Use only in an ICU setting; monitoring essential

Uses/Indications

In human medicine, nitroprusside is indicated for the management of hypertensive crises, acute heart failure secondary to mitral regurgitation, and severe refractory CHF (often in combination with dopamine). Its use in veterinary medicine is generally reserved for the treatment of critically ill patients with those conditions only when constant blood pressure monitoring can be performed.

Pharmacology/Actions

Nitroprusside is an immediate acting intravenous hypotensive agent that directly causes peripheral vasodilation (arterial and venous) independent of autonomic innervation. It produces a lowering of blood pressure, an increase in heart rate, a mild decrease in cardiac output, and a significant reduction in total peripheral resistance. Unlike the organic nitrates, tolerance does not develop to nitroprusside.

Pharmacokinetics

After starting an IV infusion of nitroprusside, reduction in blood pressure and other pharmacologic effects begin almost immediately. Blood pressure will return to pretreatment levels within 1–10 minutes following cessation of therapy.

Nitroprusside is metabolized non-enzymatically in the blood and tissues to cyanogen (cyanide radical). Cyanogen is converted in the liver to thiocyanate where it is eliminated in the urine, feces, and exhaled air. The half-life of cyanogen is 2.7–7 days if renal function is normal, but prolonged in patients with impaired renal function or with hyponatremia.

Contraindications/Precautions/Warnings

Nitroprusside is contraindicated in patients with compensatory hypertension (*e.g.*, AV shunts or coarctation of the aorta; Cushing's reflex), inadequate cerebral circulation, or during emergency surgery in patients near death.

Nitroprusside must be used with caution in patients with hepatic insufficiency, severe renal impairment, hyponatremia, or hypothyroidism. When nitroprusside is used for controlled hypotension during surgery, patients may have less tolerance to hypovolemia, anemia, or blood loss. Geriatric patients may be more sensitive to the hypotensive effects of nitroprusside.

Adverse Effects

Most adverse reactions from nitroprusside are associated with its hypotensive effects, particularly if blood pressure is reduced too rapidly. Clinical signs such as nausea, retching, restlessness, apprehension, muscle twitching, and dizziness have been reported in humans. These effects disappear when the infusion rate is reduced or stopped. Nitroprusside may be irritating at the infusion site; avoid extravasation.

Continued use may lead to potential thiocyanate and cyanide toxicity (see Overdosage section).

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as class: ***C*** (*These drugs may have potential risks. Studies in people or laboratory animals have uncovered risks, and these drugs should be used cautiously as a last resort when the benefit of therapy clearly outweighs the risks.*)

It is not known whether nitroprusside and its metabolites are excreted in maternal milk.

Overdosage/Acute Toxicity

Acute overdosage is manifested by a profound hypotension. Treat by reducing or stopping the infusion and giving fluids. Monitor blood pressure constantly.

Excessive doses, prolonged therapy, a depleted hepatic thiosulfate (sulfur) supply, or severe hepatic or renal insufficiency may lead to profound hypotension, cyanogen, or thiocyanate toxicity. Acid/base status should be monitored to evaluate therapy and to detect metabolic acidosis (early sign of cyanogen toxicity). Tolerance to therapy is also an early sign of nitroprusside toxicity. Hydroxocobalamin (Vitamin B_{12a}) may prevent cyanogen toxicity. Thiocyanate toxicity may be exhibited as delirium in dogs. Serum thiocyanate levels may need to be monitored in patients on prolonged therapy, especially in those patients with concurrent renal dysfunction. Serum levels >100 micrograms/mL are considered toxic. It is suggested to refer to other references or contact an animal poison control center for further information should cyanogen or thiocyanate toxicity be suspected.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving nitroprusside and may be of significance in veterinary patients:

- **ANESTHETICS, GENERAL:** The hypotensive effects of nitroprusside may be enhanced by concomitant administration of general anesthetics (*e.g.*, **halothane, enflurane**), or other circulatory depressants
- **DOBUTAMINE:** Synergistic effects (increased cardiac output and reduced wedge pressure) may result if dobutamine is used with nitroprusside
- **HYPOTENSIVE AGENTS, OTHER:** Patients receiving other hypotensive agents (*e.g.*, **beta-blockers, ACE inhibitors**, etc.) may be more sensitive to the hypotensive effects of nitroprusside

Doses

Directions for preparation of infusion: Add 2–3 mL D_5W to 50 mg vial to dissolve powder. Add dissolved solution to 1000 mL of D_5W and promptly protect solution from light (using aluminum foil or other opaque covering). Resultant solution contains 50 micrograms/mL of nitroprusside. Higher concentrations may be necessary in treating large animals. The administration set need not be protected from light. Solution may have a slight brownish tint, but discard solutions that turn to a blue, dark red or green color. Solution is stable for 24 hours after reconstitution. Do not add any other medications to IV running nitroprusside. Avoid extravasation at IV site. If using a Mini-Drip IV set (for small animals) (60 drops ≈ 1 mL; 1 drop contains approximately 0.83 micrograms of nitroprusside). Use an accurate flow control device (pump, controller, etc.) for administration.

- **DOGS:**

  For hypertensive crisis (systolic arterial BP >200 mm Hg):

  a) Initiate dose at 1–2 mcg/kg/minute; increase dosage incrementally every 3–5 minutes until a predetermined target BP is attained. Reduce BP 25% over 4-hour period to allow readaptation of cerebral blood vessels. (Proulx and Dhupa 2000)

  For adjunctive treatment of heart failure (cardiogenic shock; fulminant pulmonary edema):

  a) Goal is to decrease or maintain mean arterial pressure to support vital organ functions—approx. 70 mmHg): Dose as above (in "a"); concurrent use of dobutamine (5–10 mcg/kg/min) often indicated. (Proulx and Dhupa 2000)

  b) 0.5–10 mcg/kg/min IV at a low fluid rate (≤2 mL/kg/hr) using D5W or other low sodium fluid. Usually start at 2 mcg/kg/min and increase the base concentration by 1 mcg/kg every 20–30 minutes until there is an improvement in respiratory effort and thoracic auscultation. The patient is maintained on the effective dose for 48 hours. Monitor blood pressure; cyanide poisoning can occur if infusion lasts more than 3 days. After stabilized, drip is tapered as therapy with enalapril is initiated. (Macintire 2006a)

  c) For catastrophic pulmonary edema: As a CRI initiated at 1 mcg/kg/min and carefully titrated to effect by increasing by 1 mcg/kg/min increments every 15 minutes as long as BP remains stable and until perfusion and pulmonary function improves (usually requires between 2–5 mcg/kg/min with the upper limit being 8–10 mcg/kg/min). Maintain most effective dose for 12–15 hours until respiratory distress resolves, lungs are clear, and the patient is stable with a normal blood pressure, pink mucous membranes, normal capillary refill time, and normal heart rate. Most animals at our clinic require 12 hours of treatment. The systolic blood pressure must remain greater than 90 mm Hg. If hypotension develops, the CRI should be stopped. Blood pressure will return to pretreatment levels within 1–10 minutes of discontinuing treatment and administration can be reinstituted at the previous lower dose. Administer with dobutamine to treat or prevent hypotension if severe myocardial failure is present based on an echocardiogram evaluation. Wean sodium nitroprusside over 6 hours first and then dobutamine over 6

hours. ACE inhibitor is added before tapering the infusions over 3–6 hours. (Lichtenberger 2006b)

■ **CATS:**

For hypertensive crisis (systolic arterial BP >200 mm Hg):

a) Initiate dose at 0.5 mcg/kg/minute; increase dosage incrementally every 3–5 minutes until a predetermined target BP is attained. Reduce BP 25% over 4-hour period to allow readaptation of cerebral blood vessels. (Proulx and Dhupa 2000)

For adjunctive treatment of heart failure (cardiogenic shock; fulminant pulmonary edema:

a) Goal to decrease or maintain mean arterial pressure to support vital organ functions—approx. 70 mmHg): Dose as above; concurrent use of dobutamine (1–5 mcg/kg/min) often indicated. (Proulx and Dhupa 2000)

b) Initiate dose at 0.5 mcg/kg/minute constant rate infusion and increase by 0.5–1 mcg/minute every 5 minutes to desired systolic pressure (90–100 mmHg). Cats are more sensitive to the oxidative damage that can be induced by nitroprusside and total dosages should be kept to a minimum. Use a dedicated line with an infusion pump; IV line and catheter should never be flushed. A nurse devoted for continuous monitoring should be in place during administration. Cover IV solution and IV line with opaque material and discard after 24 hours. (Proulx 2003)

c) For catastrophic pulmonary edema: As a CRI initiated at 1 mcg/kg/min and carefully titrated to effect by increasing by 1 mcg/kg/min increments every 15 minutes as long as BP remains stable and until perfusion and pulmonary function improves (cats usually requires between 1–2 mcg/kg/min with the upper limit being 2 mcg/kg/min). Maintain most effective dose for 12–15 hours until respiratory distress resolves, lungs are clear, and the patient is stable with a normal blood pressure, pink mucous membranes, normal capillary refill time and normal heart rate. Most animals at our clinic require 12 hours of treatment. The systolic blood pressure must remain greater than 90 mm Hg. If hypotension develops, the CRI should be discontinued. Blood pressure will return to pretreatment levels within 1–10 minutes of discontinuing treatment and administration can be reinstituted at the previous lower dose. Administer with dobutamine to treat or prevent hypotension if severe myocardial failure is present based on an echocardiogram evaluation. Wean sodium nitroprusside over 6 hours first and then dobutamine over 6 hours. ACE inhibitor is added before tapering the infusions over 3–6 hours. (Lichtenberger 2006b)

Monitoring

- Blood pressure must be constantly monitored
- Acid/base balance
- Electrolytes (especially Na^+)

Client Information

- Must only be used by professionals in a setting where precise IV infusion and constant blood pressure monitoring can be performed.

Chemistry/Synonyms

A vascular smooth muscle relaxant, nitroprusside sodium occurs as practically odorless, reddish-brown crystals or powder. It is freely soluble in water and slightly soluble in alcohol. After reconstitution in D_5W, solution may have a brownish, straw, or light orange color and have a pH of 3.5–6.

Nitroprusside sodium may also be known as: disodium (OC-6-22)-pentakis(cyano-C)nitrosylferrate dihydrate, natrii nitroprussias, sodium nitroferricyanide dihydrate, sodium nitroprusside, or sodium nitroprussiate, and *Nitropress*®.

Storage/Stability/Compatibility

Nitroprusside sodium powder for injection should be stored protected from light and moisture and kept at room temperature (15–30°C). Nitroprusside solutions exposed to light will cause a reduction of the ferric ion to the ferrous ion with a resultant loss in potency and a change from a brownish-color to a blue color. Degradation is enhanced with nitroprusside solutions in *Viaflex*® (Baxter) plastic bags exposed to fluorescent light. After reconstitution, protect immediately by covering vial or infusion bag with aluminum foil or other opaque material. Discard solutions that turn to a blue, dark red, or green color. Solutions protected from light will remain stable for 24 hours after reconstitution. IV infusion tubing need not be protected from light while the infusion is running. It is not recommended to use IV infusion solutions other than D_5W or to add any other medications to the infusion solution.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Nitroprusside Sodium Powder for Injection: 50 mg/vial in 2 mL Flip-top vials and 5 mL vials; *Nitropress*® (Abbott); generic; (Elkins-Sinn); (Rx)

NIZATIDINE

(ni-*za*-ti-dine) Axid®

H2-RECEPTOR ANTAGONIST; PROKINETIC

Prescriber Highlights

- H_2 receptor antagonist similar to ranitidine; used primarily for its prokinetic activity; may be useful in preventing hemorrhagic necrosis in cats with pancreatitis
- Contraindications: Hypersensitivity to the drug; Caution: Geriatric patients or those with hepatic or renal insufficiency
- Adverse Effects are rare

Uses/Indications

While nizatidine acts similarly to cimetidine and ranitidine as an H_2 blocker to reduce gastric acid secretion in the stomach, in small animal medicine its use has been primarily for its prokinetic effects. It may be useful to treat delayed gastric emptying, pseudo-obstruction of the intestine and constipation.

H2 blockers may be useful in preventing hemorrhagic necrosis in feline pancreatitis.

Pharmacology/Actions

At the H_2 receptors of the parietal cells, nizatidine competitively inhibits histamine, thereby reducing gastric acid output both during basal conditions and when stimulated by food, amino acids, pentagastrin, histamine, or insulin.

While nizatidine may cause gastric emptying times to be delayed, it more likely will stimulate GI motility by inhibiting acetylcholinesterase (thereby increasing acetylcholine at muscarinic receptors). It may also have direct agonist effects on M_3 muscarinic