NITROGLYCERIN, TOPICAL

(nye-troe-***gli***-ser-in) NTG, Nitro-bid®, Minitran®

VENODILATOR

Prescriber Highlights

- Topical, oral, & injectable venodilator; usually used topically in veterinary medicine for CHF or hypertension
- Contraindications: anemia or hypersensitivity to nitrates. Caution: cerebral hemorrhage or head trauma, diuretic-induced hypovolemia, or other hypotensive conditions.
- Adverse Effects: rashes at the application sites & orthostatic hypotension; transient headaches common in humans & may be a problem for some animals
- Rotate application sites
- Wear gloves when applying; avoid human skin contact

Uses/Indications

Topical nitroglycerin in small animal medicine is used primarily as an adjunctive vasodilator in heart failure and cardiogenic edema. It is also used as an anti-anginal agent, antihypertensive (acute), and topically to treat Raynaud's disease in humans.

Pharmacology/Actions

Nitroglycerin relaxes vascular smooth muscle primarily on the venous side, but a dose related effect on arterioles is possible. Preload (left end-diastolic pressure) is reduced from the peripheral pooling of blood and decreased venous return to the heart. Because of its arteriolar effects, depending on the dose, afterload may also be reduced. Myocardial oxygen demand and workload are reduced and coronary circulation can be improved.

Pharmacokinetics

Nitroglycerin topical ointment is absorbed through the skin, with an onset of action usually within 1 hour and duration of action of 2–12 hours. It is generally dosed in dogs and cats q6–8 hours (three to four times a day). The transdermal patches have a wide inter-patient bioavailability. Nitroglycerin has a very short half-life (1–4 minutes in humans) and is metabolized in the liver. At least two metabolites have some vasodilator activity and have longer half-lives than NTG.

Contraindications/Precautions/Warnings

Nitrates are contraindicated in patients with severe anemia or those hypersensitive to them. They should be used with caution (if at all) in patients with cerebral hemorrhage or head trauma, diuretic-induced hypovolemia or other hypotensive conditions.

Adverse Effects

Most common side effects seen are rashes at the application sites and orthostatic hypotension. If hypotension is a problem, reduce dosage. Transient headaches are a common side effect seen in humans and may be a problem for some animals.

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 nitrates are excreted in maternal milk; use with caution in nursing animals.

Overdosage/Acute Toxicity

If severe hypotension results after topical administration, wash the site of application to prevent any more absorption of ointment. Fluids may be administered if necessary. Epinephrine is contraindicated as it is ineffective and may complicate the animal's condition.

Drug Interactions

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

- **ANTIHYPERTENSIVE DRUGS, OTHER**: Use of nitroglycerin with other antihypertensive drugs may cause additive hypotensive effects
- **PHENOTHIAZINES**: May increase hypotensive effects
- **SILDENAFIL** (and other **PDE INHIBITORS**): May profoundly increase risk for hypotension

Doses

Note: For the treatment of heart failure, nitroglycerin is not generally used alone.

- **DOGS:**

  For adjunctive treatment of heart failure:

  a) 1/2 inch per 2.27 kg (5 lbs) of body weight applied to a hairless area (*e.g.*, inside the earflap) every 12 hours. Person applying should use gloves and avoid contact with the product. (Kittleson 2000)

  b) If nitroprusside not used, 2% NTG at 1/4 to 1 inch q6–12h; apply to hairless area in the axilla or groin. (Macintire 2006a)

  c) Using the 2.5–10 mg/24hr transdermal patch: 12 hours on, 12 hours off (Fox 2003a)

  d) 1/4–2 inches applied directly to the patient's tongue every 8 hours during the first 48 hours. All animals tolerate the ointment given orally. (Lichtenberger 2006b)

  e) For any patient with cardiogenic pulmonary edema that is headed for oxygen: 1/4 inch for small dogs up to 1 inch for large dogs on the inner ear pinnae, groin or axilla as needed q8h for the first 24 hours. Wear gloves to apply. (DeFrancesco 2006)

- **CATS:**

  For adjunctive treatment of heart failure:

  a) 1/8th to 1/4 inch applied to a hairless area (*e.g.*, inside the earflap) every 4–6 hours. Person applying should use gloves and avoid contact with the product. (Kittleson 2000)

  b) To enhance resolution of pulmonary edema: 1/4 to 1/2 inch topically q6h; to reduce nitrate tolerance, alternate 12 hrs with and 12 hrs without nitroglycerin therapy. (Fox 2007b)

  c) Using the 2.5–5 mg/24hr transdermal patch: 12 hours on, 12 hours off (Fox 2003a)

  d) 1/4 inch applied directly to the patient's tongue every 8 hours during the first 48 hours. All animals tolerate the ointment given orally. (Lichtenberger 2006b)

  e) For any patient with cardiogenic pulmonary edema that is headed for oxygen: 1/4 inch on the inner ear pinnae, groin or axilla as needed q8h for the first 24 hours. Wear gloves to apply. (DeFrancesco 2006)

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.