

NADA #140-994, Approved by FDA

Tolazine® INJECTION

Tolazoline HCl, USP
100 mg Tolazoline per mL
Sterile Solution

Xylazine Reversing Agent and Antagonist
For Intravenous Use in Horses Only

PRECAUTIONS: The safety of Tolazine has not been evaluated in horses with metabolically unstable conditions. Tolazine should not be administered to animals exhibiting signs of stress, debilitation, cardiac disease, sympathetic blockage, hypovolemia or shock.

The safety of Tolazine has not been evaluated for reversing xylazine used as a preanesthetic to a general anesthetic.

The safety of Tolazine has not been established in pregnant mares, lactating mares, horses intended for breeding, or foals.

Tolazine should be administered carefully and at a slow rate to allow venous dilution to occur prior to the drug reaching the brain and heart. An administration rate of 1 mL/second was shown to be safe at the recommended dose.

Tolazine reverses the analgesic effects of xylazine as well as the sedative effects. If the animal was given xylazine for its analgesic properties, reversal may result in return of normal pain perception.

SAFETY: The safety of Tolazine alone without prior xylazine administration was evaluated in healthy horses. Tolazine was administered at 1, 3, and 5 times the recommended dose of 4 mg/kg, every 6 hours for 3 doses. When administered alone, Tolazine caused gastrointestinal hypermotility as horses defecated or attempted to defecate with flatulence within minutes after injection. Some horses exhibited abdominal discomfort (mild colic) and displayed transient diarrhea. Gastrointestinal disturbances were seen in all dose groups.

The safety of Tolazine was evaluated following administration of xylazine in healthy horses. The frequency of gastrointestinal disturbances was decreased in the presence of xylazine. Most horses experienced xylazine-induced hypomotility. A return to normal intestinal motility occurred within 5 minutes after Tolazine administration. A single incidence of mild colic was observed at three times the recommended Tolazine dose, and one instance of transient diarrhea was exhibited at three times the recommended Tolazine dose.

The heart rate may briefly increase immediately after Tolazine injection at the recommended dose with return to pretreatment rates within 5-10 minutes. The degree and duration of tachycardia increased with higher doses, although the increased rate usually lasted less than 60 minutes.

When Tolazine was administered at higher than the recommended dose in healthy horses, intraventricular conduction was slowed, as demonstrated by a prolongation of the QRS complex of the ECG. This effect was not observed at the 1X dose, only a mild prolongation occurred in a single horse at the 2X dose, and it was seen in most horses that received the 3X and 5X doses. Abnormalities of intraventricular conduction can predispose to ventricular arrhythmias and possibly death.

Overdoses of Tolazine at 5 times the recommended dose have been associated with fatalities in horses.

Tolazine reverses blood pressure reduction induced by xylazine in healthy horses, and may result in mild hypertension in some animals at the recommended dose.

Tolazine at doses less than or equal to 5 times the recommended dose did not affect any hematologic, serum biochemical, or urinalysis measurements.

WARNING: Keep out of reach of children. Not for human use.

This drug is for use in horses only and not for use in food-producing animals.

Avoid contact with eyes, skin and mucous membranes. In case of eye contact flush with plenty of water. Exposed skin should be washed with soap and water. In case of accidental oral exposure or injection, seek emergency medical attention.

Users with cardiovascular disease (for example, hypertension or ischemic heart disease) should take special precautions to avoid accidental exposure to this product.

To report adverse reactions in users or to obtain a copy of the material safety data sheet for this product, call 1-800-831-0004.

NOTE TO PHYSICIAN: This product contains an alpha-2 adrenoreceptor antagonist. Epinephrine should not be used to treat hypotension in humans resulting from exposure to this product since tolazoline may cause "epinephrine reversal" (further reduction in blood pressure, followed by an exaggerated rebound).

STORAGE: Protect from light. Store at controlled room temperature 15° to 30°C (59° to 86°F).

HOW SUPPLIED: 100 mL multiple-dose vial.

REFERENCES:

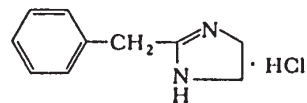
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3. Tranquilli, W.J. and Thurmon, J.C. Alpha adrenoreceptor pharmacology. *JAVMA* 1984; 184:1400-1402.
4. LLOYD, Inc. Research, 1989-1995.
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Manufactured by
Akorn Manufacturing, Inc.
Decatur, IL 62525

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CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Tolazine contains tolazoline hydrochloride with the chemical name 1H-Imidazole,4,5-dihydro-2-(phenylmethyl)-monohydrochloride. Tolazoline hydrochloride has a molecular weight of 196.68 and the molecular formula is C₁₀H₁₂N₂·HCl. The structural formula is



Each mL contains: tolazoline hydrochloride equivalent to 100 mg base activity, chlorobutanol 5.0 mg, tartaric acid 7.8 mg, sodium citrate dihydrate 7.8 mg and water for injection. The pH is adjusted with hydrochloric acid and sodium citrate.

CLINICAL PHARMACOLOGY: Tolazine belongs to the synthetic group of alpha-adrenergic blocking agents known as the imidazoline derivatives.¹ It is a mixed alpha-1 and alpha-2 adrenergic receptor antagonist that competitively inhibits alpha-adrenoceptors.^{2,3} Tolazine is also a direct peripheral vasodilator that decreases the peripheral resistance and increases venous capacitance.³

Xylazine is an alpha-2 adrenergic agonist with sedative and analgesic properties related to central nervous system depression. Administration of Tolazine reverses xylazine's central nervous system depressant effects resulting in rapid recovery from sedation. The competitive blocking of the alpha-2 adrenergic receptor by Tolazine displaces xylazine from these sites and thereby rapidly cancels the effect of the xylazine.⁴

Onset of arousal is usually apparent within 5 minutes of Tolazine administration, depending on the depth and duration of xylazine induced sedation.⁴

INDICATIONS: Tolazine should be used in horses when it is desirable to reverse the effects of sedation and analgesia caused by xylazine.

DOSAGE AND ADMINISTRATION: The Tolazine dose is 4.0 mg/kg body weight or 1.8 mg/lb (4 mL/100 kg or 4 mL/220 lb) to reverse the sedative effects of xylazine. The carefully calculated dose of Tolazine should be given slowly by intravenous injection. Administration rate should approximate 1 mL/second.^{1,5}

The table demonstrates the correct injection volume based on body weight:

Body Weight (kg)	Body Weight (lb)	Tolazine Injection Volume
250 kg	550 lb	10 mL
500 kg	1100 lb	20 mL

SIDE EFFECTS: Temporary side effects of Tolazine may be mild increases in blood pressure; tachycardia; peripheral vasodilatation, evidenced by injected mucous membranes of the gingiva and conjunctiva; and sweating. A few horses may show hyperalgesia of the lips, evidenced by licking or flipping of the lips. Some horses may exhibit piloerection soon after dosing. Clear lacrimal and nasal discharges may be noted. Muscle fasciculations may be observed. Some horses may show signs of temporary apprehensiveness. All clinical side effects should dissipate within 60-120 minutes.

The potential for side effects increases when higher than recommended doses are given or when Tolazine is given without prior administration of xylazine.

Manufactured for:

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