***Tolazoline***

**Pharmacology**

Tolazoline belongs to the synthetic group of alpha-adrenergic blocking agents known as the imidazoline derivatives. It is a mixed alpha-1 and alpha-2 adrenergic receptor antagonist which competitively reverses the effects of xylazine. Tolazoline is also a direct peripheral vasodilatator that decreases the peripheral resistance and increases venous capacitance. Tolazoline competitively blocks and antagonizes central nervous system depression caused by xylazine.

Xylazine, an alpha-2 adrenergic agonist with potent sedative, analgesic and muscle relaxant properties has been used extensively as an analgesic-sedative restraining agent. It has also been used as a preanesthetic agent for many general anesthetics. The central nervous system depressant effect, as well as other pharmacologic effects of xylazine, is dose-dependent.

Tolazoline is useful to counteract the sedation after standard doses of xylazine. The competitive selective blocking of the alpha-2 adrenergic receptor by tolazoline displaces xylazine from these sites and thereby rapidly cancels the effect of the xylazine.

**Tolazine Injection Indications**

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

**Contraindications**

Avoid giving overdoses of this drug, especially to animals with cardiac or circulatory compromise.

**Dosage and Administration**

For intravenous injection. The usual dose is 4 mL per 100 kg body weight (0.04 mL/kg) or 4 mL/220 lb (4.0 mg/kg or 1.8 mg/lb of tolazoline) to reverse the sedative effects of xylazine. The carefully calculated dose of tolazoline should be given slowly by intravenous injection.

**Side Effects**

Temporary side effects of tolazoline may be tachycardia; peripheral vasodilatation, evidenced by bright pink to dark red mucous membranes of the gingiva and conjunctiva; and hyperalgesia of the lips, evidenced by licking or flipping of the lips even before the injection is completed. Some horses may exhibit pilo-erection, especially in the rump and neck regions, 4 to 12 minutes after dosing. Clear lacrimal and nasal discharges may be noted. Some horses may also show signs of apprehensiveness, but this state quickly subsides. All side effects should dissipate within 30-60 minutes. The potential for adverse effects increases when higher than recommended doses are administered, or when tolazoline is given without prior administration of xylazine.

**Precautions**

The safety of tolazoline in pregnant mares or in horses intended for breeding has not been established.

This drug should be administered with greater care to animals exhibiting signs of stress, debilitation, cardiac disease, sympathetic blockage, hypovolemia or shock. The safety of this drug has not been evaluated in horses with metabolically unstable conditions. This drug should be administered with extreme care to horses that are exhibiting any type of circulatory compromise particularly that associated with blood loss.

In general, all drugs, including Tolazine, when given intravenously, should be administered carefully and at a slow rate to allow venous dilution to occur prior to the drug reaching the brain and heart.

The drug 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.

The use of Tolazine has not been evaluated for reversing xylazine used as a pre-anaesthetic to a general anaesthetic.

**SAFETY:**

Tolazine was tolerated in horses at 3 times (12 mg/kg) and 5 times (20 mg/kg) the recommended dose administered without prior xylazine injection at 3 intervals of 6 hours. Lacrimation was most evident when tolazoline was dosed at the 5x magnitude, and it appeared that tolazoline, when administered alone, increased gut motility as the horses would attempt to defecate with flatulence within minutes of injection. Some horses were uneasy or restless, giving the appearance of abdominal discomfort, especially those in the 5x group. Following the second and third doses, the horses manifested a greater degree of gut motility. Some horses had transient diarrhoea with signs of mild colic, i.e., shifting of their weight, borborygmus and tenesmus. However, these horses made no attempt to lie down or roll or kick at their abdomen.

Profuse sweating was noted with some of the 5x horses following their third dose. Fine localized muscle tremors were seen in the neck and rump of 5x horses. As with other side effects they were transient. Tolazoline, when administered at high doses, exerted either a direct or indirect negative dromo-tropic effect (slowing of conduction) in the heart. All side effects had dissipated within 35 to 60 minutes, and by two hours all horses appeared to be completely normal. Horses that were given xylazine prior to tolazoline administration demonstrated no clinical signs of diarrhoea or colic at 1x or 2x dosages.

No young horses or foals were used in any of the safety studies. Care should be taken when treating young animals with this product since the effects are not known precisely.

**Warning**

This drug is not to be administered to horses that are to be slaughtered for use in food.

**Storage**

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

**How Supplied**

100 mL multiple-dose vial.